	assigned at birth females (transmales) is low. Duration of gender-affirming hormones not reported. **Adverse effects** One uncontrolled, retrospective chart review provided evidence for adverse effects from gender-affirming hormones in transmales (Khatchadourian et al. 2014). See the safety results table above for full details of the results. **This study provides very low certainty evidence about the potential adverse effects of gender-affirming hormones in sex assigned at birth females (transmales). No conclusions could be drawn. Duration of gender-affirming hormones not reported.**
Duration of gender dysphoria	No evidence was identified.
Age at onset of gender dysphoria	No evidence was identified.
Age at onset of puberty	No evidence was identified.
Tanner stage at which GnRH analogue or gender-affirming hormones started	One uncontrolled, prospective, longitudinal study (Kuper et al. 2020) reported the impact of Tanner stage on outcomes, although it is not clear whether this is referring to Tanner stage at initial assessment, at the start of GnRH analogues or at another timepoint.
Diagnosis of autistic spectrum disorder	No evidence was identified.
Diagnosis of a mental health condition	One uncontrolled, prospective, longitudinal study (Achille et al. 2020) reported outcomes that were adjusted for engagement in counselling and medicines for mental health problems. Information about diagnoses and treatment were not provided. Rates of mental health issues appear to be high in the cohort. **Impact on mental health** Achille et al. 2020 reported the change in depression scores, controlled for engagement in counselling and medicines for mental health problems (measured using the Center for Epidemiologic Studies Depression [CESD-R] scale and Patient Health Questionnaire Modified for Teens [PHQ 9_Modified for Teens] score: • There was no statistically significant change in CESD-R from baseline to about 12-months follow-up. • There was no statistically significant change in PHQ 9_Modified for Teens score from baseline to about 12-months follow-up **(VERY LOW)**. **Impact on quality of life** Achille et al. 2020 reported the change in quality of life scores, controlled for engagement in counselling and medicines for mental health problems (measured using the Quality of Life Enjoyment and Satisfaction Questionnaire [QLES-Q-SF] score: • There was no statistically significant change in QLES-Q-SF score from baseline to about 12-months follow-up **(VERY LOW)**.

	This study provides very low certainty evidence about outcomes that were adjusted for engagement in counselling and medicines for mental health problems. No conclusions could be drawn.

Abbreviations: ASQ: Ask Suicide-Screening Questions; CESD-R: Center for Epidemiologic Studies Depression; GnRH: Gonadotrophin releasing hormone; GWBS: General Well-Being Scale; HDL: high-density lipoproteins; LDL: low-density lipoproteins; p: p-value; PHQ 9_Modified for Teens: Patient Health Questionnaire Modified for Teens; QLES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire.

From the evidence selected,

(a) what are the criteria used by the research studies to define gender dysphoria, gender identity disorder and gender incongruence of childhood?

(b) what were the ages at which participants commenced treatment with gender-affirming hormones?

(c) what was the duration of treatment with GnRH analogues?

Outcome	Evidence statement
Diagnostic criteria	The DSM-IV-TR criteria was used in 3 studies (Klaver et al. 2020, Klink et al. 2015 and Vlot et al. 2017). The DSM-V criteria was used in 2 studies (Kuper et al. 2020 and Stoffers et al. 2019). The DSM-V has one overarching definition of gender dysphoria with separate specific criteria for children and for adolescents and adults. The general definition describes a conflict associated with significant distress and/or problems functioning associated with this conflict between the way they feel and think of themselves which must have lasted at least 6 months. The ICD-10 diagnosis of 'transsexualism' was used in 1 study (Kaltiala et al. 2020). The authors state that this is the corresponding diagnosis to 'gender dysphoria' in the DSM-V, and that diagnostic assessments in the study location (Finland) take place according to ICD-10. It was not reported how gender dysphoria was defined in the remaining 4 studies **(VERY LOW)**. **From the evidence selected, the most commonly reported diagnostic criteria for gender dysphoria (5/10 studies) was the DSM criteria in use at the time the study was conducted.**
Age when gender-affirming hormones started	8/10 studies reported the age at which participants started treatment with gender-affirming hormones, either as the mean age (with SD) or median age (with the range): **Study** — **Mean age (± SD)** Allen et al. 2019 — 16.7 years (not reported) Khatchadourian et al. 2014 — 17.4 years (1.9) Klaver et al. 2020 — 16.4 years (1.1) in transfemales; 16.9 years (0.9) in transmales Kuper et al. 2020 — 16.2 (1.2) Klink et al. 2015 — 16.6 years (1.4) in transfemales; 16.4 years (2.3) in transmales

<table>
<tr><td></td><td>
<table>
<tr><th>Study</th><th>Median age (range)</th></tr>
<tr><td>Stoffers et al. 2019</td><td>17.2 years (15 to 19.5)</td></tr>
<tr><td>Vlot et al. 2017</td><td>16.3 years (15.9 to 19.5) in transfemales
16.0 years (14.0 to 18.9) in transmales</td></tr>
</table>

Age at the start of treatment was not reported in 3 studies:
• In Achille et al. 2020 the mean age at initial assessment (baseline) was 16.2 years (SD ±2.2)
• In Kaltiala et al. 2020 the mean age at diagnosis was 18.1 years (range 15.2 to 19.9)
• In Lopez de Lara et al. 2020 the mean age of participants was 16 years (range 14 to 18), although it is not clear if this is at the initial assessment or at the start of gender-affirming hormones.

The evidence included showed that most children and adolescents started treatment with gender-affirming hormones at about 16 to 17 years, with a range of about 14 to 19 years.</td></tr>
<tr><td>Duration of treatment with GnRH analogues</td><td>The duration of treatment with GnRH analogues was reported in 3/10 studies:

<table>
<tr><th>Study</th><th>Median duration</th></tr>
<tr><td>Klaver et al. 2020</td><td>2.1 years (IQR 1.0 to 2.7) in transfemales
1.0 years (IQR 0.5 to 2.9) in transmales</td></tr>
<tr><td>Klink et al. 2015</td><td>1.3 years (range 0.5 to 3.8) in transfemales
1.5 years (range 0.25 to 5.2) in transmales
(GnRH analogue monotherapy)</td></tr>
<tr><td>Stoffers et al. 2019</td><td>8 months (range 3 to 39)</td></tr>
</table>

The evidence included showed wide variation in the duration of treatment with gender-affirming hormones, but most studies did not report this information. Treatment duration ranged from a few months up to about 5 years.</td></tr>
</table>

Abbreviations: DSM, Diagnostic and Statistical Manual of Mental Disorders criteria; GnRH, Gonadotrophin-releasing hormone; ICD, International Statistical Classification of Diseases and Related Health Problems; IQR, interquartile range; SD, standard deviation.

6. Discussion

A key limitation to identifying the effectiveness and safety of gender-affirming hormones for children and adolescents with gender dysphoria is the lack of reliable comparative studies. All the studies included in this evidence review are uncontrolled observational studies, which are subject to bias and confounding and were of very low certainty using modified GRADE. The size of the population with gender dysphoria means conducting a prospective trial may be unrealistic, at least on a single centre basis. There may also be ethical issues with a 'no treatment arm' in comparative trials of gender-affirming hormones, where there may be poor mental health outcomes if treatment is withheld. However, the use of an active comparator such as close psychological support may reduce ethical concerns in future trials. A fundamental limitation of all the uncontrolled studies included in this review is that any changes in scores from baseline to follow-up could be attributed to a regression-to-the-mean.

The included studies have relatively short follow-up, with an average duration of treatment with gender-affirming hormones between around 1 year and 5.8 years. Further studies with a longer follow-up are needed to determine the long-term effect of gender-affirming hormones for children and adolescents with gender dysphoria.

Most studies included in this review did not report comorbidities (physical or mental health) and no study reported concomitant treatments in detail. Because of this it is not clear whether any changes observed were due to gender-affirming hormones or other treatments the participants may have received. For example, we do not know if any improvement in depression symptom score over time was the result of gender-affirming hormones or the mental health support the person may be receiving (including medicines or counselling). This may be of particular importance for the mental health outcomes discussed in this review, since depression, anxiety and other related symptoms are common in children and adolescents with gender dysphoria. In Achille et al. 2020, at baseline around one-third of participants were taking medicines for mental health problems and around two-thirds reported being depressed in the past year. In Kaltiala et al. 2020, half the participants needed mental health treatment during and before gender identity assessment, with the most common reasons for treatment being depression, anxiety and suicidality. Only 1 study reported outcomes adjusted for engagement in counselling and medicines for mental health problems (Achille et al. 2020). This study found that gender-affirming hormones had no significant impact on depression and quality of life when adjusted for mental health care, despite significant approvements reported for the unadjusted results. However, it is not possible to draw conclusions on the impact of concurrent mental health treatment on the effect of gender-affirming hormones based on this study alone. Details of the mental health care provided are not reported in the study and results are presented for transfemales and transmales separately, resulting in small patient numbers and possible underpowering.

In most of the included studies, details of the gender-affirming hormone treatment regimens are poorly reported, with limited information provided about the medicines, doses and routes of administration used. It is not clear whether the interventions used in the studies are reflective of current UK practice for children and adolescents with gender dysphoria. There is also the suggestion that the hormone dose used in 1 study may have been too low; the authors of Klink et al. 2015 suggest that the relatively low initial dose of oestrogen for transfemales may be the reason for the observed lack of effect on lumber spine bone density. Duration of treatment with a GnRH analogue is also poorly reported and is only stated in 3/10 studies.

There is a degree of indirectness in some studies, with some participants included that fall outside of the population of this evidence review. For example, in Kuper et al. 2020 17% of participants received puberty suppression alone, and in Achille et al. 2020, 30% of participants received no treatment or puberty suppression alone. Some results and statistical analyses are only reported for the whole cohort in these studies and not the subgroup of participants who received gender-affirming hormones.

Participant numbers are poorly reported in some of the included studies. In Achille et al. 2020, 47% (45/95) of the people who entered the study did not have follow-up data and were excluded from the analyses, with no explanation or description of those people lost to follow-up. In Kuper et al. 2020, the number of participants varied by outcome, with less than

two-thirds of participants providing data for some outcomes. The authors provide no explanation for this incomplete reporting.

It is not clear whether some outcome measures, specifically those related to psychosocial functioning, are relevant to the UK population. In Kaltiala et al. 2020, an observational study conducted in Finland, the proportion of participants living with parents or guardians is reported as marker of appropriate functioning. The authors state that in Finnish culture young people tend to leave the parental home early, with only around one-quarter of 20 to 24 year olds still living at home. This is lower than in the UK, where around half of 20 to 24 year olds live with their parents or guardians (ONS: Why are more young people living with their parents?).

It is difficult to draw firm conclusions for many of the effectiveness and safety outcomes reported in the included studies because many different scoring tools and methods were used to assess the same outcome, often with conflicting results. For example, bone density is reported as bone mineral density (BMD) and bone mineral apparent density (BMAD) in the same study, the latter being a size-adjusted measure often useful for people whose bones are still growing. For some populations (transfemale versus transmale) and bone regions (lumber spine versus femoral neck), statistically significant differences in BMD are reported but not for BMAD, and vice versa.

In addition to this, most outcomes reported across the included studies do not have an accepted minimal clinically important difference (MCID), making it difficult the determine whether any observed statistically significant changes are clinically meaningful. However, the authors of some studies report thresholds to interpret the results of the scoring tools, so some conclusions can be made. For example, the mean Utrecht Gender Dysphoria Scale (UGDS) score (a measure of gender dysphoria symptoms) reduced to about 15 points after treatment with gender-affirming hormones (Lopez de Lara et al. 2020). The authors state that scores of 40 points or above signify gender dysphoria, suggesting that after about 12 months of treatment with gender-affirming hormones, the majority of participants did not have symptoms of gender dysphoria.

The impact of gender-affirming hormones on bone density was reported in 3 studies (Klink et al. 2015, Stoffers et al. 2019 and Vlot et al. 2017). Although these studies did not include a control group, comparisons to a reference population are reported using z-scores. Comparisons were made to a cisgender population, meaning for example that bone density in transfemales was compared with bone density in cisgender males. The authors of Klink et al. 2015 note that this may not be the ideal comparison, because androgens and oestrogens affect bone differently, and that bone properties in a trans population differ from their age- and sex assigned at birth-matched controls. Beyond this, a major limitation when trying to determine the impact of gender-affirming hormones on the short- and long-term bone health of children and adolescents is the lack of data on fracture rates and other patient-orientated outcomes, including rates of osteoporosis. Studies of GnRH analogues in children and adolescents with gender dysphoria suggest that GnRH analogue treatment may reduce the expected increase in bone density (which is expected during puberty). Although improvements in bone density were reported following treatment with gender-affirming hormones, Z-scores suggest that bone density remained lower in transfemales and transmales compared with an equivalent cisgender population.

One study reported on cardiovascular risk factors at age 22 years in people who started gender-affirming hormones for gender dysphoria as adolescents. While glucose levels, insulin levels and insulin resistance were broadly unchanged at 22 years, statistically significant increases in blood pressure and body mass index were seen. A small but statistically significant worsening of the lipid profile in transmales who received testosterone was also seen at age 22 years. However, further studies with a considerably longer follow-up and a focus on patient-oriented outcomes, including cardiovascular events and mortality are needed to determine the long-term impact on cardiovascular health of starting gender-affirming hormones during childhood and adolescence.

Only 1 study reported adverse events and discontinuation rates with gender-affirming hormones in children and adolescents. Conclusions on these outcomes cannot be made based on this study alone.

This review did not identify sub-groups of people who may benefit more from gender-affirming hormones. Limited evidence from 2 studies suggests there was no difference in response to treatment between transfemales and transmales for mental health and quality of life (Achille et al. 2020 and Allen et al. 2019).

7. Conclusion

This evidence review found limited evidence for the effectiveness and safety of gender-affirming hormones in children and adolescents with gender dysphoria, with all studies being uncontrolled, observational studies, and all outcomes of very low certainty. Any potential benefits of treatment must be weighed against the largely unknown long-term safety profile of these treatments.

The results from 5 uncontrolled, observational studies (Achille et al. 2020, Allen et al. 2019, Kaltiala et al. 2020. Kuper et al. 2020, Lopez de Lara et al. 2020) suggest that, in children and adolescents with gender dysphoria, gender-affirming hormones are likely to improve symptoms of gender dysphoria, and may also improve depression, anxiety, quality of life, suicidality, and psychosocial functioning. The impact of treatment on body image is unclear. All results were of very low certainty. The clinical relevance of any improvements to the person is difficult to determine because most outcomes do not have a recognised minimal clinically important difference, and the authors do not present statistical analysis for some outcomes.

A further 5 uncontrolled, observational studies (Khatchadourian et al. 2014, Klaver et al. 2020, Klink et al. 2015, Stoffers et al. 2019 and Vlot et al. 2017) reported on safety outcomes, all of which provided very low certainty evidence. Statistically significant increases in some measures of bone density were seen following treatment with gender-affirming hormones, although results varied by bone region (lumber spine versus femoral neck) and by population (transfemales versus transmales). However, z-scores suggest that bone density remained lower in transfemales and transmales compared with an equivalent cisgender population. Results from 1 study of gender-affirming hormones started during adolescence reported statistically significant increases in blood pressure and body mass index, and worsening of the lipid profile (in transmales) at age 22 years, although longer term studies that report on cardiovascular event rates are needed. Adverse events and discontinuation rates associated with gender-affirming hormones were only reported in 1 study, and no conclusions can be made on these outcomes.

This review did not identify sub-groups of people who may benefit more from gender-affirming hormones. Limited evidence from 2 studies suggests there was no difference in response to treatment between transfemales and transmales for mental health and quality of life (Achille et al. 2020 and Allen et al. 2019).

No cost-effectiveness evidence was found to determine whether gender-affirming hormones are a cost-effective treatment for children and adolescents with gender dysphoria.

Appendix A PICO

The review questions for this evidence review are:

1. For children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention?
2. For children and adolescents with gender dysphoria, what is the short-term and long-term safety of gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention?
3. For children and adolescents with gender dysphoria, what is the cost-effectiveness of gender-affirming hormones compared to one or a combination of psychological support, social transitioning to the desired gender or no intervention?
4. From the evidence selected, are there particular sub-groups of children and adolescents with gender dysphoria that derive comparatively more (or less) benefit from treatment with gender-affirming hormones than the wider population of children and adolescents with gender dysphoria?
5. From the evidence selected,
   (a) what are the criteria used by the research studies to define gender dysphoria, gender identity disorder and gender incongruence of childhood?
   (b) what were the ages at which participants commenced treatment with gender-affirming hormones?
   (c) what was the duration of GnRH analogues treatment?

PICO table

P –Population and Indication	Children and adolescents aged 18 years or less who have gender dysphoria, gender identity disorder or gender incongruence of childhood as defined by the study. The following subgroups of children and adolescents with gender dysphoria, gender identity disorder or gender incongruence of childhood need to be considered:

	• Sex assigned at birth males • Sex assigned at birth females • The duration of gender dysphoria: less than 6 months, 6-24 months, and more than 24 months) • The age at which treatment was initiated with GnRH analogues and with gender-affirming hormones. • The age of onset of gender dysphoria • The age of onset of puberty • Adolescents with gender dysphoria who have a pre-existing diagnosis of autistic spectrum disorder. • Adolescents with gender dysphoria who had a significant mental health symptom load at diagnosis including anxiety, depression (with or without a history of self-harm and suicidality), psychosis, personality disorder, Attention Deficit Hyperactivity Disorder and eating disorders.
I – Intervention	Gender-affirming hormone treatments: • A testosterone preparation for sex assigned at birth female patients which may include testosterone in the form of Sustanon injections*; testosterone enantate injections; Tostran gel*; Testogel; Testim gel; oral testosterone capsules in the form of testosterone undecanoate (Restandol); Andriol testocaps; Nebido • An oestradiol preparation** for sex assigned at birth male patients which may include: oral estradiol valerate*; oestrogen patches (7β-oestradiol patches e.g. Evorel or Estradem); Estradot patches; ethinyloestradiol *** *These are the used by Leeds Hospital, England. ** Be aware that the American spelling is oestrogen without the 'o'. ***Ethinyloestradiol is rarely used.
C – Comparator(s)	One or a combination of: • Psychological support • Social transitioning to the gender with which the individual identifies. No intervention
O – Outcomes	There are no known minimal clinically important differences and there are no preferred timepoints for the outcome measures selected. **All outcomes should be stratified by:** • The age at which treatment with gender-affirming hormones was initiated • The length of treatment with GnRH analogues where possible. **A: Clinical Effectiveness** *Critical to decision making* • **Impact on gender dysphoria** This outcome is critical because gender dysphoria in adolescents and children is associated with significant distress and problems functioning. Impact on gender

	dysphoria may be measured by the Utrecht Gender Dysphoria Scale. Other measures as reported in studies may be used as an alternative to the stated measure. • **Impact on mental health** Examples of mental health problems include self-harm, thoughts of suicide, suicide attempts, suicide, eating disorders, depression/low mood and anxiety. These outcomes are critical because self-harm and thoughts of suicide have the potential to result in significant physical harm and for completed suicides the death of the young person. Disordered eating habits may cause significant morbidity in young people. Depression and anxiety are also critical outcomes because they may impact on social, occupational, or other areas of functioning of children and adolescents. The Child and Adolescent Psychiatric Assessment (CAPA) may be used to measure depression and anxiety. The impact on self-harm and suicidality (ideation and behaviour) may be measured using the Suicide Ideation Questionnaire Junior. Other measures may be used as an alternative to the stated measure. • **Impact on Quality of Life** This outcome is critical because gender dysphoria in children and adolescents may be associated with a significant reduction in health-related quality of life. Quality of Life may be measured by the KINDL questionnaire, Kidscreen 52. Other measures as reported in studies may be used as an alternative to the stated measures. *Important to decision making* • **Impact on body image** This outcome is important because some young people with gender dysphoria may desire to take steps to suppress features of their physical appearance associated with their sex assigned at birth or accentuate physical features of their experienced gender. The Body Image Scale could be used as a measure. Other measures as reported in studies may also be used as an alternative to the stated measure. • **Psychosocial Impact** Examples of psychosocial impact are: coping mechanisms which may impact on substance misuse; family relationships; peer relationships. This outcome is important because gender dysphoria in adolescents and children is associated with internalising and externalising behaviours and emotional and behavioural problems which may impact on social and occupational functioning. The child behavioural check list (CBCL) may be used to measure the impact on psychosocial functioning. Other measures as reported in studies may be used as an alternative to the stated measure. • **Engagement with health care services** This outcome is important because patient engagement with healthcare services will impact on their clinical outcomes. Engagement with health care services may be measured using the Youth Health Care measure-satisfaction, utilization, and needs (YHC-SUN) questionnaire. Loss to follow up and

	should also be ascertained as part of this outcome. Alternative measures to the YHC-SUN questionnaire may be used as reported in studies. • **Transitioning surgery - Impact on extent of and satisfaction with surgery** This outcome is important because some children and adolescents with gender dysphoria may in adulthood proceed to transitioning surgery. Stated measures of the extent of surgery and satisfaction with surgery in studies may be reported. • **De-transition** The proportion of patients who de-transition following the commencement of gender-affirming hormone treatment and the reasons why. This outcome is important to patients because there is uncertainty about the short and long term safety and adverse effects of gender-affirming hormones in children and adolescents with gender dysphoria. **B: Safety** • Short and long -term safety and adverse effects of taking gender-affirming hormones is important to assess whether treatment causes acute side effects that may lead to withdrawing the treatment or long term effects that may impact on decisions for transitioning or de-transitioning. Aspects to be reported on should include Impact of the drug use such as clinically relevant derangement in renal and liver function tests, lipids, glucose, insulin and glycosylated haemoglobin, cognitive development and functioning. The clinical and physical impact of temporary and permanent withdrawal the drug such as when patients decide to de-transition – e.g. delay in the attainment of peak bone mass, attenuation of peak bone mass, permanent physical effects. **C: Cost effectiveness** Cost effectiveness studies should be reported.
Inclusion criteria	
Study design	Systematic reviews, randomised controlled trials, controlled clinical trials, cohort studies. If no higher level quality evidence is found, case series can be considered.
Language	English only
Patients	Human studies only
Age	18 years or less
Date limits	2000-2020

Exclusion criteria	
Publication type	Conference abstracts, non-systematic reviews, narrative reviews, commentaries, letters, editorials, guidelines and pre-publication prints
Study design	Case reports, resource utilisation studies

Appendix B Search strategy

Medline, Embase, the Cochrane Library, HTA and APA PsycInfo were searched on 21 July 2020, limiting the search to papers published in English language in the last 20 years. Conference abstracts, non-systematic reviews, narrative reviews, commentaries, letters, editorials, guidelines, pre-publication prints, case reports and resource utilisation studies were excluded.

Database: Medline
Platform: Ovid
Version: Ovid MEDLINE(R) <1946 to July 17, 2020>
Search date: 21 Jul 2020
Number of results retrieved: 650
Search strategy:
Database: Ovid MEDLINE(R) <1946 to July 17, 2020>
Search Strategy:
---
1 Gender Dysphoria/ (485)
2 Gender Identity/ (18431)
3 "Sexual and Gender Disorders"/ (75)
4 Transsexualism/ (3758)
5 Transgender Persons/ (3134)
6 Health Services for Transgender Persons/ (136)
7 exp Sex Reassignment Procedures/ (835)
8 (gender* adj3 (dysphori* or incongru* or identi* or disorder* or confus* or minorit* or queer*)).tw. (7223)
9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (12665)
10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (102312)
11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (6969)
12 (male-to-female or m2f or female-to-male or f2m).tw. (114785)
13 or/1-12 (252562)
14 exp Infant/ or Infant Health/ or Infant Welfare/ (1137237)
15 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (852126)
16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1912796)
17 Minors/ (2572)
18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2360626)
19 exp pediatrics/ (58102)
20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (835833)
21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (2023650)
22 Puberty/ (13277)

23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (424041)
24 Schools/ (38087)
25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7199)
26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (468784)
27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (89314)
28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (887443)
29 or/14-28 (5532185)
30 13 and 29 (79220)
31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (7)
32 30 or 31 (79220)
33 Hormones/ad, tu, th (4514)
34 exp Progesterone/ad, tu, th (10899)
35 exp Estrogens/ad, tu, th (28936)
36 exp Gonadal Steroid Hormones/ad, tu, th (34137)
37 (progesteron* or oestrogen* or estrogen*).tw. (196074)
38 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).tw. (544)
39 exp Estradiol/ad, tu, th (10823)
40 exp Testosterone/ad, tu, th (8318)
41 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).tw. (74936)
42 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).tw. (90464)
43 or/33-42 (304239)
44 32 and 43 (3183)
45 limit 44 to yr="2000 -Current" (2019)
46 animals/ not humans/ (4685420)
47 45 not 46 (1194)
48 limit 47 to english language (1155)
49 (MEDLINE or pubmed).tw. (163678)
50 systematic review.tw. (121198)
51 systematic review.pt. (130231)
52 meta-analysis.pt. (117148)
53 intervention$.ti. (123904)
54 or/49-53 (380217)
55 randomized controlled trial.pt. (509468)
56 randomi?ed.mp. (796957)
57 placebo.mp. (194937)
58 or/55-57 (848627)
59 exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/ (5562241)
60 ((control and (group* or study)) or (time and factors)).mp. (3274107)
61 (program or survey* or ci or cohort or comparative stud* or evaluation studies or follow-up*).mp. (4624419)
62 or/59-61 (9030680)
63 Observational Studies as Topic/ (5177)
64 Observational Study/ (81866)
65 Epidemiologic Studies/ (8358)

66 exp Case-Control Studies/ (1090891)
67 exp Cohort Studies/ (2011414)
68 Cross-Sectional Studies/ (332273)
69 Controlled Before-After Studies/ (526)
70 Historically Controlled Study/ (185)
71 Interrupted Time Series Analysis/ (913)
72 Comparative Study.pt. (1866044)
73 case control$.tw. (112152)
74 case series.tw. (59119)
75 (cohort adj (study or studies)).tw. (170281)
76 cohort analy$.tw. (6758)
77 (follow up adj (study or studies)).tw. (45131)
78 (observational adj (study or studies)).tw. (86247)
79 longitudinal.tw. (204239)
80 prospective.tw. (495367)
81 retrospective.tw. (442876)
82 cross sectional.tw. (284856)
83 or/63-82 (4368140)
84 54 or 58 or 62 or 83 (9402123)
85 48 and 84 (683)
86 limit 85 to (letter or historical article or comment or editorial or news or case reports) (33)
87 85 not 86 (650)

Database: Medline in-process
Platform: Ovid
Version: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to July 17, 2020>
Search date: 21 July 2020
Number of results retrieved: 122
Search strategy:
Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to July 17, 2020>
Search Strategy:
---
1 Gender Dysphoria/ (0)
2 Gender Identity/ (0)
3 "Sexual and Gender Disorders"/ (0)
4 Transsexualism/ (0)
5 Transgender Persons/ (0)
6 Health Services for Transgender Persons/ (0)
7 exp Sex Reassignment Procedures/ (0)
8 (gender* adj3 (dysphori* or incongru* or identi* or disorder* or confus* or minorit* or queer*)).tw. (1473)
9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (2315)
10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (20821)
11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (963)
12 (male-to-female or m2f or female-to-male or f2m).tw. (15453)
13 or/1-12 (39735)
14 exp Infant/ or Infant Health/ or Infant Welfare/ (0)
15 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (80295)

16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)
17 Minors/ (0)
18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (320315)
19 exp pediatrics/ (0)
20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (119124)
21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)
22 Puberty/ (0)
23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (59969)
24 Schools/ (0)
25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)
26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (68979)
27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (10287)
28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (112220)
29 or/14-28 (523053)
30 13 and 29 (9143)
31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (3)
32 30 or 31 (9144)
33 Hormones/ad, tu, th (0)
34 exp Progesterone/ad, tu, th (0)
35 exp Estrogens/ad, tu, th (0)
36 exp Gonadal Steroid Hormones/ad, tu, th (0)
37 (progesteron* or oestrogen* or estrogen*).tw. (13291)
38 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).tw. (241)
39 exp Estradiol/ad, tu, th (0)
40 exp Testosterone/ad, tu, th (0)
41 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).tw. (5458)
42 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).tw. (4772)
43 or/33-42 (19706)
44 32 and 43 (316)
45 limit 44 to yr="2000 -Current" (303)
46 animals/ not humans/ (1)
47 45 not 46 (303)
48 limit 47 to english language (303)
49 (MEDLINE or pubmed).tw. (36030)
50 systematic review.tw. (29830)
51 systematic review.pt. (1007)
52 meta-analysis.pt. (49)
53 intervention$.ti. (21354)
54 or/49-53 (68976)
55 randomized controlled trial.pt. (277)
56 randomi?ed.mp. (74978)
57 placebo.mp. (18290)
58 or/55-57 (81427)
59 exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/ (455)

60 ((control and (group* or study)) or (time and factors)).mp. (214372)
61 (program or survey* or ci or cohort or comparative stud* or evaluation studies or follow-up*).mp. (339764)
62 or/59-61 (507046)
63 Observational Studies as Topic/ (0)
64 Observational Study/ (91)
65 Epidemiologic Studies/ (0)
66 exp Case-Control Studies/ (1)
67 exp Cohort Studies/ (1)
68 Cross-Sectional Studies/ (0)
69 Controlled Before-After Studies/ (0)
70 Historically Controlled Study/ (0)
71 Interrupted Time Series Analysis/ (0)
72 Comparative Study.pt. (46)
73 case control$.tw. (14451)
74 case series.tw. (13070)
75 (cohort adj (study or studies)).tw. (29119)
76 cohort analy$.tw. (1039)
77 (follow up adj (study or studies)).tw. (3540)
78 (observational adj (study or studies)).tw. (17421)
79 longitudinal.tw. (34485)
80 prospective.tw. (63689)
81 retrospective.tw. (73761)
82 cross sectional.tw. (60195)
83 or/63-82 (250805)
84 54 or 58 or 62 or 83 (687622)
85 48 and 84 (126)
86 limit 85 to (letter or historical article or comment or editorial or news or case reports) (4)
87 85 not 86 (122)

Database: Medline epubs ahead of print
Platform: Ovid
Version: Ovid MEDLINE(R) Epub Ahead of Print <July 17, 2020>
Search date: 21 July 2020
Number of results retrieved: 32
Search strategy:
Database: Ovid MEDLINE(R) Epub Ahead of Print <July 17, 2020>
Search Strategy:
---
1 Gender Dysphoria/ (0)
2 Gender Identity/ (0)
3 "Sexual and Gender Disorders"/ (0)
4 Transsexualism/ (0)
5 Transgender Persons/ (0)
6 Health Services for Transgender Persons/ (0)
7 exp Sex Reassignment Procedures/ (0)
8 (gender* adj3 (dysphori* or incongru* or identi* or disorder* or confus* or minorit* or queer*)).tw. (430)
9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (637)
10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (1499)
11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (179)
12 (male-to-female or m2f or female-to-male or f2m).tw. (2460)

13 or/1-12 (4883)
14 exp Infant/ or Infant Health/ or Infant Welfare/ (0)
15 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (15416)
16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)
17 Minors/ (0)
18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (53285)
19 exp pediatrics/ (0)
20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (22649)
21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)
22 Puberty/ (0)
23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (13005)
24 Schools/ (0)
25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)
26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (12420)
27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (1407)
28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (20083)
29 or/14-28 (87968)
30 13 and 29 (1618)
31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (1)
32 30 or 31 (1618)
33 Hormones/ad, tu, th (0)
34 exp Progesterone/ad, tu, th (0)
35 exp Estrogens/ad, tu, th (0)
36 exp Gonadal Steroid Hormones/ad, tu, th (0)
37 (progesteron* or oestrogen* or estrogen*).tw. (1876)
38 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).tw. (63)
39 exp Estradiol/ad, tu, th (0)
40 exp Testosterone/ad, tu, th (0)
41 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).tw. (846)
42 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).tw. (665)
43 or/33-42 (2850)
44 32 and 43 (64)
45 limit 44 to yr="2000 -Current" (61)
46 animals/ not humans/ (0)
47 45 not 46 (61)
48 limit 47 to english language (61)
49 (MEDLINE or pubmed).tw. (7948)
50 systematic review.tw. (7508)
51 systematic review.pt. (28)
52 meta-analysis.pt. (37)
53 intervention$.ti. (4267)
54 or/49-53 (15048)
55 randomized controlled trial.pt. (1)

56 randomi?ed.mp. (14113)
57 placebo.mp. (3097)
58 or/55-57 (15128)
59 exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/ (34)
60 ((control and (group* or study)) or (time and factors)).mp. (31615)
61 (program or survey* or ci or cohort or comparative stud* or evaluation studies or follow-up*).mp. (65735)
62 or/59-61 (88222)
63 Observational Studies as Topic/ (0)
64 Observational Study/ (4)
65 Epidemiologic Studies/ (0)
66 exp Case-Control Studies/ (0)
67 exp Cohort Studies/ (0)
68 Cross-Sectional Studies/ (0)
69 Controlled Before-After Studies/ (0)
70 Historically Controlled Study/ (0)
71 Interrupted Time Series Analysis/ (0)
72 Comparative Study.pt. (0)
73 case control$.tw. (2577)
74 case series.tw. (2480)
75 (cohort adj (study or studies)).tw. (7959)
76 cohort analy$.tw. (287)
77 (follow up adj (study or studies)).tw. (632)
78 (observational adj (study or studies)).tw. (3763)
79 longitudinal.tw. (7079)
80 prospective.tw. (12148)
81 retrospective.tw. (16600)
82 cross sectional.tw. (9459)
83 or/63-82 (48534)
84 54 or 58 or 62 or 83 (119752)
85 48 and 84 (32)
86 limit 85 to (letter or historical article or comment or editorial or news or case reports) (0)
87 85 not 86 (32)

Database: Medline daily update
Platform: Ovid
Version: Ovid MEDLINE(R) Daily Update <July 21, 2020>
Search date: 22 July 2020
Number of results retrieved: 3
Search strategy

Database: Ovid MEDLINE(R) Daily Update <July 21, 2020>
Search Strategy:
---
1 Gender Dysphoria/ (4)
2 Gender Identity/ (38)
3 "Sexual and Gender Disorders"/ (0)
4 Transsexualism/ (2)
5 Transgender Persons/ (26)
6 Health Services for Transgender Persons/ (1)
7 exp Sex Reassignment Procedures/ (3)
8 (gender* adj3 (dysphori* or incongru* or identi* or disorder* or confus* or minorit* or queer*)).tw. (22)

9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (39)
10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (87)
11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (15)
12 (male-to-female or m2f or female-to-male or f2m).tw. (181)
13 or/1-12 (358)
14 exp Infant/ or Infant Health/ or Infant Welfare/ (932)
15 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (981)
16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1756)
17 Minors/ (3)
18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (3672)
19 exp pediatrics/ (75)
20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (1658)
21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (2006)
22 Puberty/ (8)
23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (732)
24 Schools/ (56)
25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (5)
26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (622)
27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (98)
28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (1301)
29 or/14-28 (6705)
30 13 and 29 (130)
31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (0)
32 30 or 31 (130)
33 Hormones/ad, tu, th (3)
34 exp Progesterone/ad, tu, th (3)
35 exp Estrogens/ad, tu, th (8)
36 exp Gonadal Steroid Hormones/ad, tu, th (22)
37 (progesteron* or oestrogen* or estrogen*).tw. (161)
38 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).tw. (3)
39 exp Estradiol/ad, tu, th (8)
40 exp Testosterone/ad, tu, th (8)
41 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).tw. (79)
42 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).tw. (61)
43 or/33-42 (261)
44 32 and 43 (7)
45 limit 44 to yr="2000 -Current" (7)
46 animals/ not humans/ (3647)
47 45 not 46 (6)
48 limit 47 to english language (6)
49 (MEDLINE or pubmed).tw. (529)
50 systematic review.tw. (512)

51 systematic review.pt. (522)
52 meta-analysis.pt. (370)
53 intervention$.ti. (247)
54 or/49-53 (1065)
55 randomized controlled trial.pt. (595)
56 randomi?ed.mp. (1203)
57 placebo.mp. (219)
58 or/55-57 (1234)
59 exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/ (7958)
60 ((control and (group* or study)) or (time and factors)).mp. (4307)
61 (program or survey* or ci or cohort or comparative stud* or evaluation studies or follow-up*).mp. (5828)
62 or/59-61 (11814)
63 Observational Studies as Topic/ (27)
64 Observational Study/ (449)
65 Epidemiologic Studies/ (7)
66 exp Case-Control Studies/ (2173)
67 exp Cohort Studies/ (3287)
68 Cross-Sectional Studies/ (837)
69 Controlled Before-After Studies/ (1)
70 Historically Controlled Study/ (0)
71 Interrupted Time Series Analysis/ (6)
72 Comparative Study.pt. (768)
73 case control$.tw. (182)
74 case series.tw. (139)
75 (cohort adj (study or studies)).tw. (561)
76 cohort analy$.tw. (22)
77 (follow up adj (study or studies)).tw. (40)
78 (observational adj (study or studies)).tw. (253)
79 longitudinal.tw. (429)
80 prospective.tw. (778)
81 retrospective.tw. (1032)
82 cross sectional.tw. (739)
83 or/63-82 (5471)
84 54 or 58 or 62 or 83 (12581)
85 48 and 84 (3)
86 limit 85 to (letter or historical article or comment or editorial or news or case reports) (0)
87 85 not 86 (3)

Database: Embase
Platform: Ovid
Version: Embase <1974 to 2020 July 22>
Search date: 23 July 2020
Number of results retrieved: 1207
Search strategy:

Database: Embase <1974 to 2020 July 22>
Search Strategy:
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1 exp Gender Dysphoria/ (5399)
2 Gender Identity/ (16820)
3 "Sexual and Gender Disorders"/ (24689)
4 Transsexualism/ (3869)
5 exp Transgender/ (6597)

6 Health Services for Transgender Persons/ (158848)
7 exp Sex Reassignment Procedures/ (1108)
8 (gender* adj3 (dysphori* or incongru* or identi* or disorder* or confus* or minorit* or queer*)).tw. (12470)
9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (22509)
10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (154446)
11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (10327)
12 (male-to-female or m2f or female-to-male or f2m).tw. (200166)
13 or/1-12 (581748)
14 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ or adolescent health/ or middle school student/ or high school student/ (3440943)
15 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (1186161)
16 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (3586795)
17 exp pediatrics/ (106214)
18 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (1491597)
19 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (105108)
20 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (641660)
21 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (103791)
22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (687437)
23 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (138908)
24 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (1562903)
25 or/14-24 (7130881)
26 13 and 25 (181778)
27 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (17)
28 26 or 27 (181778)
29 hormone/bd, ad, an, cr, do, it, dt, to, ei, ih, ia, ar, cv, dl, im, na, ip, ut, va, iv, ve, vi, po, pa, pr, sc, li, th, tp, td (5160)
30 exp progesterone derivative/bd, ad, an, cr, do, it, dt, to, ei, ih, ia, ar, cv, dl, im, na, ip, ut, va, iv, ve, vi, po, pa, pr, sc, li, th, tp, td (23479)
31 exp estrogen/bd, ad, an, cr, do, it, dt, to, ei, ih, ia, ar, cv, dl, im, na, ip, ut, va, iv, ve, vi, po, pa, pr, sc, li, th, tp, td (57641)
32 steroid hormone/bd, ad, an, cr, do, it, dt, to, ei, ih, ia, ar, cv, dl, im, na, ip, ut, va, iv, ve, vi, po, pa, pr, sc, li, th, tp, td (372)
33 sex hormone/bd, ad, an, cr, do, it, dt, to, ei, ih, ia, ar, cv, dl, im, na, ip, ut, va, iv, ve, vi, po, pa, pr, sc, li, th, tp, td (1984)
34 hormonal therapy/ (42222)
35 (progesteron* or oestrogen* or estrogen*).tw. (254142)
36 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).tw. (1224)
37 exp estradiol derivative/bd, ad, an, cr, do, it, dt, to, ei, ih, ia, ar, cv, dl, im, na, ip, ut, va, iv, ve, vi, po, pa, pr, sc, li, th, tp, td (30740)

38 exp testosterone derivative/bd, ad, an, cr, do, it, dt, to, ei, ih, ia, ar, cv, dl, im, na, ip, ut, va, iv, ve, vi, po, pa, pr, sc, li, th, tp, td (15868)
39 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).tw. (99596)
40 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).tw. (114290)
41 or/29-40 (438737)
42 28 and 41 (6053)
43 limit 42 to yr="2000 -Current" (4741)
44 nonhuman/ not human/ (4649157)
45 43 not 44 (3636)
46 limit 45 to english language (3513)
47 (MEDLINE or pubmed).tw. (261145)
48 exp systematic review/ or systematic review.tw. (302985)
49 meta-analysis/ (191173)
50 intervention$.ti. (200041)
51 or/47-50 (660206)
52 random:.tw. (1552336)
53 placebo:.mp. (455979)
54 double-blind:.tw. (210671)
55 or/52-54 (1807280)
56 cohort analysis/ (596360)
57 exp epidemiology/ (3434332)
58 exp clinical trial/ (1504711)
59 evaluation study/ (45870)
60 statistics/ (301181)
61 ((control and (group* or study)) or (time and factors)).mp. (3324555)
62 (program or survey* or ci or cohort or comparative stud* or evaluation studies or follow-up*).mp. (6067112)
63 or/56-62 (11048972)
64 Clinical study/ (155444)
65 Case control study/ (157943)
66 Family study/ (26047)
67 Longitudinal study/ (141660)
68 Retrospective study/ (937696)
69 comparative study/ (859061)
70 Prospective study/ (613138)
71 Randomized controlled trials/ (182542)
72 70 not 71 (606604)
73 Cohort analysis/ (596360)
74 cohort analy$.tw. (13020)
75 (Cohort adj (study or studies)).tw. (302159)
76 (Case control$ adj (study or studies)).tw. (137432)
77 (follow up adj (study or studies)).tw. (63423)
78 (observational adj (study or studies)).tw. (168428)
79 (epidemiologic$ adj (study or studies)).tw. (106448)
80 (cross sectional adj (study or studies)).tw. (220073)
81 case series.tw. (104089)
82 prospective.tw. (861922)
83 retrospective.tw. (886445)
84 or/64-69,72-83 (4047788)
85 51 or 55 or 63 or 84 (12494560)
86 46 and 85 (2151)
87 86 not (letter or editorial).pt. (2137)

88 87 not (conference abstract or conference paper or conference proceeding or "conference review").pt. (1207)

Database: APA PsycInfo

Platform: Ovid
Version: APA PsycInfo <1806 to July Week 2 2020>
Search date: 22 July 2020
Number of results retrieved: 581
Search strategy:

Database: APA PsycInfo <1806 to July Week 2 2020>
Search Strategy:
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1 Gender Dysphoria/ (936)
2 Gender Identity/ (8648)
3 Transsexualism/ (2825)
4 Transgender/ (5257)
5 exp Gender Reassignment/ (568)
6 (gender* adj3 (dysphori* or incongruen* or identi* or disorder* or confus* or minorit* or queer*)).tw. (15276)
7 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (13028)
8 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (7679)
9 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (5796)
10 (male-to-female or m2f or female-to-male or f2m).tw. (63688)
11 or/1-10 (99498)
12 exp Infant Development/ (21841)
13 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (150219)
14 Child Characteristics/ or exp Child Behavior/ or Child Psychology/ or exp Child Welfare/ or Child Psychiatry/ (23423)
15 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (984230)
16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (78962)
17 Adolescent Psychiatry/ or Adolescent Behavior/ or Adolescent Development/ or Adolescent Psychology/ or Adolescent Characteristics/ or Adolescent Health/ (62142)
18 Puberty/ (2753)
19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (347604)
20 Schools/ (29181)
21 Child Day Care/ or Nursery Schools/ (2836)
22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (772814)
23 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (21475)
24 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (285697)
25 or/12-24 (1765408)
26 11 and 25 (49560)
27 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (14)

28 26 or 27 (49561)
29 hormones/ (8408)
30 sex hormones/ (1777)
31 exp progestational hormones/ (2409)
32 estrogens/ (3889)
33 steroids/ (3797)
34 (progesteron* or oestrogen* or estrogen*).tw. (11188)
35 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)).tw. (457)
36 estradiol/ (3120)
37 testosterone/ (5606)
38 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan).tw. (9625)
39 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle).tw. (6741)
40 or/29-39 (30344)
41 28 and 40 (1005)
42 limit 41 to yr="2000 -Current" (749)
43 limit 42 to english language (692)
44 limit 43 to ("0200 book" or "0240 authored book" or "0280 edited book" or "0300 encyclopedia" or "0400 dissertation abstract") (111)
45 43 not 44 (581)

Database: Cochrane Library – incorporating Cochrane Database of Systematic Reviews (CDSR); CENTRAL

Platform: Wiley
Version:
CDSR –Issue 7 of 12, July 2020
CENTRAL – Issue 7 of 12, July 2020
Search date: 22 July 2020
Number of results retrieved: CDSR 0 ; CENTRAL 67.

ID Search Hits
#1 MeSH descriptor: [Gender Dysphoria] this term only 3
#2 MeSH descriptor: [Gender Identity] this term only 227
#3 MeSH descriptor: [Sexual and Gender Disorders] this term only 2
#4 MeSH descriptor: [Transsexualism] this term only 27
#5 MeSH descriptor: [Transgender Persons] this term only 36
#6 MeSH descriptor: [Health Services for Transgender Persons] this term only 0
#7 MeSH descriptor: [Sex Reassignment Procedures] explode all trees 4
#8 (gender* near/3 (dysphori* or incongru* or identi* or disorder* or confus* or minorit* or queer*)):ti,ab,kw 702
#9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*):ti,ab,kw 959
#10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*):ti,ab,kw 3969
#11 ((sex or gender*) near/3 (reassign* or chang* or transform* or transition*)):ti,ab,kw 524
#12 (male-to-female or m2f or female-to-male or f2m):ti,ab,kw 516
#13 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 6413
#14 MeSH descriptor: [Infant] explode all trees 28440
#15 MeSH descriptor: [Infant Health] this term only 49
#16 MeSH descriptor: [Infant Welfare] this term only 82

#17 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*):ti,ab,kw,so 89530
#18 MeSH descriptor: [Child] explode all trees 44089
#19 MeSH descriptor: [Child Behavior] explode all trees 2061
#20 MeSH descriptor: [Child Health] this term only 98
#21 MeSH descriptor: [Child Welfare] this term only 325
#22 MeSH descriptor: [Minors] this term only 8
#23 (child* or minor or minors or boy* or girl* or kid or kids or young*):ti,ab,kw,so 265417
#24 MeSH descriptor: [Pediatrics] explode all trees 661
#25 (pediatric* or paediatric* or peadiatric*):ti,ab,kw,so 57725
#26 MeSH descriptor: [Adolescent] this term only 102154
#27 MeSH descriptor: [Adolescent Behavior] this term only 1358
#28 MeSH descriptor: [Adolescent Health] this term only 29
#29 MeSH descriptor: [Puberty] this term only 295
#30 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*):ti,ab,kw,so 140927
#31 MeSH descriptor: [Schools] this term only 1914
#32 MeSH descriptor: [Child Day Care Centers] this term only 231
#33 MeSH descriptor: [Nurseries, Infant] explode all trees 17
#34 MeSH descriptor: [Schools, Nursery] this term only 37
#35 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*):ti,ab,kw,so 97810
#36 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") near/2 (year or years or age or ages or aged)):ti,ab 6710
#37 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") near/2 (year or years or age or ages or aged)):ti,ab 196881
#38 #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 516067
#39 #13 and #38 2488
#40 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*):ti,ab,kw 0
#41 #39 or #40 2488
#42 MeSH descriptor: [Hormones] this term only 2241
#43 MeSH descriptor: [Progesterone] explode all trees 3135
#44 MeSH descriptor: [Estrogens] explode all trees 1841
#45 MeSH descriptor: [Gonadal Steroid Hormones] explode all trees 10747
#46 (progesteron* or oestrogen* or estrogen*):ti,ab,kw 18387
#47 ((cross-sex or crosssex or gender-affirm*) and (hormon* or steroid* or therap* or treatment* or prescri* or pharm* or medici* or drug* or intervention* or care)):ti,ab,kw 24
#48 MeSH descriptor: [Estradiol] explode all trees 4434
#49 MeSH descriptor: [Testosterone] explode all trees 2945
#50 (testosteron* or sustanon* or tostran or testogel or testim or restandol or andriol or testocaps* or nebido or testavan):ti,ab,kw 7386
#51 (oestrad* or estrad* or evorel or ethinyloestrad* or ethinylestrad* or elleste or progynova or zumenon or bedol or femseven or nuvelle):ti,ab,kw 11410
#52 #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 31870
#53 #41 and #52 121
#54 "conference":pt or (clinicaltrials or trialsearch):so 492465
#55 #53 not #54 72

Database: HTA

Platform: Wiley
Version: up to 2018
Search date: 22nd July 2020
Number of results retrieved: 4
Search strategy:

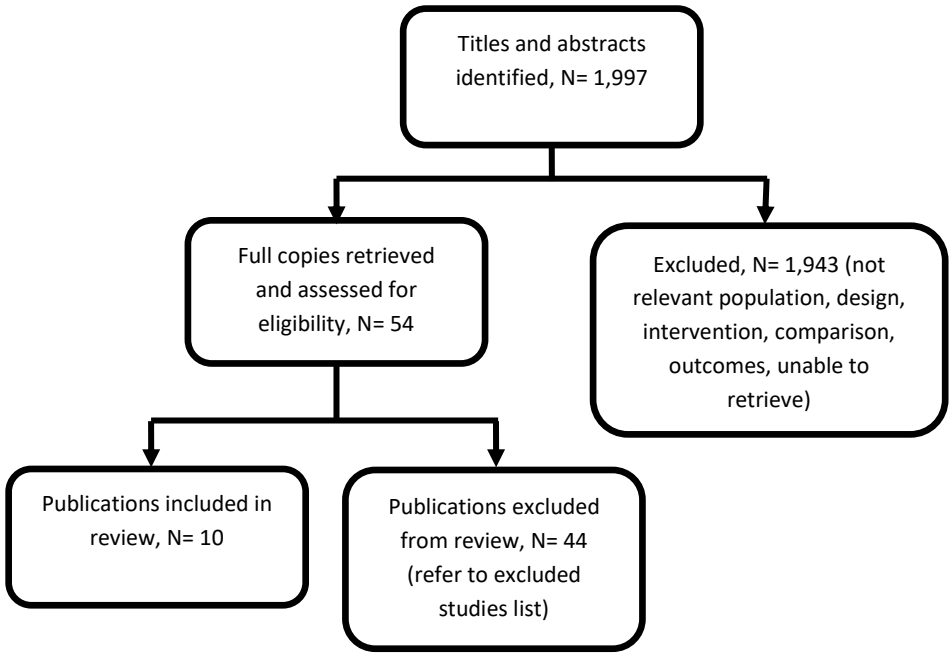
#1 MeSH DESCRIPTOR Gender Dysphoria 0
#2 MeSH DESCRIPTOR Gender Identity 12
#3 MeSH DESCRIPTOR Sexual and Gender Disorders 2
#4 MeSH DESCRIPTOR Transsexualism 12
#5 MeSH DESCRIPTOR Transgender Persons 3
#6 MeSH DESCRIPTOR Health Services for Transgender Persons 0
#7 MeSH DESCRIPTOR Sex Reassignment Procedures EXPLODE ALL TREES 1
#8 ((gender* near3 (dysphori* or incongru* or identi* or disorder* or confus* or minorit* or queer*))) 28
#9 ((transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*)) 76
#10 ((trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*)) 83
#11 (((sex or gender*) near3 (reassign* or chang* or transform* or transition*))) 24
#12 ((male-to-female or m2f or female-to-male or f2m)) 86
#13 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 261
#14 MeSH DESCRIPTOR Infant EXPLODE ALL TREES 2964
#15 MeSH DESCRIPTOR Infant Health 0
#16 MeSH DESCRIPTOR Infant Welfare 22
#17 ((prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*)) 5510
#18 MeSH DESCRIPTOR Child EXPLODE ALL TREES 4935
#19 MeSH DESCRIPTOR Child Behavior EXPLODE ALL TREES 64
#20 MeSH DESCRIPTOR Child Health 2
#21 MeSH DESCRIPTOR Child Welfare 80
#22 MeSH DESCRIPTOR Minors 2
#23 ((child* or minor or minors or boy* or girl* or kid or kids or young*)) 13575
#24 MeSH DESCRIPTOR Pediatrics EXPLODE ALL TREES 119
#25 ((pediatric* or paediatric* or peadiatric*)) 2842
#26 MeSH DESCRIPTOR Adolescent 4594
#27 MeSH DESCRIPTOR Adolescent Behavior 94
#28 MeSH DESCRIPTOR Adolescent Health 0
#29 MeSH DESCRIPTOR Puberty 3
#30 ((adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*)) 5621
#31 MeSH DESCRIPTOR Schools 168
#32 MeSH DESCRIPTOR Child Day Care Centers 12
#33 MeSH DESCRIPTOR Schools, Nursery 3
#34 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)) 4454
#35 ((("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") near2 (year or years or age or ages or aged))) 380
#36 ((("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") near2 (year or years or age or ages or aged))) 7996

#37 #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 22640
#38 #13 AND #37 116
#39 (#13 AND #37) IN HTA 4

Appendix C Evidence selection

The literature searches identified 1,997 references. These were screened using their titles and abstracts and 54 references were obtained and assessed for relevance. Of these, 10 references are included in the evidence review. The remaining 44 references were excluded and are listed in appendix D.

Figure 1 – Study selection flow diagram



References submitted with Preliminary Policy Proposal

There is no preliminary policy proposal for this policy.

Appendix D Excluded studies table

Study reference	Reason for exclusion
Aranda G, Mora M, Hanzu FA et al. (2019) Effects of sex steroids on cardiovascular risk profile in transgender men under gender affirming hormone therapy. Endocrinologia, diabetes y nutricion 66(6): 385–392	Excluded on population – adult study, participants not 18 years or less (mean age 27.1 years).
Arnold, Justin D, Sarkodie, Eleanor P, Coleman, Megan E et al. (2016) Incidence of Venous Thromboembolism in Transgender Women	Excluded on population – adult study, participants not 18 years or less (mean age 33.2 years).

Study reference	Reason for exclusion
Receiving Oral Estradiol. The journal of sexual medicine 13(11): 1773–1777	
Asscheman, Henk, Giltay, Erik J, Megens, Jos A J et al. (2011) A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. European journal of endocrinology 164(4): 635–42	Excluded on population – although some participants started gender-affirming hormones when young, the study does not report the proportion who started treatment when 18 years or less. Mean ages at start of treatment were 31.4 years (transfemales) and 26.1 years (transmales), suggesting the majority of participants were older than 18 years at the start of treatment. Outcomes not reported separately for people aged 18 years or less.
Author not, found (2014) Hormone therapy for the treatment of gender dysphoria. Lansdale, PA: HAYES, Inc	Full text paper not available.
Baba, T., Endo, T., Honnma, H. et al. (2007) Association between polycystic ovary syndrome and female-to-male transsexuality. Human Reproduction 22(4): 1011–1016	Excluded on population – although study included some younger people (age range 17 to 47), most participants were adults (mean age around 25 years) and the proportion who started treatment when 18 years or less is not reported. Outcomes not reported separately for people aged 18 years or less.
Becerra-Fernandez A, Perez-Lopez G, Roman MM et al. (2014) Prevalence of hyperandrogenism and polycystic ovary syndrome in female to male transsexuals. Endocrinologia y Nutricion: Organo de la Sociedad Espanola de Endocrinologia y Nutricion 61(7): 351–8	Excluded on population – although study included some younger people (age range 18 to 45), most participants were adults (mean age around 25 years) and the proportion who started treatment when 18 years or less is not reported. Outcomes not reported separately for people aged 18 years or less.
Becker I, Auer M, Barkmann C et al. (2018) A Cross-Sectional Multicenter Study of Multidimensional Body Image in Adolescents and Adults with Gender Dysphoria Before and After Transition-Related Medical Interventions. Archives of Sexual Behavior 47(8): 2335–2347	Excluded on population – study included people aged 14 to 21 years. Outcomes not reported separately for people aged 18 years or less. Better evidence available – only 11 participants received gender-affirming hormones. The majority of the study cohort were either pre-treatment, received puberty suppression alone, or received hormones and underwent surgery.
Chew D, Anderson J, Williams K et al. (2018) Hormonal Treatment in Young People With Gender Dysphoria: A Systematic Review. Pediatrics 141(4): e20173742	Excluded on better available evidence - systematic review did not meta-analyse results from. Individual studies from this systematic review are either

Study reference	Reason for exclusion
	included, or excluded because they did not meet the PICO criteria.
Connolly MD, Zervos MJ, Barone CJ 2nd et al. (2016) The Mental Health of Transgender Youth: Advances in Understanding. The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine 59(5): 489–495	Excluded on intervention - review did not investigate gender-affirming hormones
de Vries ALC, McGuire JK, Steensma TD et al. (2014) Young adult psychological outcome after puberty suppression and gender reassignment. Pediatrics 134(4): 696–704	Exclude on intervention – all participants had surgery after gender-affirming hormones. Unable to determine whether changes were due to hormones or surgery. Complete data only available for 40 patients. Details of gender-affirming hormones are poorly reported. Outcomes reported in other study (with a population that more closely matches PICO)
Elamin MB, Garcia MZ, Murad MH et al. (2010) Effect of sex steroid use on cardiovascular risk in transsexual individuals: a systematic review and meta-analyses. Clinical Endocrinology 72(1): 1–10	Exclude on population – all included studies conducted in adult population. Unclear whether hormones were started when participants were aged 18 years or less. Outcomes not reported by age at treatment initiation.
Fernandez JD and Tannock LR (2016) Metabolic effects of hormone therapy in transgender patients. Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 22(4): 383–8	Excluded on population – adult study, participants not 18 years or less (mean ages 31 and 27 years).
Fighera TM, Ziegelmann PK, Da Silva TR et al. (2019) Bone mass effects of cross-sex hormone therapy in transgender people: Updated systematic review and meta-analysis. Journal of the Endocrine Society 3(5): 943–964	Excluded on population – all included studies conducted in adult population. Unclear whether hormones were started when participants were aged 18 years or less. Outcomes not reported by age at treatment initiation.
Getahun D, Nash R, Flanders WD et al. (2018) Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons: A Cohort Study. Annals of Internal Medicine 169(4): 205–213	Excluded on population – adult study, participants not 18 years or less.
Gomez-Gil E, Zubiaurre-Elorza L, de Antonio IE et al. (2014) Determinants of quality of life in Spanish transsexuals attending a gender unit before genital sex reassignment surgery. Quality of Life Research: an International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation 23(2): 669–76	Excluded on population – although study included some younger people (age range 16 to 67), most participants were adults (mean age 31.2 years) and the proportion who started treatment when 18 years or less is not reported. Outcomes not reported separately for people aged 18 years or less.
Gomez-Gil E, Zubiaurre-Elorza L, Esteva I et al. (2012) Hormone-treated transsexuals report less	Excluded on population – adult study, participants not 18 years or less (mean age 24.6 years).

Study reference	Reason for exclusion
social distress, anxiety and depression. Psychoneuroendocrinology 37(5): 662–70	
Gooren LJ, van Trotsenburg MAA, Giltay EJ et al. (2013) Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. The Journal of Sexual Medicine 10(12): 3129–34	Excluded on population – study reports on cancer rates in people aged 18-80 years. The 3 cases of cancer all started gender-affirming hormone treatment >18 years.
Grimstad FW, Boskey E, Grey M (2020) New-Onset Abdominopelvic Pain After Initiation of Testosterone Therapy Among TransMasculine Persons: A Community-Based Exploratory Survey. LGBT health 7(5): Published Online:13 Jul 2020https://doi.org/10.1089/lgbt.2019.0258	Excluded on population – adult study, participants not 18 years or less.
Hannema SE, Schagen SEE, Cohen-Kettenis PT et al. (2017) Efficacy and Safety of Pubertal Induction Using 17beta-Estradiol in Transgirls. The Journal of Clinical Endocrinology and Metabolism 102(7): 2356–2363	Excluded on better evidence available – small study (n=28) with high drop-out rate (n=16 at final follow-up). Same outcomes reported in larger studies.
Jarin J, Pine-Twaddell E, Trotman G et al. (2017) Cross-Sex Hormones and Metabolic Parameters in Adolescents With Gender Dysphoria. Pediatrics 139(5)	Excluded on population and better evidence available. Although the study included some younger people (age range 13 to 25; mean age 16 and 18), the proportion who started treatment when 18 years or less is not reported. Outcomes not reported separately for people aged 18 years or less. Outcomes were limited to physiological results (including haemoglobin, lipids and BMI). Follow-up only 6 months, other included studies report same outcomes with longer follow-up (12 to 31 months).
Keo-Meier CL, Herman LI, Reisner SL et al. (2015) Testosterone treatment and MMPI-2 improvement in transgender men: a prospective controlled study. Journal of consulting and clinical psychology 83(1): 143–56	Excluded on population – although study included some younger people (age range 18 to 54), most participants were adults (mean age 26.6 years) and the proportion who started treatment when 18 years or less is not reported. Outcomes not reported separately for people aged 18 years or less.
Klaver M, de Mutsert R, Wiepjes CM et al. (2018) Early Hormonal Treatment Affects Body Composition and Body Shape in Young Transgender Adolescents. The Journal of Sexual Medicine 15(2): 251–260	Excluded on outcomes – reported outcomes not included in PICO document. The risk of obesity with gender-affirmed hormones was reported in an included study.
McFarlane T, Zajac JD, Cheung AS (2018) Gender-affirming hormone therapy and the risk of sex hormone-dependent tumours in transgender individuals-A systematic review. Clinical Endocrinology 89(6): 700-711	Exclude on population – all included studies conducted in adult population.

Study reference	Reason for exclusion
Meriggiola MC, Armillotta F, Costantino A et al. (2008) Effects of testosterone undecanoate administered alone or in combination with letrozole or dutasteride in female to male transsexuals. The Journal of Sexual Medicine 5(10): 2442–53	Excluded on population – adult study, participants not 18 years or less.
Nota NM, Wiepjes CM, de Blok, CJM et al. (2018) The occurrence of benign brain tumours in transgender individuals during cross-sex hormone treatment. Brain: A Journal of Neurology 141(7): 2047–2054	Excluded on population – adult study, participants not 18 years or less.
Oda H and Kinoshita T (2017) Efficacy of hormonal and mental treatments with MMPI in FtM individuals: Cross-sectional and longitudinal studies. BMC Psychiatry 17(1): 256	Excluded on population – although study included some younger people (age range 15 to 43), most participants were adults (mean age around 25.6 years) and the proportion who started treatment when 18 years or less is not reported. Outcomes not reported separately for people aged 18 years or less.
Olson-Kennedy J, Okonta V, Clark LF et al. (2018) Physiologic Response to Gender-Affirming Hormones Among Transgender Youth. The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine 62(4): 397–401	Excluded on population – although study included some younger people (age range 12 to 23; mean age 18 years). Outcomes not reported separately for people aged 18 years or less. Outcomes limited to physiological results (including haemoglobin, lipids, liver enzymes and BMI). Same outcomes reported in included studies that had a less indirect population and a longer follow-up.
Ott J, Kaufmann U, Bentz K et al. (2010) Incidence of thrombophilia and venous thrombosis in transsexuals under cross-sex hormone therapy. Fertility and sterility 93(4): 1267–72	Excluded on population – adult study, participants not 18 years or less.
Pakpoor J, Wotton CJ, Schmierer K et al. (2016) Gender identity disorders and multiple sclerosis risk: A national record-linkage study. Multiple sclerosis. Multiple Sclerosis Journal. 22(13): 1759–1762	Excluded on population – although study included some younger people, outcomes not reported separately for people aged 18 years or less. Also exclude for intervention – unclear if people received gender-affirming hormones.
Pyra M, Casimiro I, Rusie L et al. (2020) An Observational Study of Hypertension and Thromboembolism among Transgender Patients Using Gender-Affirming Hormone Therapy. Transgender Health 5(1): 1–9	Excluded on population – adult study (age range 20-70). Age at which gender-affirming hormones started not reported.
Quiros C, Patrascioiu I, Mora M et al. (2015) Effect of cross-sex hormone treatment on cardiovascular risk factors in transsexual individuals. Experience in a specialized unit in Catalonia. Endocrinologia y nutricion : organo de la Sociedad Espanola de Endocrinologia y Nutricion 62(5): 210–6	Excluded on population – adult study, participants not 18 years or less.

Study reference	Reason for exclusion
Rowniak S, Bolt L, Sharifi C (2019) Effect of cross-sex hormones on the quality of life, depression and anxiety of transgender individuals: A quantitative systematic review. JBI Database of Systematic Reviews and Implementation Reports 17(9): 1826–1854	Exclude on population – all included studies conducted in adult population.
Sequeira GM, Kidd K, El Nokali NE et al. (2019) Early Effects of Testosterone Initiation on Body Mass Index in Transmasculine Adolescents. Journal of Adolescent Health 65(6): 818–820	Exclude on outcome - study only reports BMI z-score over 12 month testosterone treatment. BMI not listed as an outcome of interest in the PICO document. Other included studies have investigated the impact of gender-affirming hormone treatment on CV risk profile, including longer term obesity rates, with a longer follow-up and more participants.
Shim JY, Laufer MR, Grimstad FW (2020) Dysmenorrhea and Endometriosis in Transgender Adolescents. Journal of Pediatric and Adolescent Gynecology. Available online 11 June 2020. https://doi.org/10.1016/j.jpag.2020.06.001	Exclude on population – only 2 participants taking testosterone before diagnosis of dysmenorrhea.
Slabbekoorn D, Van Goozen SHM, Gooren, LJG et al. (2001) Effects of cross-sex hormone treatment on emotionality in transsexuals. International Journal of Transgenderism 5(3): http://www.symposion.com/ijt/ijtvo05no03_02.htm	Excluded on population – adult study (age range 21 to 28 years)
Smith YLS., Van Goozen SHM, Kuiper AJ et al. (2005) Sex reassignment: Outcomes and predictors of treatment for adolescent and adult transsexuals. Psychological Medicine 35(1): 89–99	Excluded on population – results on adults only used to assess hormone treatment.
Sutherland N, Espinel W, Grotzke M et al. (2020) Unanswered Questions: Hereditary breast and gynecological cancer risk assessment in transgender adolescents and young adults. Journal of Genetic Counseling 29(4): 625–633	Excluded on study type – narrative review of 3 case reports.
van Velzen DM, Paldino A, Klaver M et al. (2019) Cardiometabolic Effects of Testosterone in Transmen and Estrogen Plus Cyproterone Acetate in Transwomen. The Journal of Clinical Endocrinology and Metabolism 104(6): 1937–1947	Excluded on population – adult study, participants not 18 years or less.
White Hughto JM and Reisner SL (2016) A Systematic Review of the Effects of Hormone Therapy on Psychological Functioning and Quality of Life in Transgender Individuals. Transgender Health 1(1): 21–31	Exclude on population – all included studies conducted in adult population.
Wiepjes CM, de Blok CJM, Staphorsius AS et al. (2020) Fracture Risk in Trans Women and Trans Men Using Long-Term Gender-Affirming Hormonal Treatment: A Nationwide Cohort Study. Journal of Bone and Mineral Research 35(1): 64–70	Excluded on population – adult study, all participants started gender-affirming hormones after 18 years.
Wierckx K, Mueller S, Weyers S et al. (2012) Long-term evaluation of cross-sex hormone treatment in	Excluded on population – adult study, participants not 18 years or less.

Study reference	Reason for exclusion
transsexual persons. The Journal of Sexual Medicine 9(10): 2641–51	
Wierckx K, Van Caenegem E, Schreiner T et al. (2014) Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the European network for the investigation of gender incongruence. The journal of sexual medicine 11(8): 1999–2011	Excluded on population – adult study, participants not 18 years or less.
Wilson R, Jenkins C, Miller H et al. (2006) The effect of oestrogen on cytokine and antioxidant levels in male to female transsexual patients. Maturitas 55(1): 14–8	Excluded on population – adult study, participants not 18 years or less.
Witcomb GL, Bouman WP, Claes L et al. (2018) Levels of depression in transgender people and its predictors: Results of a large matched control study with transgender people accessing clinical services. Journal of Affective Disorders 235: 308–315	Excluded on population – although study included some younger people (age range 15 to 79), most participants were adults (mean age around 30.4 years) and the proportion who started treatment when 18 years or less is not reported. Outcomes not reported separately for people aged 18 years or less.

Appendix E Evidence tables

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Achille, C., Taggart, T., Eaton, N.R. et al. (2020) Longitudinal impact of gender-affirming endocrine intervention on the mental health and well-being of transgender youths: Preliminary results. International Journal of Pediatric Endocrinology 2020(1): 8 **Study location** Single centre, New York, United States **Study type** Prospective longitudinal study **Study aim** To assess the psychological wellbeing and quality of life in children and adolescents who have sought endocrine	Inclusion and exclusion not reported- it appears from the description in the publication that all people referred for gender dysphoria were invited to participate, and the vast majority agreed. Of the 95 treatment naïve people who entered the study, 50 people completed all follow-up questionnaires and were included in the analysis. No description of the 45 people without follow-up data reported. The study included 50 children, adolescents and young adults with gender dysphoria.	**Intervention** Endocrine interventions (the collective term used by authors for puberty suppression and gender-affirming hormones) were introduced as per Endocrine Society and the World Professional Association for	**Critical Outcomes** ***Impact on mental health*** Depression symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CESD-R). Statistically significant improvements in CESD-R score were observed from baseline (initial assessment; 21.4 points) to about 12 months follow-up (13.9 points; p<0.001). Regression analysis, controlling for reported medicines for mental health problems and engagement in counselling, found no statistically significant change from baseline in transfemales (p=0.27) and transmales (p=0.43). The Patient Health Questionnaire Modified for Teens (PHQ 9_Modified for Teens) was also used to assess depression symptoms. Depression scores improved from baseline (p< 0.001; absolute scores not reported numerically). Regression analysis, controlling for reported medicines for mental health problems and engagement in counselling, found no statistically significant change from baseline in transfemales (p=0.07) and transmales (p=0.67). Suicidal ideation measured using the additional questions from the PHQ 9_Modified for Teens, was presented in 10% (5/50) of	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record 4. b) no **Domain 2: Comparability** 1. c) no comparator **Domain 3: Outcome** 1. c) self-report 2. a) yes – 6 monthly assessment up to 12 months (preliminary results from an ongoing study) 3. c) Follow up rate less than 80% and no description of those lost **Overall quality is assessed as poor** Other comments: Although regression analysis results for some outcomes were controlled for use of medicines for mental health problems,

intervention to help with gender dysphoria. **Study dates** Study recruitment ran from December 2013 to December 2018; study is ongoing	17 transfemales and 33 transmales. Diagnostic criteria for gender dysphoria not reported. Mean age at baseline was 16.2 years (SD 2.2). Mean age at the start of gender-affirming hormone treatment not reported.	Transgender Health (WPATH) guidelines. Puberty suppression was: • GnRH agonist and/or anti-androgens (transfemales) • GnRH agonist or medroxyprogesterone (transmales) Average duration of GnRH analogue treatment not reported. Once eligible, gender-affirming hormones were offered, these were: • Oestradiol (transfemales) • Testosterone (transmales) Doses and route of administration not reported. After about 12-months treatment ('wave 3' in the study): • 24 people (48%) were on gender-affirming hormones alone • 12 people (24%) were on puberty suppression alone	participants at baseline and 6% (3/50) at about 12-month follow-up, no statistical analysis reported. The study also reported results by gender: In transfemales, 11.8% (2/17) had suicidal ideation at baseline compared with 5.9% (1/17) at 12-month follow-up (no statistically analysis reported) In transmales, 9.1% (3/33) had suicidal ideation at baseline compared with 6.1% (2/33) at 12-month follow-up (no statistically analysis reported) ***Impact on quality of life*** Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q-SF) scores: there was no statistically significant change in score from baseline to about 12-months (p=0.085; absolute scores not reported numerically). Regression analysis, controlling for reported medicines for mental health problems and engagement in counselling, found not statistically significant change from baseline in transfemales (p=0.06) and transmales (p=0.08). *No other critical or important outcomes reported*	details of these is not reported. Other co-morbidities not reported. Source of funding: None

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
		• 11 people (22%) were on both gender-affirming hormones and puberty suppression • 3 people (6%) were on no endocrine intervention Results not represented separately for the sub-group of people who received gender-affirming hormones. Average duration of treatment with gender-affirming hormones not reported. **Comparison** No comparison group. Change overtime reported.		

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Allen, LR, Watson, LB, Egan, AM et al. (2019) Well-being and suicidality among transgender youth after gender-affirming hormones. Clinical Practice in Pediatric	The study included adolescents and young adults (age range 13-20 years) who received services for gender dysphoria in a clinic in the United States. Participants were required to have received gender-	39 participants received gender-affirming hormones only 8 participants received a GnRH analogue followed by gender-affirming hormones.	**Critical Outcomes** ***Impact on mental health*** The Ask Suicide-Screening Questions (ASQ) instrument was used to assess suicidality. Following an average of about 12 months treatment with gender-affirming hormones, adjusted mean ASQ score was statistically significantly lower (from 1.11 [standard error	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Psychology 7(3): 302-311 **Study location** Single centre, Kansas City, United States **Study type** Retrospective longitudinal study **Study aim** To examine suicidality and general well-being following administration of gender-affirming hormones. **Study dates** Participants first presented to the clinic between 2015 and 2018.	affirming hormones for at least 3 months, and have pre-test and final assessment data points. No exclusion criteria reported. In total 47 adolescents and young adults with gender dysphoria were included: 14 transfemales (sex assigned at birth male) and 33 transmales (sex assigned at birth female). Diagnostic criteria for gender dysphoria not reported. Mean age at pre-test (before administration of gender-affirming hormones) was 16.59 years (range 13.73 to 19.04). Mean age at the start of treatment in the sub-group who received gender-affirming hormones-only was 16.72 years. Mean age at the start of treatment with gender-affirming hormones in people who previously	Mean duration of treatment in the gender-affirming hormones only subgroup was 366 days. Mean duration of gender-affirming hormone treatment in people who had previously received a GnRH analogue was not reported. Mean duration of treatment with a GnRH analogue was not reported. Participants were assessed at the start of treatment and at least 3 months after treatment.	(SE) 0.22] at baseline to 0.27 [SE 0.12] at final assessment; p<0.001). The authors also reported change in ASQ separately for transfemales (from 1.21 [SE 0.36] at baseline to 0.24 [SE 0.19] at final assessment) and transmales (from 1.01 [SE 0.36] at baseline to 0.29 [0.13] at final assessment). There was no statistically significant difference in change from baseline between transfemales and transmales (p=0.79) ***Impact on quality of life*** Assessed using the General Well-Being Scale (GWBS) of the Pediatric Quality of Life Inventory. Following an average of about 12 months treatment with gender-affirming hormones, adjusted mean GWBS score was statistically significantly higher (from 61.7 [SE 2.43] at baseline to 70.23 [2.15] at final assessment; p<0.002). The authors also reported change in GWBS of the Pediatric Quality of Life Inventory for transfemales (from 58.44 [SE 4.09] at baseline to 69.52 [SE 3.62] at final assessment) and transmales (from 64.95 [SE 2.66] at baseline to 70.94 [2.35] at final assessment). There was no statistically significant difference in change from baseline between transfemales and transmales (p=0.32) *No other critical or important outcomes reported*	3. a) secure record 4. b) no **Domain 2: Comparability** 2. c) no comparator **Domain 3: Outcome** 1. b) record linkage 2. a) yes – mean duration of treatment was 366 days 3. a) complete follow up - all subjects accounted for **Overall quality is assessed as poor** Other comments: None Source of funding: Not reported

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
	received a GnRH analogue was not reported.			

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Kaltiala, R., Heino, E., Tyolajarvi, M. et al. (2020) Adolescent development and psychosocial functioning after starting cross-sex hormones for gender dysphoria. Nordic Journal of Psychiatry 74(3): 213-219 **Study location** Single centre, Tampere, Finland **Study type** Retrospective chart review **Study aim** To evaluate the psychosocial functioning and need for mental health treatment during the gender identity diagnostic phase and after about	The study included adolescents who were referred to the gender identity service before they 18 years old, were diagnosed with gender dysphoria, received gender-affirming hormones and completed a follow-up of approximately 12 months after starting hormones. In total 52 adolescents were included, comprising of 11 transfemales and 41 transmales. Gender dysphoria was diagnosed according to International Classification of Disease 10 (ICD-10). The authors state that the corresponding diagnosis to 'gender dysphoria' in	Intervention referred to as 'hormonal sex reassignment treatment' – details of intervention not reported, although gender-affirming hormones were prescribed to all participants. It is not clear from the study whether additional interventions were prescribed. Medical records reviewed for the 'real-life phase' – the approximately 12 months follow-up period for this population in Finland.	**Critical Outcomes** ***Impact on mental health*** Of the 52 people who received gender-affirming hormones, 50% (26/52) needed mental health treatment before or during the assessment and 46% (24/51) needed mental health treatment during the 12-month 'real life' phase (no statistically significant difference). For specific symptoms / conditions: • depression: 54% (28/52) needed treatment before or during the assessment and 15% (8/52) needed treatment during the 12-month 'real life' phase (statistically significant reduction, p<0.001) • anxiety: 48% (25/52) needed treatment before or during the assessment and 15% (8/52) needed treatment during the 12-month 'real life' phase (statistically significant reduction, p<0.001) • suicidality/self-harm: 35% (18/52) needed treatment before or during the assessment and 4% (2/52) needed treatment during the 12-month 'real life' phase (statistically significant reduction, p<0.001) • conduct problems/antisocial: 14% (7/52) needed treatment before or during the	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record 4. b) no **Domain 2: Comparability** 1. c) cohorts are not comparable on the basis of the design or analysis controlled for confounders **Domain 3: Outcome** 1. b) record linkage 2. a) yes – 12 month follow-up 3. a) complete follow up - all subjects accounted for **Overall quality is assessed as poor**

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
a year on gender-affirming hormones. **Study dates** 2011 to 2017	the ICD-10 is 'transsexualism'. Mean age at diagnosis 18.1 years (range 15.2 to 19.9)		assessment and 6% (3/52) needed treatment during the 12-month 'real life' phase (no statistically significant difference, p= 0.18) • psychotic symptoms/psychosis: 2% (1/52) needed treatment before or during the assessment and 4% (2/52) needed treatment during the 12-month 'real life' phase (no statistically significant difference, p= 0.56) • substance abuse: 4% (2/52) needed treatment before or during the assessment and 2% (1/52) needed treatment during the 12-month 'real life' phase (no statistically significant difference, p= 0.56) • autism: 12% (6/52) needed treatment before or during the assessment and 6% (3/52) needed treatment during the 12-month 'real life' phase (no statistically significant difference, p= 0.30) • ADHD: 10% (5/52) needed treatment before or during the assessment and 2% (1/52) needed treatment during the 12-month 'real life' phase (no statistically significant difference, p= 0.09) • eating disorder: 2% (1/52) needed treatment before or during the assessment and 2% (1/52) needed treatment during the 12-month 'real life' phase (no statistically significant difference, p= 1.0). No details of actual treatment reported. **Important Outcomes** ***Psychosocial Impact*** Study reported on measures of functioning in different domains of adolescent development,	Other comments: None Source of funding: No source of funding reported

			reported over the approximately 12-month period after starting gender-affirming hormones (referred to as the 'real-life phase' in Finland) Significantly fewer participants were living with parent(s)/ guardians during the real-life phase (40%; 21/50) compared with during gender identity assessment (73%; 38/52; p=0.001)) There was a statistically significant reduction in the number of participants with normative peer contacts, from gender identity assessment (89%; 46/52) to the real-life phase (81%; 42/52; p<0.001). There was no significant difference in the number of participants who were progressing normally in school or work during gender identity assessment (64%; 33/52) compared with the real-life phase (60%; 31/52). There was no significant difference in the number of participants who have been dating or were in steady relationships during gender identity assessment (62%; 32/50) compared with the real-life phase (58%; 30/52). There was no significant difference in the number of participants who were able to deal with matters outside of the home in an age-appropriate manner during gender identity assessment (81% (42/52) compared with the real-life phase (81%; 42/52)	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			No other critical or important outcomes reported	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Khatchadourian K, Amed S, Metzger DL (2014) Clinical management of youth with gender dysphoria in Vancouver. The Journal of pediatrics 164(4): 906-11 **Study location** Single centre study, Vancouver, Canada **Study type** Retrospective chart review **Study aim** To describe the patient characteristics, clinical management, and response to treatment in a cohort of people seen in a single clinic. **Study dates** 1998 to 2011	Inclusion criteria were at least Tanner stage 2 pubertal development, previous assessment by a mental health professional and a confirmed diagnosis of gender dysphoria (diagnostic criteria not specified). No exclusion criteria are specified. 63 children, adolescents and young people with gender dysphoria who started gender-affirming hormones, out of 84 young people seen in the unit between 1998 and 2011. 39 transfemales and 24 transmales. Diagnostic criteria for gender dysphoria not reported. Mean age at the start of gender-affirming hormone treatment was 17.4 years (SD 1.9).	**Intervention** Transfemales: Oestrogen (oral micronized 17β-oestradiol) Transmales: Testosterone (injectable testosterone enanthate and/or cypionate) 19 participants (30%) had previously received a GnRH analogue. The median time from start of GnRH analogue to start of gender-affirming hormones was 11.3 months (range 2.2 to 42.0). 11 participants continued GnRH analogues after starting gender-affirming hormones. Average duration of treatment with a GnRH analogue not reported **Comparison** No comparator	**Critical Outcomes** No critical outcomes assessed. **Important outcomes** ***Safety*** Of the 63 participants who received gender-affirming hormones: • No participants permanently discontinued gender-affirming hormones • 3 participants (5%) temporarily discontinued treatment: ○ 2 transmales due to concomitant mental health comorbidities ○ 1 transmale due to androgenic alopecia. ○ No transfemale stopped treatment. The authors report that all patients eventually restarted gender-affirming hormones, although they do not report how long treatment was	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record* 4. b) no **Domain 2: Comparability** 1. c) cohorts are not comparable on the basis of the design or analysis controlled for confounders **Domain 3: Outcome** 1. b) record linkage 2. b) no – although follow-up time is reported for patients with more than 1 clinic visit, duration of treatment with gender-affirming hormones is not reported 3. c) incomplete - missing data **Overall quality is assessed as poor**

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			stopped for, or what the effect of stopped treatment was. • No participants reported major complications • 12 participants (19%) had minor complications: ○ 7 transmales had severe acne (requiring isotretinoin) ○ 1 transmale had andogenic alopecia ○ 3 transmales had mild dyslipidaemia (levels not reported) ○ 1 transmale had significant mood swings ○ No transfemales had minor complications	Other comments: Mental health comorbidity was reported for all participants but not for the gender-affirming hormone cohort separately. Concomitant use of other medicines was not reported. Source of funding: No source of funding identified.

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Klaver, Maartje, de Mutsert, Renee, van der Loos, Maria A T C et al. (2020) Hormonal Treatment and Cardiovascular Risk Profile in Transgender Adolescents. Pediatrics 145(3) **Study location** Single centre, Amsterdam, Netherlands	Participants were included if i) they had started GnRH analogue treatment before 18 years, ii) if whole body dual-energy radiograph absorptiometry was performed at least once during treatment (4 months before or after the start of GnRH analogues or gender-affirming hormones, or	Transfemales: Oestrogen (17-β oestradiol [E2]) orally, starting with 5 mcg/kg body weight per day, which was increased every 6 months until the maintenance dose of 2 mg per day was reached. Transmales: mixed testosterone esters (Sustanon), 25 mg/m^2 body surface area every 2 weeks intramuscularly,	**Critical Outcomes** No critical outcomes assessed. **Important outcomes** ***Safety*** Safety outcomes reported separately for transfemales and transmales. **For transfemales**, from the start of gender-affirming hormone treatment to age 22 years: • Mean BMI statistically significantly increased (mean change +1.9, 95% CI 0.6 to 3.2, p<0.005; mean BMI at	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record* 4. b) no **Domain 2: Comparability** 1. c) cohorts are not comparable on the basis

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Study type Retrospective chart review **Study aim** To examine the effects of treatment on changes in cardiovascular risk factors, including BMI, blood pressure, insulin sensitivity, and lipid levels. **Study dates** 1998-2015	within 1.5 years before or after the 22nd birthday), iii) if they were likely to have had at least 1 medical consultation in young adulthood. The study included 192 young people with dysphoria who met the above inclusion criteria: 71 transfemales and 121 transmales. Gender dysphoria was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria. Mean age at the start of gender-affirming hormones was 16.4 years (SD 1.1) for transfemales and 16.9 years (SD 0.9) for transmales.	increased every 6 months to maintenance dose of 250 mg every 3 to 4 weeks. When GnRH analogues were started after the age of 16 years a different hormone starter dose was used (1 mg oestrogen daily and 75 mg testosterone weekly). Median (IQR) duration of GnRH analogue (monotherapy) was 2.1 years (1.0 to 2.7) in transfemales and 1.0 (0.5 to 2.9) for transmales.	22 years= 23.2, 95% CI 21.6 to 24.8). At age 22 years, 9.9% of the cohort were obese, compared with 3.0% in reference cisgender population[1]. • Mean systolic blood pressure (SBP) did not significantly change (mean change -3 mmHg, 95% CI -8 to 2; mean SBP at 22 years= 117 mmHg, 95% CI 113 to 122) • Mean diastolic blood pressure (DBP) statistically significantly increased (mean change +6 mmHg, 95% CI 3 to 10, p<0.001; mean DBP at 22 years= 75 mmHg, 95% CI 72 to 78) • Mean glucose level did not significantly change (mean change +0.1 mmol/L, 95% CI -0.1 to 0.2; mean glucose level at 22 years= 5.0 mmol/L, 95% CI 4.8 to 5.1) • Mean insulin level did not significantly change (mean change +2.7 mU/L, 95% CI -1.7 to 7.1; mean insulin level at 22 years= 5.0 mU/L (4.8 to 5.1) • Insulin resistance (mean Homeostatic Model Assessment of Insulin Resistance [HOMA-IR]) did not significantly change (mean change +0.7, 95% CI -0.2 to 1.5; mean HOMA-IR at 22 years 2.9, 95% CI 1.9 to 3.9) • Mean total cholesterol did not significantly change (mean change +0.1 mmol/L, 95% CI -0.2 to 0.4; mean total cholesterol at 22 years 4.1 mmol/L, 95% CI 3.8 to 4.4) • Mean HDL cholesterol did not significantly change (mean change +0.0 mmol/L, 95% CI -0.1 to 0.2; mean HDL cholesterol at 22 years 1.6 mmol/L, 95% CI 1.4 to 1.7) • Mean LDL cholesterol did not significantly change (mean change +0.0 mmol/L, 95%	of the design or analysis controlled for confounders **Domain 3: Outcome** 1. b) record linkage 2. a) yes- follow-up from start of gender-affirming hormones to age 22 years, around 5 years 3. a) complete follow up - all subjects accounted for **Overall quality is assessed as poor** Other comments: None Source of funding: No external funding

			CI -0.3 to 0.2; mean LDL cholesterol at 22 years 2.0 mmol/L, 95% CI 1.8 to 2.3) • Mean triglycerides statistically significantly increased (mean change +0.2 mmol/L, 95% CI 0.0 to 0.5, p<0.05; triglyceride level at 22 years 1.1 mmol/L, 95% CI 0.9 to 1.4) **For transmales**, from the start of gender-affirming hormone treatment to age 22 years: • Mean BMI statistically significantly increased (mean change +1.4, 95% CI 0.8 to 2.0, p<0.005; mean BMI at 22 years= 23.9, 95% CI 23.0 to 24.7). At age 22 years, 6.6% of the cohort were obese, compared with 2.2% in reference cisgender population[1]. • Mean systolic blood pressure (SBP) statistically significantly increased (mean change +5 mmHg, 95% CI 1 to 9; mean SBP at 22 years= 126 mmHg, 95% CI 122 to 130) • Mean diastolic blood pressure (DBP) statistically significantly increased (mean change +6 mmHg, 95% CI 4 to 9, p<0.001; mean DBP at 22 years= 74 mmHg, 95% CI 72 to 77) • Mean glucose level did not significantly change (mean change 0.0 mmol/L, 95% CI -0.2 to 0.2; mean glucose level at 22 years= 4.8 mmol/L, 95% CI 4.7 to 5.0) • Mean insulin level statistically significantly decreased (mean change -2.1 mU/L, 95% CI -3.9 to -0.3, p<0.05; mean insulin level at 22 years= 8.6 mU/L (6.9 to 10.2) • Insulin resistance (mean Homeostatic Model Assessment of Insulin Resistance [HOMA-IR]) statistically significantly	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			decreased (mean change -0.5, 95% CI -1.0 to -0.1, p<0.05; mean HOMA-IR at 22 years 1.8, 95% CI 1.4 to 2.2) • Mean total cholesterol statistically significantly increased (mean change +0.4 mmol/L, 95% CI 0.2 to 0.6, p<0.001; mean total cholesterol at 22 years 4.6 mmol/L, 95% CI 4.3 to 4.8) • Mean HDL cholesterol statistically significantly decreased (mean change -0.3 mmol/L, 95% CI -0.4 to -0.2, p<0.001; mean HDL cholesterol at 22 years 1.3 mmol/L, 95% CI 1.2 to 1.3) • Mean LDL cholesterol statistically significantly increased (mean change +0.4 mmol/L, 95% CI 0.2 to 0.6, p<0.001; mean LDL cholesterol at 22 years 2.6 mmol/L, 95% CI 2.4 to 2.8) • Mean triglycerides statistically significantly increased (mean change +0.5 mmol/L, 95% CI 0.3 to 0.7, p<0.001; triglyceride level at 22 years 1.3 mmol/L, 95% CI 1.1 to 1.5)	

[1] Reference population taken from Fredriks et al. (2000)

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Klink D, Caris M, Heijboer A et al. (2015) Bone mass in young adulthood following gonadotropin-releasing hormone analog treatment and cross-sex hormone treatment in adolescents with gender dysphoria. The Journal of Clinical Endocrinology and Metabolism 100(2): e270-5 **Study location** Single centre, Amsterdam, Netherlands **Study type** Retrospective longitudinal study **Study aim** To assess peak bone mass in young adults with gender dysphoria who had received GnRH analogues and gender-affirming hormones during their pubertal years. **Study dates**	34 young people with gender dysphoria who received GnRH analogues, gender-affirming hormones and gonadectomy. The study included 15 transfemales and 19 transmales; mean age at start of gender-affirming hormones was 16.6 years (SD 1.4) and 16.4 years (SD 2.3) respectively. Participants were required to meet the DSM-IV-TR criteria for gender identity disorder of adolescence. Participants were included if they had undergone gonadectomy between June 1998 and August 2012, and they were at least 21 years old when they had the surgery. Bone mineral density data were also required at the start of GnRH analogue, gender-affirming hormones and at the age of 22 years. No concomitant treatments were reported.	**Intervention** Transfemales - oral 17-β oestradiol (incremental dosing) Transmales – IM testosterone (Sustanon 250 mg/ml; incremental dosing) Median duration of treatment with gender-affirming hormones for transfemales was 5.8 years (range 3.0 to 8.0) and for transmales was 5.4 years (range 2.8 to 7.8). The GnRH analogue was SC triptorelin 3.75 mg every 4 weeks. No details of gonadectomy reported. **Comparison** No comparison group. Comparison over time reported.	**Critical outcomes** No critical outcomes reported **Important outcomes** **Safety** ***Bone density: lumbar spine*** **Lumbar spine bone mineral apparent density (BMAD)** Change from starting gender-affirming hormones to age 22 years in transfemales-Mean (SD); g/m^3 • Start of gender-affirming hormones: 0.22 (0.02) • Age 22 years: 0.23 (0.03) • p=0.003 z-score (range) • Start of gender-affirming hormones: -0.90 (0.80) • Age 22 years: -0.78 (1.03) • No statistically significant difference Change from starting gender-affirming hormones to age 22 years in transmales-Mean (SD); g/m^3 • Start of gender-affirming hormones: 0.24 (0.02) • Age 22 years: 0.25 (0.28 • p=0.001 z-score (SD) • Start of gender-affirming hormones: -0.50 (0.81) • Age 22 years: -0.033 (0.95) • p=0.002	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record* 4. b) no **Domain 2: Comparability** 1. c) cohorts are not comparable on the basis of the design or analysis controlled for confounders **Domain 3: Outcome** 1. b) record linkage 2. a) yes – mean duration of gender-affirming hormone treatment was 5.8 and 5.4 years. 3. c) follow-up rate variable across timepoints and no description of those lost **Overall quality is assessed as poor** Other comments: Within person comparison. Small numbers of participants in each subgroup. No

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Gonadectomy took place between June 1998 and August 2012	At the start of gender-affirming hormone treatment, in the transfemale subgroup the median Tanner P was 4 (IQR 2) and the median Tanner G was 12 (IQR 11). In the transmale subgroup the median Tanner B was 5 (IQR 2) and the median Tanner P was 5 (IQR 0).		**Lumbar spine bone mineral density (BMD)** Change from starting gender-affirming hormones to age 22 years in transfemales- Mean (SD); g/m^2 • Start of gender-affirming hormones: 0.84 (0.11) • Age 22 years: 0.93 (0.10) • p<0.001 z-score (range) • Start of gender-affirming hormones: -1.01 (0.98) • Age 22 years: -1.36 (0.83) • No statistically significant difference Change from starting gender-affirming hormones to age 22 years in transmales- Mean (SD); g/m^2 • Start of gender-affirming hormones: 0.91 (0.10) • Age 22 years: 0.99 (0.13) • P<0.001 z-score (range) • Start of gender-affirming hormones: -0.72 (0.99) • Age 22 years: -0.33 (1.12) • No statistically significant difference ***Bone density: femoral region, nondominant side*** **Femoral region, nondominant side BMAD** Change from starting gender-affirming hormones to age 22 years in transfemales- Mean (SD); g/m^3 • Start of gender-affirming hormones: 0.26 (0.04) • Age 22 years: 0.28 (0.05)	concomitant treatments or comorbidities were reported. Source of funding: None disclosed

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			• No statistically significant difference z-score (SD) • Start of gender-affirming hormones: -1.57 (1.74) • Age 22 years: Not reported • No statistical analysis reported Change from starting gender-affirming hormones to age 22 years in transmales-Mean (SD); g/m^3 • Start of gender-affirming hormones: 0.31 (0.04) • Age 22 years: 0.33 (0.05) • p=0.010 z-score (SD) • Start of gender-affirming hormones: -0.28 (0.74) • Age 22 years: Not reported • No statistical analysis reported **Femoral region, nondominant side BMD** Change from starting gender-affirming hormones to age 22 years in transfemales-Mean (SD); g/m^2 • Start of gender-affirming hormones: 0.87 (0.08) • Age 22 years: 0.94 (0.11) • P=0.009 z-score (SD) • Start of gender-affirming hormones: -0.95 (0.63) • Age 22 years: -0.69 (0.74) • No statistically significant difference Change from starting gender-affirming hormones to age 22 years in transmales-Mean (SD); g/m^2 • Start of gender-affirming hormones: 0.88 (0.09) • Age 22 years: 0.95 (0.10)	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			• P<0.001 z-score (SD) • Start of gender-affirming hormones: -0.35 (0.79) • Age 22 years: -0.35 (0.74) • p=0.006	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Kuper, Laura E, Stewart, Sunita, Preston, Stephanie et al. (2020) Body Dissatisfaction and Mental Health Outcomes of Youth on Gender-Affirming Hormone Therapy. Pediatrics 145(4) **Study location** Single centre, Texas, USA **Study type** Prospective longitudinal study **Study aim** To: • explore how baseline body dissatisfaction, depression, and anxiety symptoms vary by gender,	148 children and adolescents with gender dysphoria, n=148, of whom: • 25 received puberty suppression only • 93 received gender-affirming hormone therapy only • 30 received both Results for treatments reported separately. Mean age at initial assessment was 15.4 years (range 9 to 18). Mean age at start of gender-affirming hormone therapy was 16.2 years (range 13.2 to 18.6). All participants met the Diagnostic and Statistical	Hormone therapy, guided by Endocrine Society Clinical Practice Guidelines Follow-up at least 18 months from initial assessment at the clinic. Mean duration of gender-affirming hormone therapy before follow-up was 10.9 months (range 1 to 18; SD 3.3)	**Critical Outcomes** ***Impact on mental health*** Mean depression score, assessed using the Quick Inventory of Depressive Symptoms (QIDS), self-reported was 9.6 (SD 5.0) at baseline and 7.4 (SD 4.5) at follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. Mean depression score, assessed using the QIDS, clinician-reported was 5.9 (SD 4.1) at baseline and 6.0 (SD 3.8) at follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. Mean anxiety score, assessed using the Screen for Child Anxiety Related Emotional Disorders (SCARED) questionnaire was 32.6 (SD 16.3) at baseline and 28.4 (SD 15.9) at	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record 4. b) no **Domain 2: Comparability** 1. c) cohorts are not comparable on the basis of the design or analysis controlled for confounders **Domain 3: Outcome** 1. d) assessors not blinded to treatment 2. a) yes – follow-up at least 18 months from initial assessment. Mean duration of gender-affirming hormone

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
age at initial assessment, and Tanner stage at first medical visit • examine how body dissatisfaction, depression, and anxiety symptoms change over the first year of gender-affirming hormone treatment • explore how any changes vary by affirmed gender, Tanner stage, age, type of treatment, months on gender-affirming hormone therapy, mental health treatment received, and whether chest surgery was also obtained (among transmales). **Study dates** Initial participant assessments took place between August 2014 and March 2018.	Manual of Mental Disorders, Fifth Edition criteria for gender dysphoria. Specific inclusion and exclusion criteria for the study are not reported. It would appear that all children and adolescents eligible for gender-affirming hormones were considered eligible for the study. The authors state that before initial assessment with a psychologist, psychiatrist, and/or clinical therapist, parents completed a phone intake survey. Around one-third of families did not follow-up after the phone intake.		follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. Mean panic score, assessed using specific questions from the SCARED questionnaire was 8.1 (SD 6.3) at baseline and 7.1 (SD 6.5) at follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. Mean generalised anxiety score, assessed using specific questions from the SCARED questionnaire was 10.0 (SD 5.1) at baseline and 8.8 (SD 6.5) at follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. Mean social anxiety score, assessed using specific questions from the SCARED questionnaire was 8.5 (SD 4.1) at baseline and 7.7 (SD 4.2) at follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. Mean separation anxiety score, assessed using specific questions from the SCARED	treatment was 10.9 months. 3. c) patient numbers vary by outcome with no explanation **Overall quality is assessed as poor** Other comments: None Source of funding: Supported by Children's Health. The Research Electronic Data Capture database was funded by the Clinical and Translational Science Awards program

			questionnaire was 3.5 (SD 3.0) at baseline and 3.1 (SD 2.5) at follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. Mean school avoidance score, assessed using specific questions from the SCARED questionnaire was 2.6 (SD 2.1) at baseline and 2.0 (SD 2.0) at follow-up. The authors did not present statistical analysis for the sub-group of participants receiving gender-affirming hormones and it is unclear whether the change in score was statistically significant. The authors also reported results separately for transfemales and transmales: **Transfemales** No statistical analyses were reported for this sub-group and it is unclear whether any changes in score were statistically significant. • Mean depression symptoms, assessed using the QIDS, self-reported was 7.5 (SD 4.9) at baseline and 6.6 (SD 4.4) at follow-up. • Mean depression symptoms, assessed using the QIDS, clinician-reported was 4.2 (SD 3.2) at baseline and 5.4 (SD 3.4) at follow-up. • Mean anxiety symptoms, assessed using the SCARED questionnaire was 26.4 (SD 14.2) at baseline and 24.3 (SD 15.4) at follow-up.	

			• Mean panic symptoms, assessed using specific questions from the SCARED questionnaire was 5.7 (SD 4.9) at baseline and 5.1 (SD 4.9) at follow-up. • Mean generalised anxiety symptoms, assessed using specific questions from the SCARED questionnaire was 8.6 (SD 5.1) at baseline and 8.0 (SD 5.1) at follow-up. • Mean social anxiety symptoms, assessed using specific questions from the SCARED questionnaire was 7.1 (SD 3.9) at baseline and 6.8 (SD 4.4) at follow-up. • Mean separation anxiety symptoms, assessed using specific questions from the SCARED questionnaire was 3.4 (SD 3.3) at baseline and 2.7 (SD 2.3) at follow-up. • Mean school avoidance symptoms, assessed using specific questions from the SCARED questionnaire was 1.8 (SD 1.7) at baseline and 1.9 (SD 2.1) at follow-up. **Transmales** No statistical analyses were reported for this sub-group and it is unclear whether any changes in score were statistically significant. • Mean depression symptoms, assessed using the QIDS, self-reported was 10.4 (SD 5.0) at baseline and 7.5 (SD 4.5) at follow-up. • Mean depression symptoms, assessed using the QIDS, clinician-reported was 6.7 (SD 4.4) at baseline and 6.2 (SD 4.1) at follow-up. • Mean anxiety symptoms, assessed using the SCARED questionnaire was 35.4 (SD	

			16.5) at baseline and 29.8 (SD 15.5) at follow-up. • Mean panic symptoms, assessed using specific questions from the SCARED questionnaire was 9.3 (SD 6.5) at baseline and 7.9 (SD 6.5) at follow-up. • Mean generalised anxiety symptoms, assessed using specific questions from the SCARED questionnaire was 10.4 (SD 5.0) at baseline and 9.0 (SD 5.1) at follow-up. • Mean social anxiety symptoms, assessed using specific questions from the SCARED questionnaire was 8.5 (SD 4.0) at baseline and 7.8 (SD 4.1) at follow-up. • Mean separation anxiety symptoms, assessed using specific questions from the SCARED questionnaire was 4.2 (SD 3.4) at baseline and 3.4 (SD 2.6) at follow-up. • Mean school avoidance symptoms, assessed using specific questions from the SCARED questionnaire was 2.6 (SD 2.1) at baseline and 2.0 (SD 2.0) at follow-up. No difference in impact on mental health found by Tanner age. Numerical results, statistical analysis and information on specific outcomes not reported. It is unclear from the paper whether Tanner age is at initial assessment, start of GnRH analogues, start of gender-affirming hormones, or another timepoint. **Important Outcomes** ***Impact on body image***	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			Mean Body Image Scale (BIS) score was 70.7 (SD 15.2) at baseline and 51.4 (SD 18.3) at follow-up. The authors do not present statistical analysis for this population and it is unclear whether the change in score was statistically significant. The authors also reported body image results separately for transfemales and transmales. No statistical analyses were reported for this sub-groups and it is unclear whether changes in score were statistically significant. • In transfemales, BIS score was 67.5 (SD 19.5) at baseline and 49.0 (SD 21.6) at follow-up. • In transmales, BIS score was 71.1 (SD 13.4) at baseline and 52.9 (SD 16.8) at follow-up. No difference in body image score found by Tanner age. Numerical results, statistical analysis and information on specific outcomes not reported. It is unclear from the paper whether Tanner age is at initial assessment, start of GnRH analogues, start of gender-affirming hormones, or another timepoint. *No other critical or important outcomes reported*	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Study dates Lopez de Lara, D., Perez Rodriguez, O., Cuellar Flores, I. et al. (2020) Psychosocial assessment in transgender adolescents. Anales de Pediatria **Study location** Single centre in Madrid, Spain **Study type** Prospective analytical study **Study aim** To assess the psychosocial status of patients seeking care in the paediatric endocrinology clinic for gender dysphoria, and the impact on psychosocial status of gender-affirming hormone therapy at 12 months of treatment **Study dates** Not reported	23 adolescents with gender dysphoria; 16 transmale and 7 transfemale. Participants were required to be at a stage of pubertal development of Tanner 2 or higher. People with mental health comorbidity that could affect the experience of gender dysphoria were excluded. Mean age at baseline was 16 years (range 14 to 18). 30 cisgender controls, matched for age, ethnicity, and socioeconomic status	Gender-affirming hormones- • Oral oestradiol • Intramuscular testosterone Participants had previously received gonadotropin-releasing hormone (GnRH) analogues in the intermediate pubertal stages (Tanner 2---3).	**Critical Outcomes** ***Impact on gender dysphoria*** Following gender-affirming hormones for 12 months, mean (±SD) Utrecht Gender Dysphoria Scale (UGDS) score statistically significantly improved, from 57.1 (±4.1) at baseline to 14.7 (±3.2; p<0.001) ***Impact on mental health*** Mean depression score statistically significantly improved following treatment with gender-affirming hormones. Mean Beck Depression Inventory II (BDI-II) score (±SD) reduced from 19.3 points (±5.5) at baseline to 9.7 points (±3.9) at 12 months (p<0.001). Mean anxiety scores statistically significantly improved following treatment with gender-affirming hormones. Mean (±SD) State-Trait Anxiety Inventory (STAI) State subscale score improved from 33.3 points (±9.1) at baseline to 16.8 points (±8.1) at 12 months (p<0.001). Mean (±SD) State-Trait Anxiety Inventory (STAI) Trait subscale score improved from 33.0 points (±7.2) at baseline to 18.5 points (±8.4) at 12 months (p<0.001). **Important Outcomes** ***Psychosocial Impact*** There was not change in family functioning, measured using the Family APGAR test, from baseline (17.9 points) to 1 year after starting	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. Not applicable – although a control group is reported on, people in this group did not have gender dysphoria. 3. a) secure record* 4. b) no **Domain 2: Comparability** 1. Not applicable – although a control group is reported on, people in this group did not have gender dysphoria. **Domain 3: Outcome** 1. d) assessors not blinded to treatment 2. a) yes – 12 months treatment with gender-affirming hormones 3. a) complete follow up - all subjects accounted for **Overall quality is assessed as poor**

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			gender-affirming hormones (18.0 points; no statistical analysis reported). Results from the Strengths and Difficulties Questionnaire, Spanish Version (SDQ-Cas) showed statistically significant improvements from baseline (14.7 points; SD±3.3) to 12 months after gender-affirming hormones (10.3 points; SD±2.9; p<0.001) *No other critical or important outcomes reported*	Other comments: None Source of funding: Not reported

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Stoffers, Iris E; de Vries, Martine C; Hannema, Sabine E (2019) Physical changes, laboratory parameters, and bone mineral density during testosterone treatment in adolescents with gender dysphoria. The journal of sexual medicine 16(9): 1459-1468 **Study location** Single centre, Leiden, Netherlands **Study type** Retrospective chart review **Study aim** To report changes in height, BMI, blood pressure, laboratory parameters and bone density. **Study dates** November 2010 to August 2018	62 transmales with gender dysphoria. participants were required to have been receiving testosterone therapy for at least 6 months. Further inclusion or exclusion criteria not reported. Gender dysphoria was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria. .	Testosterone intramuscular injection (Sustanon 250 mg). Dose escalated every 6 months up to the standard adult dose of 125 mg every 2 weeks or 250 mg every 3-4 weeks. A more rapid dose escalation was using in patients who started GnRH analogue treatment at 16 years or older. Median age at start of testosterone treatment was 17.2 years (range 14.9 to 18.4) Median duration of testosterone treatment was 12 months (range 5 to 33) Median duration of GnRH analogue treatment was 8 months (range 3 to 39)	**Critical Outcomes** No critical outcomes assessed. **Important outcomes** ***Safety*** ***Bone mineral density (BMD): lumbar spine*** There was no statistically significant difference in lumber spine bone mineral density (BMD) from start of testosterone treatment to any timepoint, up to 24 months follow-up. Mean (±SD), g/cm^2: • Start of testosterone: 0.90 (±0.11) • 6 months: 0.94 (±0.10) • 12 months: 0.95 (±0.09) • 24 months: 0.95 (±0.11) z-score (±SD): • Start of testosterone: -0.81 (±1.02) • 6 months: -0.67 (±0.95) • 12 months: -0.66 (±0.81) • 24 months: -0.74 (±1.17) ***Bone mineral density (BMD): femoral neck (hip)*** There was no statistically significant difference in right or left femoral neck (hip) bone mineral density (BMD) from start of	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record* 4. b) no **Domain 2: Comparability** 1. c) cohorts are not comparable on the basis of the design or analysis controlled for confounders **Domain 3: Outcome** 1. b) record linkage 2. a) yes – mean duration of gender-affirming hormone treatment was 5.8 and 5.4 years. 3. a) complete follow up - all subjects accounted for **Overall quality is assessed as poor** Other comments: None Source of funding: None

			testosterone treatment to any timepoint, up to 24 months follow-up. **Right** Mean (±SD), g/cm^2: • Start of testosterone: 0.77 (±0.08) • 6 months: 0.84 (±0.11) • 12 months: 0.82 (±0.08) • 24 months: 0.85 (±0.11) z-score (±SD): • Start of testosterone: -0.97 (0.79) • 6 months: -0.54 (±0.96) • 12 months: -0.80 (±0.69) • 24 months: -0.31 (±0.84) **Left** Mean (±SD), g/cm^2: • Start of testosterone: 0.76 (±0.09) • 6 months: 0.83 (±0.12) • 12 months: 0.81 (±0.08) • 24 months: 0.86 (±0.09) z-score (±SD): • Start of testosterone: -1.07 (0.85) • 6 months: -0.62 (±1.12) • 12 months: -0.93 (±0.63) • 24 months: -0.20 (±0.70) ***Other safety-related outcomes*** • Alkaline phosphatase: statistically significant increases observed from start of testosterone treatment to 6 months and 12 months ($p<0.001$), although difference at 24 months was not statistically significant. Median (IQR), U/L ○ Start of testosterone: 102 (78 to 136) ○ 6 months: 115 (102 to 147) ○ 12 months: 112 (88 to 143) ○ 24 months: 81 (range 69 to 98) • Creatinine: statistically significant increases observed from start of	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			testosterone treatment to 6, 12 and 24 months (p<0.001). Mean (±SD), umol/L ○ Start of testosterone: 62 (±7) ○ 6 months: 70 (±9) ○ 12 months: 74 (±10) ○ 24 months: 81 (±10) There was no statistically significant change from start of testosterone treatment in: • HbA1c • Aspartate aminotransferase (AST) • Alanine aminotransferase (ALT) • Gamma-glutamyl transferase • Urea Numerical results, follow-up duration and further details of statistical analysis not reported.	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
Full citation Vlot MC, Klink DT, den Heijer M et al. (2017) Effect of pubertal suppression and cross-sex hormone therapy on bone turnover markers and bone mineral apparent density (BMAD) in transgender adolescents. Bone 95: 11-19 **Study location** Single centre, Amsterdam, Netherlands **Study type** Retrospective chart review **Study aim** To investigate the impact of GnRH analogues and gender-affirming hormones on bone mineral apparent density (BMAD) in transgender adolescents. The study also report on levels of bone turnover markers, although the authors concluded that the	70 adolescents with gender dysphoria (42 transmales and 28 transfemales). Median age (range) at the start of gender-affirming hormones was 16.3 years (15.9 to 19.5) for transmales and 16.0 years (14.0 to 18.9) for transfemales. Participants were included if they had a diagnosis of gender dysphoria according to DSM-IV-TR criteria who received GnRH analogues and then gender-affirming hormones. No concomitant treatments were reported. The study categorised participants into a young and old pubertal group, based on their bone age. The young transmales had a bone age of <14 years and the old transmales had a bone age of ≥14 years. The young transfemales	Transfemales: Oestradiol oral Dose escalated every 6 months until standard adult dose of 2 mg daily was reached Transmales: Testosterone intramuscular injection (Sustanon 250 mg). Dose escalated every 6 months up to the standard adult dose of 250 mg every 4 weeks or 250 mg every 3-4 weeks. All participants previously received a GnRH analogue (triptorelin 3.75 mg subcutaneously every 4 weeks) Median duration of GnRH analogue therapy not reported.	**Critical outcomes** No critical outcomes reported **Important outcomes** ***Bone density: lumbar spine*** **Lumbar spine bone mineral apparent density (BMAD)** Transfemales (bone age <15 years), change from starting gender-affirming hormones to 24 months follow-up. Median (range), g/m^3 • Start of gender-affirming hormones (C0): 0.20 (0.18 to 0.24) • 24-month follow-up (C24): 0.22 (0.19 to 0.27) • Statistically significant increase (p≤0.01) z-score (range) • Start of gender-affirming hormones (C0): -1.52 (-2.36 to 0.42) • 24-month follow-up (C24): • Statistically significant increase (p≤0.05) Transfemales (bone age ≥15 years), change from starting gender-affirming hormones to 24 months follow-up. Median (range), g/m^3 • Start of gender-affirming hormones: 0.22 (0.19 to 0.24) • 24-months: 0.23 (0.21 to 0.26) • Statistically significant increase (p≤0.05) z-score (range) • Start of gender-affirming hormones: -1.15 (-2.21 to 0.08) • 24-months: -0.66 (-1.66 to 0.54)	This study was appraised using the Newcastle-Ottawa tool for cohort studies. **Domain 1: Selection domain** 1. b) somewhat representative 2. c) no-non exposed cohort 3. a) secure record* 4. b) no **Domain 2: Comparability** 1. c) cohorts are not comparable on the basis of the design or analysis controlled for confounders **Domain 3: Outcome** 1. b) record linkage 2. a) yes- 24 month follow-up 3. a) complete follow up - all subjects accounted for **Overall quality is assessed as poor.** Other comments: None Source of funding: grant from Abbott diagnostics

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
added value of these seems to be limited. **Study dates** Participants started gender-affirming therapy between 2001 and 2011	group had a bone age of <15 years and the old transfemales group ≥15 years.		Statistically significant increase (p≤0.05) Transmales (bone age <14 years), change from starting gender-affirming hormones to 24 months follow-up. Median (range), g/m^3 • Start of gender-affirming hormones: 0.23 (0.19 to 0.28) • 24-months: 0.25 (0.22 to 0.28) • Statistically significant increase (p≤0.01) z-score (range) • Start of gender-affirming hormones: -0.84 (-2.2 to 0.87) • 24-months: -0.15 (-1.38 to 0.94) Statistically significant increase (p≤0.01) Transmales (bone age ≥14 years), change from starting gender-affirming hormones to 24 months follow-up. Median (range), g/m^3 • Start of gender-affirming hormones: 0.24 (0.20 to 0.28) • 24-months: 0.25 (0.21 to 0.30) • Statistically significant increase (p≤0.01) z-score (range) • Start of gender-affirming hormones: -0.29 (-2.28 to 0.90) • 24-months: -0.06 (-1.75 to 1.61) Statistically significant increase (p≤0.01) ***Bone density: femoral neck*** **Femoral neck BMAD** Transfemales (bone age <15 years), change from starting gender-affirming hormones to 24 months follow-up.	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			Median (range), g/m^3 • Start of gender-affirming hormones: 0.27 (0.20 to 0.33) • 24-months: 0.27 (0.20 to 0.36) • No statistically significant change z-score (range) • Start of gender-affirming hormones: -1.32 (-3.39 to 0.21) • 24-months: -1.30 (-3.51 to 0.92) • No statistically significant change Transfemales (bone age ≥15 years), change from starting gender-affirming hormones to 24 months follow-up. Median (range), g/m^3 • Start of gender-affirming hormones: 0.30 (0.26 to 0.34) • 24-months: 0.29 (0.24 to 0.38) • No statistically significant change z-score (range) • Start of gender-affirming hormones: -0.36 (-1.50 to 0.46) • 24-months: -0.56 (-2.17 to 1.29) • No statistically significant change Transmales (bone age <14 years), change from starting gender-affirming hormones to 24 months follow-up. Median (range), g/m^3 • Start of gender-affirming hormones: 0.30 (0.22 to 0.35) • 24-months: 0.33 (0.23 to 0.37) • Statistically significant increase (p≤0.01) z-score (range) • Start of gender-affirming hormones: -0.37 (-2.28 to 0.47) • 24-months: -0.37 (-2.03 to 0.85)	

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
			• Statistically significant increase (p≤0.01) Transmales (bone age ≥14 years), change from starting gender-affirming hormones to 24 months follow-up. • Start of gender-affirming hormones: 0.30 (0.23 to 0.41) • 24-months: 0.32 (0.23 to 0.41) • Statistically significant increase (p≤0.01) z-score (range) • Start of gender-affirming hormones: -0.27 ((-1.91 to 1.29) • 24-months: 0.02 (-2.1 to 1.35) • Statistically significant increase (p≤0.05)	

Appendix F Quality appraisal checklists

Newcastle-Ottawa Quality Assessment Form for Cohort Studies

Note: A study can be given a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Selection

1) Representativeness of the exposed cohort
    a) Truly representative (one star)
    b) Somewhat representative (one star)
    c) Selected group
    d) No description of the derivation of the cohort
2) Selection of the non-exposed cohort
    a) Drawn from the same community as the exposed cohort (one star)
    b) Drawn from a different source
    c) No description of the derivation of the non exposed cohort
3) Ascertainment of exposure
    a) Secure record (e.g., surgical record) (one star)
    b) Structured interview (one star)
    c) Written self report
    d) No description
    e) Other
4) Demonstration that outcome of interest was not present at start of study
    a) Yes (one star)
    b) No

Comparability

1) Comparability of cohorts on the basis of the design or analysis controlled for confounders
    a) The study controls for age, sex and marital status (one star)
    b) Study controls for other factors (list) _____ (one star)
    c) Cohorts are not comparable on the basis of the design or analysis controlled for confounders

Outcome

1) Assessment of outcome
    a) Independent blind assessment (one star)
    b) Record linkage (one star)
    c) Self report
    d) No description
    e) Other
2) Was follow-up long enough for outcomes to occur
    a) Yes (one star)
    b) No
    Indicate the median duration of follow-up and a brief rationale for the assessment above:_____
3) Adequacy of follow-up of cohorts
    a) Complete follow up- all subject accounted for (one star)

b) Subjects lost to follow up unlikely to introduce bias- number lost less than or equal to 20% or description of those lost suggested no different from those followed. (one star)
c) Follow up rate less than 80% and no description of those lost
d) No statement

Thresholds for converting the Newcastle-Ottawa scales to AHRQ standards (good, fair, and poor):

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Appendix G Grade profiles

Table 2: Question 1: For children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? - Gender dysphoria

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
Impact on gender dysphoria (1 uncontrolled, prospective observational study)									
Change from baseline in mean gender dysphoria score, measured using the UGDS (duration of treatment 12 months). Higher scores indicate greater gender dysphoria.									
1 cohort study Lopez de Lara et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=23	None	T0 (baseline) = 57.1 (SD 4.1) T1 (12 months) = 14.7 (SD 3.2) Statistically significant improvement, p<0.001	Critical	VERY LOW

Abbreviations: p: p-value; SD: standard deviation; UGDS: Utrecht Gender Dysphoria Scale

1 Downgraded 1 level - the cohort study by Lopez de Lara et al. 2020 was assessed at high risk of bias (poor quality overall; lack of blinding and no control group)

Table 3: Question 1: For children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – Mental health

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
Impact on mental health (3 uncontrolled, prospective observational studies and 2 uncontrolled, retrospective observational studies)									
Change from baseline in mean depression score, measured using the BDI-II (duration of treatment 12 months). Higher scores indicate more severe depression.									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
1 cohort study Lopez de Lara et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=23	None	T0 (baseline) = 19.3 (SD 5.5) T1 (12 months) = 9.7 (SD 3.9) Statistically significant improvement, p<0.001	Critical	VERY LOW
Change from baseline in mean depression score, measured using the CESD-R (approximately 12-month follow-up). Higher scores indicate more severe depression.									
1 cohort study Achille et al. 2020	Serious limitations[2]	Serious indirectness[3]	No serious inconsistency	Not calculable	N=50	None	Wave 1 (baseline) = 21.4 Wave 3 (approx. 12 months) = 13.9 Statistically significant improvement (p<0.001)	Critical	VERY LOW
Change from baseline in depression score, measured using the Patient Health Questionnaire Modified for Teens (PHQ 9_Modified for Teens) (approximately 12-month follow-up). Higher scores indicate more severe depression.									
1 cohort study Achille et al. 2020	Serious limitations[2]	Serious indirectness[3]	No serious inconsistency	Not calculable	N=50	None	Statistically significant reductions in mean score, p<0.001 Results presented diagrammatically, numerical results for mean score not reported	Critical	VERY LOW
Change from baseline in depression symptoms, measured using the Quick Inventory of Depressive Symptoms (QIDS), self-reported (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe depression.									
1 cohort study Kuper et al. 2020	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=105	None	Baseline = 9.6 (SD 5.0) Follow-up = 7.4 (SD 4.5) No statistical analysis reported for the sub-group of participants receiving gender-affirming hormones	Critical	VERY LOW
Change from baseline in depression symptoms, measured using the Quick Inventory of Depressive Symptoms (QIDS), clinician-reported (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe depression.									
1 cohort study	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=106	None	Baseline = 5.9 (SD 4.1) Follow-up = 6.0 (SD 3.8)	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
Kuper et al. 2020							No statistical analysis reported for the sub-group of participants who received gender-affirming hormones		
Need for treatment due to depression, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 54% (28/52) During real life phase 15% (8/52) Statistically significant reduction (p<0.001)	Critical	VERY LOW
Change from baseline in anxiety score, measured using the STAI-State subscale (duration of treatment 12 months). Higher scores indicate more severe anxiety.									
1 cohort study Lopez de Lara et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=23	None	T0 (baseline) = 33.3 (SD 9.1) T1 (12 months) = 16.8 (SD 8.1) Statistically significant improvement, p<0.001	Critical	VERY LOW
Change from baseline in anxiety score, measured using the STAI-Trait subscale (duration of treatment 12 months). Higher scores indicate more severe anxiety.									
1 cohort study Lopez de Lara et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=23	None	T0 (baseline) = 33.0 (SD 7.2) T1 (12 months) = 18.5 (SD 8.4) Statistically significant improvement, p<0.001	Critical	VERY LOW
Change from baseline in anxiety symptoms, measured using the SCARED questionnaire (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe anxiety.									
1 cohort study Kuper et al. 2020	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=80	None	Baseline = 32.6 (SD 16.3) Follow-up = 28.4 (SD 15.9) No statistical analysis reported for the sub-group of participants	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
							who received gender-affirming hormones		
Change from baseline in panic symptoms, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=82	None	Baseline = 8.1 (SD 6.3) Follow-up = 7.1 (SD 6.5) No statistical analysis reported for the sub-group of participants who received gender-affirming hormones	Critical	VERY LOW
Change from baseline in generalised anxiety symptoms, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=82	None	Baseline = 10.0 (SD 5.1) Follow-up = 8.8 (SD 5.0) No statistical analysis reported for the sub-group of participants who received gender-affirming hormones	Critical	VERY LOW
Change from baseline in social anxiety symptoms, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=82	None	Baseline = 8.5 (SD 4.1) Follow-up = 7.7 (SD 4.2) No statistical analysis reported for the sub-group of participants who received gender-affirming hormones	Critical	VERY LOW
Change from baseline in separation anxiety symptoms, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=81	None	Baseline = 3.5 (SD 3.0) Follow-up = 3.1 (SD 2.5) No statistical analysis reported for the sub-group of participants	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
							who received gender-affirming hormones		
Change from baseline in school avoidance, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=80	None	Baseline = 2.6 (SD 2.1) Follow-up = 2.0 (SD 2.0) No statistical analysis reported for the sub-group of participants who received gender-affirming hormones	Critical	VERY LOW
Need for treatment due to anxiety, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 48% (25/52) During real life phase 15% (8/52) Statistically significant reduction (p<0.001)	Critical	VERY LOW
Change from baseline in adjusted mean suicidality score, measured using the ASQ instrument (mean treatment duration 349 days). Higher scores indicate a greater degree of suicidality.									
1 cohort study Allen et al. 2019	Serious limitations[5]	No serious indirectness	No serious inconsistency	Not calculable	N=39	None	T0 (baseline) = 1.11 (SE 0.22) T1 (final assessment) = 0.27 (SE 0.12) Statistically significant improvement in score from T0 to T1, p<0.001	Critical	VERY LOW
Change from baseline in percentage of participants with suicidal ideation, measured using the additional questions from the PHQ 9_Modified for Teens (approximately 12-month follow-up)									
1 cohort study Achille et al. 2020	Serious limitations[2]	Serious indirectness[3]	No serious inconsistency	Not calculable	N=50	None	Wave 1 (baseline) = 10% (5/50) Wave 3 (approx. 12 months) = 6% (3/50)	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
							No statistical analysis reported		
Change from baseline in suicidal ideation (passive), information on which was collected by clinician, exact methods / tools not reported (mean duration of gender-affirming hormone treatment was 10.9 months)									
1 cohort study Kuper et al. 2020	Serious limitations[4]	Serious indirectness [6]	No serious inconsistency	Not calculable	N=130	None	Lifetime = 81% (105 people) 1 month before initial assessment = 25% (33 people) Follow-up period = 38% (51 people) No statistical analysis reported	Critical	VERY LOW
Change from baseline in suicide attempts, information on which was collected by clinician, exact methods / tools not reported (mean duration of gender-affirming hormone treatment was 10.9 months)									
1 cohort study Kuper et al. 2020	Serious limitations[4]	Serious indirectness[6]	No serious inconsistency	Not calculable	N=130	None	Lifetime = 15% (20 people) 3 months before initial assessment = 2% (3 people) Follow-up period = 5% (6 people) No statistical analysis reported	Critical	VERY LOW
Change from baseline in non-suicidal self-injury, information on which was collected by clinician, exact methods / tools not reported (mean duration of gender-affirming hormone treatment was 10.9 months)									
1 cohort study Kuper et al. 2020	Serious limitations[4]	Serious indirectness[6]	No serious inconsistency	Not calculable	N=130	None	Lifetime = 52% (68 people) 3 months before initial assessment = 10% (13 people) Follow-up period = 17% (23 people) No statistical analysis reported	Critical	VERY LOW
Need for treatment due to suicidality / self-harm, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 35% (18/52) During real life phase	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
							4% (2/52) Statistically significant reduction (p<0.001)		
Need for mental health treatment, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 50% (26/52) During real life phase 46% (24/51) No statistically significant difference (p= 0.77)	Critical	VERY LOW
Need for treatment due to conduct problems / antisocial, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 14% (7/52) During real life phase 6% (3/52) No statistically significant difference (p= 0.18)	Critical	VERY LOW
Need for treatment due to psychotic symptoms or psychosis, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 2% (1/52) During real life phase 4% (2/52) No statistically significant difference (p= 0.56)	Critical	VERY LOW
Need for treatment due to substance abuse, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 4% (2/52) During real life phase 2% (1/52) No statistically significant difference (p= 0.56)	Critical	VERY LOW
Need for treatment due to autism, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 12% (6/52) During real life phase 6% (3/52) No statistically significant difference (p= 0.30)	Critical	VERY LOW
Need for treatment due to ADHD, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 10% (5/52) During real life phase 2% (1/52) No statistically significant difference (p= 0.09)	Critical	VERY LOW
Need for treatment due to eating disorder, during and before gender identity assessment, and during real life phase (approximately 12 months follow-up)									
1 cohort study Kaltiala et al. 2020	Serious limitations[7]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During and before gender identity assessment 2% (1/52)	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
							During real life phase 2% (1/52) No statistically significant difference (p=1.0)		

Abbreviations: ADHD: attention deficit hyperactivity disorder; ASQ: Ask Suicide-Screening Questions; CESD-R: Center for Epidemiologic Studies Depression Scale; BDI-II: Beck Depression Inventory II (BDI-II); p: p-value; PHQ 9_Modified for Teens: Patient Health Questionnaire Modified for Teens; SCARED: Screen for Child Anxiety Related Emotional Disorders; SD: standard deviation; STAI: State-Trait Anxiety Inventory

1 Downgraded 1 level - the cohort study by Lopez de Lara et al. (2020) was assessed at high risk of bias (poor quality; lack of blinding and no control group).
2 Downgraded 1 level - the cohort study by Achille et al (2020) was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).
3 Serious indirectness in Achille 2020- Outcome reported for full study cohort, of whom 30% were taking no treatment or puberty suppression alone at follow-up. Results for people taking gender-affirming hormones not reported separately.[4] Downgraded 1 level - the cohort study by Kuper et al. (2020) was assessed at high risk of bias (poor quality).
5 Downgraded 1 level - the cohort study by Allen et al. (2019) was assessed at high risk of bias (poor quality; lack of blinding and no control group).
6 Serious indirectness in Kuper et al. 2020- Outcome reported for full study cohort, of whom approximately 17% received puberty suppression alone and did not receive gender-affirming hormones
7 Downgraded 1 level - the cohort study by Kaltiala et al. (2020) was assessed at high risk of bias (poor quality; lack of blinding and no control group).

Table 4: Question 1: For children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – Quality of life

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
Impact on quality of life (1 uncontrolled, prospective observational study and 1 uncontrolled, retrospective observational study)									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
Change from baseline in mean quality of life score, measured using the QLES-Q-SF) (approximately 12-month follow-up). Higher scores indicated better quality of life.									
1 cohort study Achille et al. 2020	Serious limitations[1]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=50	None	Numerical improvements in mean score reported from wave 1 (baseline) to wave 3 (approx. 12 months), but difference not statistically significant (p = 0.085) Results presented diagrammatically, numerical results for mean score not reported	Critical	VERY LOW
Change from baseline in adjusted mean well-being score, measured using the GWBS of the Pediatric Quality of Life Inventory (mean treatment duration 349 days). Higher scores indicated better well-being.									
1 cohort study Allen et al. 2019	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=39	None	T0 (baseline) = 61.70 (SE 2.43) T1 (final assessment) = 70.23 (SE 2.15) Statistically significant improvement in well-being score, p<0.002	Critical	VERY LOW

Abbreviations: GWBS: General Well-Being Scale; p: p-value; QLES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire; SE: standard error

1 Downgraded 1 level - the cohort study by Achille et al (2020) was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).
2 Serious indirectness in Achille et al. 2020 - Outcome reported for full study cohort, of whom 30% were taking no treatment or puberty suppression alone at follow-up. Results for people taking gender-affirming hormones not reported separately.
3 Downgraded 1 level - the cohort study by Allen et al. (2019) was assessed at high risk of bias (poor quality; lack of blinding and no control group).

Table 5: Question 1: For children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – Body image

QUALITY	Summary of findings	IMPORTANCE	CERTAINTY

					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
Impact on body image *(1 uncontrolled, prospective observational study)*									
Change from baseline in mean body image, measured using the BIS (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores represent a higher degree of body dissatisfaction.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=86	None	Baseline = 70.7 (SD 15.2) Follow-up = 51.4 (SD 18.3) No statistical analysis reported for the sub-group of participants who received gender-affirming hormones	Important	VERY LOW

Abbreviations: BIS: Body Image Scale; p: p-value; SD: standard deviation

1 Downgraded 1 level - the cohort study by Kuper et al. (2020) was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).

Table 6: Question 1: For children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – Psychological impact

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Psychosocial Impact (1 uncontrolled, prospective observational study and 1 uncontrolled, retrospective observational study)									
Change from baseline in family functioning, measured using the Family APGAR test. Higher scores suggest more family dysfunction.									
1 cohort study Lopez de Lara et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=23	None	T0 (baseline) = 17.9 T1 (12 months) = 18.0 No statistical analysis reported	Important	VERY LOW
Change from baseline in mean patient strengths and difficulties score, measured using the SDQ, Spanish Version (total difficulties score) (duration of treatment 12 months). Higher scores suggest the presence of a behavioural disorder.									
1 cohort study	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=23	None	T0 (baseline) = 14.7 (SD 3.3) T1 (12 months) = 10.3 (SD 2.9)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Lopez de Lara et al. 2020							Statistically significant improvement p<0.001		
Functioning in adolescent development: Living with parent(s)/ guardians[2] (outcome reported for the approximately 12-month period after starting gender-affirming hormones; referred to as the 'real-life phase' in Finland). Not living with parent(s) or guardian in your early 20s is a marker of age-appropriate functioning in Finnish culture.									
1 cohort study Kaltiala et al. 2020	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During gender identity assessment = 73% (38/52) During real life phase = 40% (21/50) Statistically significant reduction (p=0.001)	Important	VERY LOW
Functioning in adolescent development: Normative peer contacts[4] (outcome reported for the approximately 12-month period after starting gender-affirming hormones; referred to as the 'real-life phase' in Finland)									
1 cohort study Kaltiala et al. 2020	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During gender identity assessment = 89% (46/52) During real life phase = 81% (42/52) Statistically significant reduction (p<0.001)	Important	VERY LOW
Functioning in adolescent development: Progresses normatively in school/ work[5] (outcome reported for the approximately 12-month period after starting gender-affirming hormones; referred to as the 'real-life phase' in Finland)									
1 cohort study Kaltiala et al. 2020	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During gender identity assessment = 64% (33/52) During real life phase = 60% (31/52) No statistically significant difference (p=0.69)	Important	VERY LOW
Functioning in adolescent development: Has been dating or had steady relationships[6] (outcome reported for the approximately 12-month period after starting gender-affirming hormones; referred to as the 'real-life phase' in Finland)									
1 cohort study	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During gender identity assessment = 62% (32/50)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Kaltiala et al. 2020							During real life phase = 58% (30/52) No statistically significant difference (p=0.51)		
Functioning in adolescent development: Is age-appropriately able to deal with matters outside of the home[7] (outcome reported for the approximately 12-month period after starting gender-affirming hormones; referred to as the 'real-life phase' in Finland)									
1 cohort study Kaltiala et al. 2020	Serious limitations[2]	No serious indirectness	No serious inconsistency	Not calculable	N=52	None	During gender identity assessment = 81% (42/52) During real life phase = 81% (42/52) No statistically significant difference (p=1.00)	Important	VERY LOW

Abbreviations: APGAR: Adaptability, Partnership, Growth, Affection and Resolve; p: p-value; SD: standard deviation; SDQ: Strengths and Difficulties Questionnaire

1 Downgraded 1 level - the cohort study by Lopez de Lara et al. (2020) was assessed at high risk of bias (poor quality; lack of blinding and no control group).
2 Living arrangements were classified as (1) living with at least one parent/guardian, (2) living in a boarding school, with an adult relative, in some form of supported accommodation or the like, where supervision and guidance by a responsible adult is provided, (3) independently alone or in a shared household with a peer, (4) with a romantic partner. In the analyses dichotomised living arrangements as (a) parent(s)/guardian(s) vs. in other arrangements.
3 Downgraded 1 level - the cohort study by Kaltiala et al. (2020) was assessed at high risk of bias (poor quality; lack of blinding and no control group).
4 Peer relationships were classified as: (1) socialises with friends in leisure time, outside of activities supervised by adults, (2) socialises with peers only at school or in the context of rehabilitative activity, (3) spends time close to peers, for example in school or rehabilitative activity, but does not connect with them, (4) does not meet peers at all. In the analyses, peer relationships during (a) gender identity assessment and (b) the real-life phase were dichotomized to age-appropriate (normative) (1) vs. restricted or lacking (2–4).
5 School/work participation was classified as (1) age appropriate participation in mainstream curriculum, progresses without difficulties, (2) participates in mainstream curriculum with difficulty, (3) participates in rehabilitative educational or work activity, (4) not involved in education and working life. Age-appropriate participation during (1) was recorded if the adolescent attended mainstream secondary education or upper secondary education at a regular rate (a class per year in comprehensive school; has not changed more than once between tracks in upper secondary education) or had proceeded to work life after completing vocational education. Participation with difficulty (2) was recorded if the adolescent was enrolled in mainstream education but had to repeat a class, studied with special arrangements (for example, in a special small group), or followed some form of adjusted curriculum. In the analyses, school/work life during (a) gender identity assessment and (b) real-life phase was dichotomised to normative (1) vs. any other (2, 3 or 4).
6 Romantic involvement was recorded (1) has or has had a dating or steady relationship, not only online, (2) has had a romantic relationship only online, (3) has not had dating or steady relationships. In the analyses we compared has or has had (1) vs. has not had (2,3) a dating or steady relationship during (a) gender identity assessment and (b) real-life phase. Sexual history was recorded in more detail in case histories during gender identity assessment, and for this period we also collected the experiences of (French) kissing (yes/no), intercourse (yes/no) and experience of any genitally intimate contact with a partner (petting under clothes or naked, intercourse, oral sex) (yes/no).

7 In recording age-appropriate competence in managing everyday matters it was expected that early adolescents (up to 14 years) would be able, for example, to do shopping and travel alone on local public transport, and to help with household duties assigned by their parents. Middle adolescents (15–17 years) were further assumed, for example, to be able make telephone calls in matters important to them (for example, when seeking a summer job), to deal with school-related issues with school personnel without parental participation, to select and start new hobbies independently and to fulfil their role in summer jobs and in similar responsibilities of young people. Late adolescents (18 years and over), legally adults, were expected to have, in addition to the above, competence to talk to authorities such as professionals in health and social services, employment or educational institutions, to deal with banks or health insurance, to manage their financial issues and to manage their housekeeping if they chose to move to live independently of parents/guardians. Competence in managing everyday matters was recorded as follows: (1) the adolescent is able to cope age appropriately outside home, (2) the adolescent needs support in age-appropriate matters outside home but functions age-appropriately in the home (manages her/his own hygiene, clothing and nutrition, participates in (younger subjects) or takes responsibility for (older subjects) housekeeping) and (3) the adolescent's functioning is inadequate both at home and outside home. For the analyses, participants were determined to be able to age-appropriately able cope with matters outside of the home (1) vs. not (2,3).

Table 7: Question 2: For children and adolescents with gender dysphoria, what is the short-term and long-term safety of gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – Bone density

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Lumbar spine bone mineral apparent density (BMAD) (2 uncontrolled, retrospective observational studies)									
Change from start of gender-affirming hormones to age 22 years in lumber spine BMAD in transfemales									
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=13 (Mean) N=14 (z-score)	None	Mean (SD), g/m^3 Start of gender-affirming hormones: 0.22 (0.02) Age 22 years: 0.23 (0.03) P=0.003 z-score (SD) Start of gender-affirming hormones: -0.90 (0.80) Age 22 years: -0.78 (1.03) No statistically significant difference	Important	VERY LOW
Change from baseline in lumbar spine BMAD in transfemales with a bone age less than 15 years ('young'; 24 months follow-up)									
1 cohort study Vlot et al. 2017	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=15	None	Median (range), g/m^3 Start of gender-affirming hormones (C0): 0.20 (0.18 to 0.24)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
							24-month follow-up (C24): 0.22 (0.19 to 0.27) Statistically significant increase (p≤0.01) z-score (range) Start of gender-affirming hormones (C0): -1.52 (-2.36 to 0.42) 24-month follow-up (C24): -1.10 (-2.44 to 0.69) Statistically significant increase (p≤0.05)		
Change from baseline in lumbar spine BMAD in transfemales with a bone age of 15 years or more ('old'; 24 months follow-up)									
1 cohort study Vlot et al. 2017	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=5	None	Median (range), g/m^3 Start of gender-affirming hormones (C0): 0.22 (0.19 to 0.24) 24-month follow-up (C24): 0.23 (0.21 to 0.26) Statistically significant increase (p≤0.05) z-score (range) Start of gender-affirming hormones (C0): -1.15 (-2.21 to 0.08) 24-month follow-up (C24): -0.66 (-1.66 to 0.54) Statistically significant increase (p≤0.05)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in lumber spine BMAD in transmales									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=19 (Mean and z-score)	None	Mean (SD), g/m^3 Start of gender-affirming hormones: 0.24 (0.02) Age 22 years: 0.25 (0.28) P=0.001 z-score Start of gender-affirming hormones: -0.50 (0.81) Age 22 years: -0.033 (0.95) P=0.002	Important	VERY LOW
Change from baseline in lumbar spine BMAD in transmales with a bone age of less than 14 years ('young'; 24 months follow-up)									
1 cohort study Vlot et al. 2017	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=11	None	Median (range), g/m^3 Start of gender-affirming hormones (C0): 0.23 (0.19 to 0.28) 24-month follow-up (C24): 0.25 (0.22 to 0.28) Statistically significant increase (p≤0.01) z-score (range) Start of gender-affirming hormones (C0): -0.84 (-2.2 to 0.87) 24-month follow-up (C24): -0.15 (-1.38 to 0.94) Statistically significant increase (p≤0.01)	Important	VERY LOW
Change from baseline in lumbar spine BMAD in transmales with a bone age of 14 years or more ('old'; 24 months follow-up)									
1 cohort study	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=23	None	Median (range), g/m^3	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Vlot et al. 2017							Start of gender-affirming hormones (C0): 0.24 (0.20 to 0.28) 24-month follow-up (C24): 0.25 (0.21 to 0.30) Statistically significant increase (p≤0.01) z-score (range) Start of gender-affirming hormones (C0): -0.29 (-2.28 to 0.90) 24-month follow-up (C24): -0.06 (-1.75 to 1.61) Statistically significant increase (p≤0.01)		
Change in femoral neck BMAD (2 uncontrolled, retrospective observational studies)									
Change from start of gender-affirming hormones to age 22 years in femoral neck BMAD in transfemales									
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=14 (Mean) N=10 (z-score)	None	Mean (SD), g/m^3 Start of gender-affirming hormones: 0.26 (0.04) Age 22 years: 0.28 (0.05) No statistically significant difference z-score (SD) Start of gender-affirming hormones: -1.57 (1.74) Age 22 years: Not reported	Important	VERY LOW
Change from baseline in femoral neck BMAD in transfemales with a bone age less than 15 years ('young'; 24 months follow-up)									
1 cohort study	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=16	None	Median (range), g/m^3 C0: 0.27 (0.20 to 0.33) C24: 0.27 (0.20 to 0.36)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Vlot et al. 2017							No statistically significant change z-score (range) C0: -1.32 (-3.39 to 0.21) C24: -1.30 (-3.51 to 0.92) No statistically significant change		
Change from baseline in femoral neck BMAD in transfemales with a bone age of 15 years or more ('old'; 24 months follow-up)									
1 cohort study Vlot et al. 2017	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=6	None	Median (range), g/m^3 C0: 0.30 (0.26 to 0.34) C24: 0.29 (0.24 to 0.38) No statistically significant change z-score (range) C0: -0.36 (-1.50 to 0.46) C24: -0.56 (-2.17 to 1.29) No statistically significant change	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in femoral neck BMAD in transmales									
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=19 (Mean) N=18 (z-score)	None	Mean (SD), g/m^3 Start of gender-affirming hormones: 0.31 (0.04) Age 22 years: 0.33 (0.05) P=0.010 z-score (SD) Start of gender-affirming hormones: -0.28 (0.74) Age 22 years: Not reported	Important	VERY LOW
Change from baseline in femoral neck BMAD in transmales with a bone age of less than 14 years ('young'; 24 months follow-up)									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
1 cohort study Vlot et al. 2017	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=10	None	Median (range), g/m^3 C0: 0.30 (0.22 to 0.35) C24: 0.33 (0.23 to 0.37) Statistically significant increase (p≤0.01) z-score (range) C0: -0.37 (-2.28 to 0.47) C24: -0.37 (-2.03 to 0.85) Statistically significant increase (p≤0.01)	Important	VERY LOW
Change from baseline in femoral neck BMAD in transmales with a bone age of 14 years or more ('old'; 24 months follow-up)									
1 cohort study Vlot et al. 2017	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=23	None	Median (range), g/m^3 C0: 0.30 (0.23 to 0.41) C24: 0.32 (0.23 to 0.41) Statistically significant increase (p≤0.01) z-score (range) C0: -0.27 ((-1.91 to 1.29) C24: 0.02 (-2.1 to 1.35) Statistically significant increase (p≤0.05)	Important	VERY LOW
Change in lumbar spine BMD (2 uncontrolled, retrospective observational studies)									
Change from start of gender-affirming hormones to age 22 years in lumbar spine BMD in transfemales									
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=15 (Mean) N=13 (z-score)	None	Mean (SD), g/m^2 Start of gender-affirming hormones: 0.84 (0.11) Age 22 years: 0.93 (0.10) P<0.001 z-score (SD)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
							Start of gender-affirming hormones: -1.01 (0.98) Age 22 years: -1.36 (0.83) No statistically significant difference		
Change from start of gender-affirming hormones to age 22 years in lumbar spine BMD in transmales									
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=19 (Mean and z-score)	None	Mean (SD), g/m^2 Start of gender-affirming hormones: 0.91 (0.10) Age 22 years: 0.99 (0.13) P<0.001 z-score (SD) Start of gender-affirming hormones: -0.72 (0.99) Age 22 years: -0.33 (1.12) No statistically significant difference	Important	VERY LOW
Change from start of testosterone treatment in lumbar spine BMD in transmen (follow-up 6 to 24 months)									
1 cohort study Stoffers et al. 2019	Serious limitations[4]	No serious indirectness	Not applicable	Not calculable	N=62 (T0 and T6) N=37 (T12) N=15 (T24)	None	Mean (SD), g/cm^2 T0: 0.90 (0.11) T6: 0.94 (0.10) T12: 0.95 (0.09) T24: 0.95 (0.11) No statistically significant difference from T0 to any timepoint z-score (SD) T0: -0.81 (1.02) T6: -0.67 (0.95) T12: -0.66 (0.81) T24: -0.74 (1.17)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
							No statistically significant difference from T0 to any timepoint		
Change in femoral neck BMD (2 uncontrolled, retrospective observational studies)									
Change from start of gender-affirming hormones to age 22 years in femoral neck BMD in transfemales									
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=15 (Mean) N=11 (z-score)	None	Mean (SD), g/m^2 Start of gender-affirming hormones: 0.87 (0.08) Age 22 years: 0.94 (0.11) P=0.009 z-score (SD) Start of gender-affirming hormones: -0.95 (0.63) Age 22 years: -0.69 (0.74) No statistically significant difference	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in femoral neck BMD in transmales									
1 cohort study Klink et al. 2015	Serious limitations[1]	Serious indirectness[2]	Not applicable	Not calculable	N=19 (Mean) N=16 (z-score)	None	Mean (SD), g/m^2 Start of gender-affirming hormones: 0.88 (0.09) Age 22 years: 0.95 (0.10) P<0.001 z-score (SD) Start of gender-affirming hormones: -0.35 (0.79) Age 22 years: -0.35 (0.74) P=0.006	Important	VERY LOW
Change from start of testosterone treatment in right femoral neck (hip) BMD in transmales (follow-up 6 to 24 months)									
1 cohort study	Serious limitations[4]	No serious indirectness	Not applicable	Not calculable	N=62 (T0 and T6)	None	Mean (SD), g/cm^2 T0: 0.77 (0.08)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Stoffers et al. 2019					N=37 (T12) N=15 (T24)		T6: 0.84 (0.11) T12: 0.82 (0.08) T24: 0.85 (0.11) No statistically significant difference from T0 to any timepoint z-score (SD) T0: -0.97 (0.79) T6: -0.54 (0.96) T12: -0.80 (0.69) T24: -0.31 (0.84) No statistically significant difference from T0 to any timepoint		
Change from start of testosterone treatment in left femoral neck (hip) BMD in transmales (follow-up 6 to 24 months)									
1 cohort study Stoffers et al. 2019	Serious limitations[4]	No serious indirectness	Not applicable	Not calculable	N=62 (T0 and T6) N=37 (T12) N=15 (T24)	None	Mean (SD), g/cm^2 T0: 0.76 (0.09) T6: 0.83 (0.12) T12: 0.81 (0.08) T24: 0.86 (0.09) No statistically significant difference from T0 to any timepoint z-score (SD) T0: -1.07 (0.85) T6: -0.62 (1.12) T12: -0.93 (0.63) T24: -0.20 (0.70) No statistically significant difference from T0 to any timepoint	Important	VERY LOW

Abbreviations: BMAD: bone mineral apparent density; BMD: bone mineral density; g: grams; m: metre; SD: standard deviation

1 Downgraded 1 level - the cohort study by Klink et al. (2015) was assessed as at high risk of bias (poor quality overall; lack of blinding, no control group and high number of participants lost to follow-up)
2 Outcomes reported after gender reassignment surgery and not after gender-affirming hormones alone. Unclear whether observed changes are due to hormones or surgery
3 Downgraded 1 level - the cohort study by Vlot et al. (2017) was assessed as at high risk of bias (poor quality overall; lack of blinding and no control)
4 Downgraded 1 level - the cohort study by Stoffers et al. (2019) was assessed as at high risk of bias (poor quality overall; lack of blinding and no control group)

Table 8: Question 2: For children and adolescents with gender dysphoria, what is the short-term and long-term safety of gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – Cardiovascular risk factors

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change in body mass index (1 uncontrolled, retrospective observational study)									
Change from start of gender-affirming hormones to age 22 years in BMI in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI) +1.9 (0.6 to 3.2) Statistically significant increase (p<0.005) Mean BMI at 22 years (95% CI): 23.2 (21.6 to 24.8)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in BMI in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI) +1.4 (0.8 to 2.0) Statistically significant increase (p<0.005) Mean BMI at 22 years (95% CI): 23.9 (23.0 to 24.7)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Obesity rates at age 22 years (1 uncontrolled, retrospective observational study)									
Obesity rates at age 22 years in transfemales who started gender-affirming hormones as adolescents (1 uncontrolled, retrospective observational study)									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	At 22 years, 9.9% of transfemales were obese, compared with 3.0% in reference cisgender population No statistically analysis reported	Important	VERY LOW
Obesity rates at age 22 years in transfemales who started gender-affirming hormones as adolescents (1 uncontrolled, retrospective observational study)									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	At 22 years, 6.6% of transmales were obese, compared with 2.2% in reference cisgender population No statistically analysis reported	Important	VERY LOW
Change in blood pressure (1 uncontrolled, retrospective observational study)									
Change from start of gender-affirming hormones to age 22 years in systolic blood pressure (SBP) in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI) -3 (-8 to 2) No statistically significant difference Mean SBP at 22 years (95% CI): 117 (113 to 122)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in diastolic blood pressure (DBP) in transfemales									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI) +6 (3 to 10) Statistically significant increase (p<0.001) Mean DBP at 22 years (95% CI): 75 (72 to 78)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in systolic blood pressure (SBP) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI): +5 (1 to 9) Statistically significant increase (p<0.05) Mean SBP at 22 years (95% CI): 126 (122 to 130)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in diastolic blood pressure (DBP) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI): +6 (4 to 9) Statistically significant increase (p<0.001) Mean DBP at 22 years (95% CI): 74 (72 to 77)	Important	VERY LOW
Change in glucose levels, insulin levels, insulin resistance and HbA1c (2 uncontrolled, retrospective observational studies)									
Change from start of gender-affirming hormones to age 22 years in glucose level (mmol/L) in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI): +0.1 (-0.1 to 0.2)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
							No statistically significant difference Mean glucose level at 22 years (95% CI): 5.0 (4.8 to 5.1)		
Change from start of gender-affirming hormones to age 22 years in insulin level (mU/L) in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI) +2.7 (-1.7 to 7.1) No statistically significant difference Mean insulin level at 22 years (95% CI): 13.0 (8.4 to 17.6)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in insulin resistance (HOMA-IR) in transfemales. Higher scores indicate more insulin resistance.									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI) +0.7 (-0.2 to 1.5) No statistically significant difference Mean HOMA-IR at 22 years (95% CI): 2.9 (1.9 to 3.9)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in glucose level (mmol/L) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI) 0.0 (-0.2 to 0.2) No statistically significant difference	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
							Mean glucose level at 22 years (95% CI): 4.8 (4.7 to 5.0)		
Change from start of gender-affirming hormones to age 22 years in insulin level (mU/L) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI) -2.1 (-3.9 to -0.3) Statistically significant decrease (p<0.05) Mean insulin level at 22 years (95% CI): 8.6 (6.9 to 10.2)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in insulin resistance (HOMA-IR) in transmales. Higher scores indicate more insulin resistance.									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI): -0.5 (-1.0 to -0.1) Statistically significant decrease (p<0.05) Mean HOMA-IR at 22 years (95% CI): 1.8 (1.4 to 2.2)	Important	VERY LOW
Change from start of testosterone in HbA1c in transmales (up to 24 months follow-up)									
1 cohort study Stoffers et al. 2019	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N= Not reported	None	No statistically significant change from start of testosterone treatment Numerical results, follow-up duration and further details of	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
							statistical analysis not reported.		
Change in lipid profile (1 uncontrolled, retrospective observational study)									
Change from start of gender-affirming hormones to age 22 years in total cholesterol (mmol/L) in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI): +0.1 (-0.2 to 0.4) No statistically significant difference Mean total cholesterol at 22 years (95% CI): 4.1 (3.8 to 4.4)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in HDL cholesterol (mmol/L) in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI): 0.0 (-0.1 to 0.2) No statistically significant difference Mean HDL cholesterol at 22 years (95% CI): 1.6 (1.4 to 1.7)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in LDL cholesterol (mmol/L) in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI): 0.0 (-0.3 to 0.2) No statistically significant difference Mean LDL cholesterol at 22 years (95% CI): 2.0 (1.8 to 2.3)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change from start of gender-affirming hormones to age 22 years in triglycerides (mmol/L) in transfemales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=71	None	Mean change (95% CI): +0.2 (0.0 to 0.5) Statistically significant increase (p<0.05) Mean triglycerides at 22 years (95% CI): 1.1 (0.9 to 1.4)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in total cholesterol (mmol/L) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI): +0.4 (0.2 to 0.6) Statistically significant increase (p<0.001) Mean total cholesterol at 22 years (95% CI): 4.6 (4.3 to 4.8)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in HDL cholesterol (mmol/L) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI) -0.3 (-0.4 to -0.2) Statistically significant decrease (p<0.001) Mean HDL cholesterol at 22 years (95% CI): 1.3 (1.2 to 1.3)	Important	VERY LOW
Change from start of gender-affirming hormones to age 22 years in LDL cholesterol (mmol/L) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI): +0.4 (0.2 to 0.6)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
							Statistically significant increase (p<0.001) Mean LDL cholesterol at 22 years (95% CI): 2.6 (2.4 to 2.8)		
Change from start of gender-affirming hormones to age 22 years in triglycerides (mmol/L) in transmales									
1 cohort study Klaver et al. 2020	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=121	None	Mean change (95% CI) +0.5 (0.3 to 0.7) Statistically significant increase (p<0.001) Mean triglycerides at 22 years (95% CI): 1.3 (1.1 to 1.5)	Important	VERY LOW

Abbreviations: BMI: boss mass index; CI: confidence interval; DBP: diastolic blood pressure; HbA1c: glycated haemoglobin; HDL: high-density lipoproteins; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; LDL: low-density lipoproteins; mmol/L: millimoles per litre; mU/L: milliunits per litre; SBP: systolic blood pressure; SD: standard deviation

1 Downgraded 1 level - the cohort study by Klaver et al. (2020) was assessed as at high risk of bias (poor quality overall; lack of blinding and no control group)
2 Downgraded 1 level - the cohort study by Stoffers et al. (2019) was assessed as at high risk of bias (poor quality overall; lack of blinding and no control group)

Table 9: Question 2: For children and adolescents with gender dysphoria, what is the short-term and long-term safety of gender-affirming hormones compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – Other safety outcomes

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Liver enzymes (1 uncontrolled, retrospective observational study)									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change from start of testosterone in aspartate aminotransferase (AST) level in transmales (up to 24 months follow-up)									
1 cohort study Stoffers et al. 2019	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N= Not reported	None	No statistically significant change from start of testosterone treatment Numerical results, follow-up duration and further details of statistical analysis not reported.	Important	VERY LOW
Change from start of testosterone in alanine aminotransferase (ALT) level in transmales (up to 24 months follow-up)									
1 cohort study Stoffers et al. 2019	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N= Not reported	None	No statistically significant change from start of testosterone treatment Numerical results, follow-up duration and further details of statistical analysis not reported.	Important	VERY LOW
Change from start of testosterone in gamma-glutamyl transferase (GGT) level in transmales (up to 24 months follow-up)									
1 cohort study Stoffers et al. 2019	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N= Not reported	None	No statistically significant change from start of testosterone treatment Numerical results, follow-up duration and further details of statistical analysis not reported.	Important	VERY LOW
Change from start of testosterone in alkaline phosphatase (ALP) level in transmales (up to 24 months follow-up)									
1 cohort study Stoffers et al. 2019	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=62 (T0 and T1) N=37 (T12)	None	Median (IQR), U/L T0: 102 (78 to 136) T6: 115 (102 to 147) T12: 112 (88 to 143) T24: 81 (range 69 to 98)	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
					N-15 (T24)		Statistically significant increase from T0 at T6 and T12 (p<0.001)		
Kidney markers (1 uncontrolled, retrospective observational study)									
Change from start of testosterone in serum creatinine level in transmales (up to 24 months follow-up)									
1 cohort study Stoffers et al. 2019	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N=62 (T0 and T1) N=37 (T12) N=15 (T24)	None	Mean (SD), umol/L T0: 62 (7) T6: 70 (9) T12: 74 (10) T24: 81 (10) Statistically significant increase from T0 at all timepoints (p<0.001)	Important	VERY LOW
Change from start of testosterone in serum urea[2] level in transmales (up to 24 months follow-up)									
1 cohort study Stoffers et al. 2019	Serious limitations[1]	No serious indirectness	Not applicable	Not calculable	N= Not reported	None	No statistically significant change from start of testosterone treatment Numerical results, follow-up duration and further details of statistical analysis not reported.	Important	VERY LOW
Adverse effects (1 uncontrolled, retrospective observational study)									
Permanent discontinuation of gender-affirming hormones (median follow-up 2.0 years (range 0.0 to 11.3)									
1 cohort study Khatchadourian et al. 2014	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=63	None	No participants permanently discontinued gender-affirming hormones.	Important	VERY LOW
Temporary discontinuation of gender-affirming hormones (median follow-up 2.0 years (range 0.0 to 11.3)									
1 cohort study	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=63	None	3/37 transmales receiving testosterone temporarily	Important	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Khatchadourian et al. 2014							discontinued treatment, 2 due to concomitant mental health comorbidities and 1 due to androgenic alopecia. All eventually resumed treatment. No transfemales receiving oestrogen temporarily discontinued treatment		
Minor complications during treatment with gender-affirming hormones (median follow-up 2.0 years (range 0.0 to 11.3)									
1 cohort study Khatchadourian et al. 2014	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=63	None	12/63 participants had minor complications during treatment with gender-affirming hormones All 12 were transmales receiving testosterone. Complications were severe acne (n=7), androgenic alopecia (n=1) mild dyslipidaemia (n=3) and significant mood swings (n=1) No transfemales receiving oestrogen had minor complications	Important	VERY LOW
Severe complications during treatment with gender-affirming hormones (median follow-up 2.0 years (range 0.0 to 11.3)									
1 cohort study Khatchadourian et al. 2014	Serious limitations[3]	No serious indirectness	Not applicable	Not calculable	N=63	None	No severe complications reported during gender-affirming treatment	Important	VERY LOW

Abbreviations: ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyl transferase; IQR: interquartile range; SD: standard deviation; U/L: units per litre; umol/L: micromole per litre

1 Downgraded 1 level - the cohort study by Stoffers et al. (2019) was assessed as at high risk of bias (poor quality overall; lack of blinding and no control group)
2 Referred to as 'ureum' in original publication
3 Downgraded 1 level - the cohort study by Khatchadourian et al. (2014) was assessed as at high risk of bias (poor quality overall; lack of blinding, no control group and high number of participants lost to follow-up)

Table 10: From the evidence selected, are there particular sub-groups of children and adolescents with gender dysphoria that derive comparatively more (or less) benefit from treatment with gender-affirming hormones than the wider population of children and adolescents with gender dysphoria? – Transfemales compared with transmales

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Transfemales	Transmales	Result (95% CI)		
Impact on mental health (1 uncontrolled, retrospective observational study)									
Change from baseline in adjusted mean suicidality score, measured using the ASQ tool (mean treatment duration 349 days). Higher scores indicate a greater degree of suicidality.									
1 cohort study Allen et al. 2019	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=14	N=33	**Transfemales** T0 (baseline) = 1.21 (SE 0.36) T1 (final assessment) = 0.24 (SE 0.19) **Transmales** T0 (baseline) = 1.01 (SE 0.23) T1 (final assessment) = 0.29 (SE 0.13) No statistically significant difference in change from baseline between transfemales and transmales (p=0.79)	Critical	VERY LOW
Impact on quality of life (1 uncontrolled, retrospective observational study)									
Change from baseline in adjusted mean well-being score, measured using the GWBS of the Pediatric Quality of Life Inventory (mean treatment duration 349 days). Higher scores indicate better well-being.									
1 cohort study Allen et al. 2019	Serious limitations[4]	No serious indirectness	No serious inconsistency	Not calculable	N=14	N=33	**Transfemales** T0 (baseline) = 58.44 (SE 4.09) T1 (final assessment) = 69.52 (SE 3.62)	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Transfemales	Transmales	Result (95% CI)		
							Transmales T0 (baseline) = 64.95 (SE 2.66) T1 (final assessment) = 70.94 (SE 2.35) No statistically significant difference in change from baseline between transfemales and transmales (p=0.32)		

Abbreviations: ASQ: Ask Suicide-Screening Questions; GWBS: General Well-Being Scale; SE: standard error

1 The cohort study by Allen et al. 2019 was assessed at high risk of bias (poor quality; lack of blinding and no control group).

Table 11: From the evidence selected, are there particular sub-groups of children and adolescents with gender dysphoria that derive comparatively more (or less) benefit from treatment with gender-affirming hormones than the wider population of children and adolescents with gender dysphoria? – Sex assigned at birth males (transfemales)

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events/No of patients% (n/N%)		Effect		
Study type and number of studies Author year	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change from baseline in mean depression symptoms in transfemales, measured using the Quick Inventory of Depressive Symptoms (QIDS), self-reported (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more depression.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=40	None	Baseline = 7.5 (SD 4.9) Follow-up = 6.6 (SD 4.4) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean depression symptoms in transfemales, measured using the Quick Inventory of Depressive Symptoms (QIDS), clinician-reported (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe depression.									
1 cohort study	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=45	None	Baseline = 4.2 (SD 3.2) Follow-up = 5.4 (SD 3.4)	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events/No of patients% (n/N%)		Effect		
Study type and number of studies Author year	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Kuper et al. 2020							No statistical analysis reported for this sub-group		
Change from baseline in mean anxiety symptoms in transfemales, measured using the SCARED questionnaire (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe anxiety.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=33	None	Baseline = 26.4 (SD 14.2) Follow-up = 24.3 (SD 15.4) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean panic symptoms in transfemales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=34	None	Baseline = 5.7 (SD 4.9) Follow-up = 5.1 (SD 4.9) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean generalised anxiety symptoms in transfemales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=34	None	Baseline = 8.6 (SD 5.1) Follow-up = 8.0 (SD 5.1) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean social anxiety symptoms in transfemales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=34	None	Baseline = 7.1 (SD 3.9) Follow-up = 6.8 (SD 4.4) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean separation anxiety symptoms in transfemales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=34	None	Baseline = 3.4 (SD 3.3) Follow-up = 2.7 (SD 2.3) No statistical analysis reported for this sub-group	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events/No of patients% (n/N%)		Effect		
Study type and number of studies Author year	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change from baseline in mean school avoidance symptoms in transfemales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=33	None	Baseline = 1.8 (SD 1.7) Follow-up = 1.9 (SD 2.1) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in percentage of participants with suicidal ideation in transfemales, measured using the additional questions from the PHQ 9_Modified for Teens (approximately 12-month follow-up)									
1 cohort study Achille et al. 2020	Serious limitations[2]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=17	None	Wave 1 (baseline) = 11.8% (2/17) Wave 2 (approx. 12 months) = 5.9% (1/17) No statistical analysis reported	Critical	VERY LOW
Impact on body image (1 uncontrolled, prospective observational study)									
Change from baseline in mean body image in transfemales, measured using the BIS (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores represent a higher degree of body dissatisfaction.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=30	None	Baseline = 67.5 (SD 19.5) Follow-up = 49.0 (SD 21.6) No statistical analysis reported for this sub-group	Important	VERY LOW

Abbreviations: BIS: Body Image Scale; PHQ 9: Patient Health Questionnaire 9; SCARED: Screen for Child Anxiety Related Emotional Disorders; SD: standard deviation

1 Downgraded 1 level - the cohort study by Kuper et al. (2020) was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).
2 Downgraded 1 level - the cohort study by Achille et al. 2020 was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).
3 Serious indirectness in Achille 2020- Approximately 30% of the full sample received puberty suppression alone or were receiving no treatment at final follow-up.

Table 12: From the evidence selected, are there particular sub-groups of children and adolescents with gender dysphoria that derive comparatively more (or less) benefit from treatment with gender-affirming hormones than the wider population of children and adolescents with gender dysphoria? – Sex assigned at birth females (transmales)

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change from baseline in mean depression symptoms in transmales, measured using the Quick Inventory of Depressive Symptoms (QIDS), self-reported (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe depression.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=76	None	Baseline = 10.4 (SD 5.0) Follow-up = 7.5 (SD 4.5) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean depression symptoms in transmales, measured using the Quick Inventory of Depressive Symptoms (QIDS), clinician-reported (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe depression.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=78	None	Baseline = 6.7 (SD 4.4) Follow-up = 6.2 (SD 4.1) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean anxiety symptoms in transmales, measured using the SCARED questionnaire (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe anxiety.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=65	None	Baseline = 35.4 (SD 16.5) Follow-up = 29.8 (SD 15.5) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean panic symptoms in transmales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=66	None	Baseline = 9.3 (SD 6.5) Follow-up = 7.9 (SD 6.5) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean generalised anxiety symptoms in transmales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=66	None	Baseline = 10.4 (SD 5.0) Follow-up = 9.0 (SD 5.1) No statistical analysis reported for this sub-group	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change from baseline in mean social anxiety symptoms in transmales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=66	None	Baseline = 8.5 (SD 4.0) Follow-up = 7.8 (SD 4.1) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean separation anxiety symptoms in transmales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=65	None	Baseline = 4.2 (SD 3.4) Follow-up = 3.4 (SD 2.6) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in mean school avoidance symptoms in transmales, measured using specific questions from the SCARED questionnaire (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores indicate more severe symptoms.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=65	None	Baseline = 2.9 (SD 2.3) Follow-up = 2.0 (SD 2.3) No statistical analysis reported for this sub-group	Critical	VERY LOW
Change from baseline in percentage of participants with suicidal ideation in transmales, measured using the additional questions from the PHQ 9_Modified for Teens (approximately 12-month follow-up)									
1 cohort study Achille et al. 2020	Serious limitations[2]	Serious indirectness[3]	No serious inconsistency	Not calculable	N=33	None	Wave 1 (baseline) = 9.1% (3/33) Wave 2 (approx. 12 months) = 6.1% (2/33) No statistical analysis reported	Critical	VERY LOW
Impact on body image (1 uncontrolled, prospective observational study)									
Change from baseline in mean body image in transmales, measured using the BIS (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores represent a higher degree of body dissatisfaction.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=66	None	Baseline = 71.1 (SD 13.4) Follow-up = 52.9 (SD 16.8) No statistical analysis reported for this sub-group	Important	VERY LOW

Abbreviations: BIS: Body Image Scale; PHQ 9: Patient Health Questionnaire 9; SCARED: Screen for Child Anxiety Related Emotional Disorders; SD: standard deviation

1 Downgraded 1 level - the cohort study by Kuper et al. (2020) was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).
2 Downgraded 1 level - the cohort study by Achille et al. 2020 was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).
3 Serious indirectness in Achille 2020- Approximately 30% of the full sample received puberty suppression alone or were receiving no treatment at final follow-up.

Table 14: From the evidence selected, are there particular sub-groups of children and adolescents with gender dysphoria that derive comparatively more (or less) benefit from treatment with gender-affirming hormones than the wider population of children and adolescents with gender dysphoria? – Outcomes controlled for concurrent counselling and medicines for mental health problems

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Impact on mental health (1 uncontrolled, retrospective observational study)									
Change from baseline in mean depression score in transfemales, measured using the CESD-R (approximately 12-month follow-up; controlled for engagement in counselling and medicines for mental health problems). Higher scores indicate more depression.									
1 cohort study Achille et al. 2020	Serious limitations[1]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=17	None	No statistically significant change from baseline (p=0.27) Numerical scores not reported	Critical	VERY LOW
Change from baseline in mean depression score in transmales, measured using the CESD-R (approximately 12-month follow-up; controlled for engagement in counselling and medicines for mental health problems). Higher scores indicate more severe depression.									
1 cohort study Achille et al. 2020	Serious limitations[1]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=33	None	No statistically significant change from baseline (p=0.43) Numerical scores not reported	Critical	VERY LOW
Change from baseline in depression score in transfemales, measured using the Patient Health Questionnaire Modified for Teens (PHQ 9_Modified for Teens) (approximately 12-month follow-up; controlled for engagement in counselling and medicines for mental health problems). Higher scores indicate more severe depression.									
1 cohort study Achille et al. 2020	Serious limitations[1]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=17	None	No statistically significant change from baseline (p=0.07) Numerical scores not reported	Critical	VERY LOW

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Change from baseline in depression score in transmales, measured using the Patient Health Questionnaire Modified for Teens (PHQ 9_Modified for Teens) (approximately 12-month follow-up; controlled for engagement in counselling and medicines for mental health problems). Higher scores indicate more severe depression.									
1 cohort study Achille et al. 2020	Serious limitations[1]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=33	None	No statistically significant change from baseline (p=0.67) Numerical scores not reported	Critical	VERY LOW
Impact on quality of life (1 uncontrolled, retrospective observational study)									
Change from baseline in mean quality of life score in transfemales, measured using the QLES-Q-SF (approximately 12-month follow-up; controlled for engagement in counselling and medicines for mental health problems). Higher scores indicated better quality of life.									
1 cohort study Achille et al. 2020	Serious limitations[1]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=17	None	No statistically significant change from baseline (p=0.06)	Critical	VERY LOW
Change from baseline in mean quality of life score in transmales, measured using the QLES-Q-SF (approximately 12-month follow-up; controlled for engagement in counselling and medicines for mental health problems). Higher scores indicated better quality of life.									
1 cohort study Achille et al. 2020	Serious limitations[1]	Serious indirectness[2]	No serious inconsistency	Not calculable	N=33	None	No statistically significant change from baseline (p=0.08)	Critical	VERY LOW
Psychosocial Impact (1 uncontrolled, retrospective observational study)									
Functioning in adolescent development: Progresses normatively in school/ work during the real-life phase – impact on need for mental health treatment before or during gender identity assessment									
1 cohort study Kaltiala et al. 2020	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=49	None	Needed mental health treatment: 47% (15/32) functioning well Did not need mental health treatment: 82% (14/17) functioning well Statistically significant difference p=0.02	Important	VERY LOW
Functioning in adolescent development: Is age-appropriately able to deal with matters outside of the home during the real-life phase – impact on need for mental health treatment before or during gender identity assessment									

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
1 cohort study Kaltiala et al. 2020	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=49	None	Needed mental health treatment: 72% (23/32) managing well Did not need mental health treatment: 94% (16/17) managing well No statistically significant difference p=0.06	Important	VERY LOW
Functioning in adolescent development: Progresses normatively in school/ work during the real-life phase – impact on need for mental health treatment during the real-life phase									
1 cohort study Kaltiala et al. 2020	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=51	None	Needed mental health treatment: 42% (10/24) functioning well Did not need mental health treatment: 74% (20/27) functioning well Statistically significant difference p=0.02	Important	VERY LOW
Functioning in adolescent development: Is age-appropriately able to deal with matters outside of the home during the real-life phase – impact on need for mental health treatment during the real-life phase									
1 cohort study Kaltiala et al. 2020	Serious limitations[3]	No serious indirectness	No serious inconsistency	Not calculable	N=51	None	Needed mental health treatment: 67% (16/24) managing well Did not need mental health treatment: 93% (25/27) managing well Statistically significant difference p=0.02	Important	VERY LOW

Abbreviations: CESD-R: Center for Epidemiologic Studies Depression; p: p-value; PHQ 9: Patient Health Questionnaire 9; QLES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire

1 Downgraded 1 level - the cohort study by Achille et al 2020 was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).
2 Serious indirectness in Achille 2020- Approximately 30% of the full sample received puberty suppression alone or were receiving no treatment at final follow-up.
3 Downgraded 1 level - the cohort study by Kaltiala et al. 2020 was assessed at high risk of bias (poor quality; lack of blinding and no control).

Table 15: From the evidence selected, are there particular sub-groups of children and adolescents with gender dysphoria that derive comparatively more (or less) benefit from treatment with gender-affirming hormones than the wider population of children and adolescents with gender dysphoria? – Tanner age

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of patients		Effect		
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result (95% CI)		
Impact on mental health (1 uncontrolled, retrospective observational study)									
Change from baseline in mental health problems – depression, anxiety and anxiety-related symptoms (mean duration of gender-affirming hormone treatment was 10.9 months)									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=105	None	No difference in outcomes found by Tanner age. Numerical results, statistical analysis and information on specific outcomes not reported. It is unclear from the paper whether Tanner age is at initial assessment, start of GnRH analogues, start of gender-affirming hormones, or another timepoint	Critical	VERY LOW
Impact on body image (1 uncontrolled, prospective observational study)									
Change from baseline in mean body image, measured using the BIS (mean duration of gender-affirming hormone treatment was 10.9 months). Higher scores represent a higher degree of body dissatisfaction.									
1 cohort study Kuper et al. 2020	Serious limitations[1]	No serious indirectness	No serious inconsistency	Not calculable	N=105	None	No difference in body image score found by Tanner age. Numerical results, statistical analysis and information on specific outcomes not reported.	Important	VERY LOW

							It is unclear from the paper whether Tanner age is at initial assessment, start of GnRH analogues, start of gender-affirming hormones, or another timepoint		

Abbreviations: BIS: Body Image Scale

1 Downgraded 1 level - the cohort study by Kuper et al. 2020 was assessed at high risk of bias (poor quality; lack of blinding, no control group and high number of participants lost to follow-up).

Glossary

Ask Suicide-Screening Questions (ASQ)	ASQ is a four-item dichotomous (yes, no) response measure with high sensitivity, designed to identify risk of suicide. A patient is considered to have screened positive if they answered yes to any item. The authors of Allen et al. 2019 altered the fourth item of the ASQ ("Have you ever tried to kill yourself?") and prefaced it with "In the past few weeks . . ." as they were not investigating lifetime suicidality. A response of 'no' was scored as 0 and a response of 'yes' was scored as 1; each item was summed, generating an overall score for suicidality on a scale ranging from 0 to 4, with higher scores indicating greater levels of suicidal ideation.
Beck Depression Inventory-II (BDI-II)	The BDI-II is a tool for assessing depressive symptoms. There are no specific scores to categorise depression severity, but it is suggested that 0 to 13 is minimal symptoms, 14 to 19 is mild depression, 20 to 28 is moderate depression, and severe depression is 29 to 63.
Body Image Scale (BIS)	The BIS is used to measure body satisfaction. The scale consists of 30 body features, which the person rates on a 5-point scale. Each of the 30 items falls into one of 3 basic groups based on its relative importance as a gender-defining body feature: primary sex characteristics, secondary sex characteristics, and neutral body characteristics. A higher score indicates more dissatisfaction.
Bone mineral apparent density (BMAD)	BMAD is a size adjusted value of bone mineral density (BMD) incorporating bone size measurements using UK norms in growing adolescents.
Center for Epidemiologic Studies Depression scale (CESD-R)	The CESD-R is a valid, widely used tool to access depressive symptoms. The CESD-R asks about how frequently a person has felt or behaved in a certain way; with 20 questions scored from 0 score is calculated as a sum of 20 questions, ranging from 0 ("not at all or less than one day") to 3 ("5–7 days" and/or "nearly every day for 2 weeks"). Total score ranges from 0 to 60, with higher scores indicating more depressive symptoms.
Cisgender	Cisgender is a term for someone whose gender identity matches their birth-registered sex.
Family APGAR (Adaptability, Partnership, Growth, Affection and Resolve) test	The Family APGAR test is a 5-item questionnaire, with higher scores indicating better family functioning. The authors reported the following interpretation of the score: functional, 17-20 points; mildly dysfunctional, 16-13 points; moderately dysfunctional, 12-10 point; severely dysfunctional, <9 points.
Gender	The roles, behaviours, activities, attributes and opportunities that any society considers appropriate for girls and boys, and women and men.
Gender dysphoria	Discomfort or distress that is caused by a discrepancy between a person's gender identity (how they see themselves regarding their gender) and that person's sex assigned at birth (and the associated gender role, and/or primary and secondary sex characteristics).

General Well-Being Scale (GWBS) of the Pediatric Quality of Life Inventory score	The GWBS of the Pediatric Quality of Life Inventory uses uses a 5-point response scale, contains seven items, and measures two dimensions: general wellbeing (6 items) and general health (1 item). Each item is scored from 0 to 4, and the total score is linearly transformed to a 0 to 100 scale. High scores reflect fewer perceived problems and greater well-being.
GnRH analogue	GnRH analogues competitively block GnRH receptors to prevent the spontaneous release of two gonadotropin hormones, Follicular Stimulating Hormone (FSH) and Luteinising Hormone (LH) from the pituitary gland. The reduction in LH and FSH secretion reduces oestradiol secretion from the ovaries in those whose sex assigned at birth was female and testosterone secretion from the testes in those whose sex assigned at birth was male.
Patient Health Questionnaire Modified for Teens score (PHQ 9_Modified for Teens)	The PHQ 9_Modified for Teens is a validated tool to assess depression, dysthymia and suicide risk. The tool consists of 9 questions scored from 0 to 3 (total score 0 to 27), plus an additional 4 questions that are not scored. A score of 0 to 4 suggests no or minimal depressive symptoms, 5 to 9 mild, 10-14 moderate, 15-19 moderate and 20-27 severe symptoms.
Quick Inventory of Depressive Symptoms (QIDS)	Both the clinician- and self-reported QIDS are validated tools to assess depressive symptoms. The tool consists of 16 items, with the highest score for 9 items (sleep, weight, psychomotor changes, depressed mood, decreased interest, fatigue, guilt, concentration, and suicidal ideation) are added to give a total score ranging from 0 to 27. A score of 0 to 5 is suggestive of no depressive symptoms, 6 to 10 mild symptoms, 11 to 15 moderate symptoms, 16-20 severe symptoms and 21 to 27 very severe symptoms.
Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q-SF)	QLES-Q-SF is a validated questionnaire, consisting of 15 questions that rate quality of life on a scale of 1 (poor) to 5 (very good).
Screen for Child Anxiety Related Emotional Disorders (SCARED) questionnaire	SCARED is a validated, 41-point questionnaire, with each item scored 0 to 2. A total score of 25 or more is suggestive of anxiety disorder, with scores above 30 being more specific. Certain scores for specific questions may indicate the presence of other anxiety-related disorders: A score of 7 or more in questions related to panic disorder or significant somatic symptoms may indicate the presence of these. A score of 9 or more in questions related to generalised anxiety disorder may indicate the presence of this. A score of 5 or more in questions related to separation anxiety may indicate the presence of this. A score of 8 or more in questions related to social anxiety disorder may indicate the presence of this. A score of 3 or more in questions related to significant school avoidance may indicate the presence of this.
State-Trait Anxiety Inventory (STAI) score	STAI is a validated and commonly used measure of state anxiety (current state of anxiety) and trait anxiety (general state of calmness, confidence and security). It has 40 items, the first 20 covering state anxiety, the second 20 covering trait anxiety. STAI

	can be used in clinical settings to diagnose anxiety and to distinguish it from depressive illness. Each subtest (state and trait) is scored between 20 and 80, with higher scores indicating greater anxiety. There is no published minimal clinically meaningful difference (MCID) for STAI or thresholds for anxiety severity.
Strengths and Difficulties Questionnaire (SDQ, Spanish version	The SDQ, Spanish version includes 25-items covering emotional symptoms, conduct problems, hyperactivity/ inattention, peer relationship problems and prosocial behaviour. The authors state that a score of more than 20 is considered indicative of risk of having a disorder (normal: 0-15; borderline: 16-19, abnormal: 20-40).
Tanner stage	Tanner staging is a scale of physical development.
Transgender (including transmale and transfemale)	Transgender is a term for someone whose gender identity is not congruent with their birth-registered sex. A transfemale is a person who identifies as female and a transmale is a person who identifies as male.
Utrecht Gender Dysphoria Scale (UGDS)	The UGDS is a validated screening tool for both adolescents and adults to assess gender dysphoria. It consists of 12 items, to be answered on a 1- to 5-point scale, resulting in a sum score between 12 and 60. Higher scores indicate higher levels of gender dysphoria.

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DEFENDANT'S EXHIBIT 11

Socialstyrelsen
THE NATIONAL BOARD OF HEALTH AND WELFARE

Care of children and adolescents with gender dysphoria

Summary

Summary

The National Board of Health and Welfare (NBHW) has been commissioned by the Swedish government to update the national guidelines on care of children and adolescents with gender dysphoria, first published in 2015 [1]. Guidelines chapters are updated stepwise and this report contains revised guidance on psychosocial support and diagnostic assessment, and on puberty suppressing treatment with GnRH-analogues and gender-affirming hormonal treatment. This report thus replaces the corresponding chapters in the publication from 2015. Remaining chapters and the updated guidelines as a whole will be published later in 2022. In response to comments received during external review, two new chapters have been added, named *New recommendations on hormonal treatment – their reasons and consequences and Non-binary gender identity – current knowledge and a need for clarification*. Another difference compared to the guidelines from 2015 [1] is that the term "gender incongruence" is used alongside the term "gender dysphoria". For explanations of terms and abbreviations, see Appendix 2. For a description of the scientific evidence and clinical experience underlying the recommendations and the work process, see Appendices 3 and 4.

The guidelines apply to children and adolescents, i.e. people under 18 years of age. In the medical text sections, the term children (barn) refers to persons who have not yet entered puberty, while the term adolescents (ungdomar) refers to people whose puberty has started. In the text sections relating to juridical regulations, only the term children (barn) is used and denotes people younger than 18 years of age. Finally, the term "young people" (unga) is sometimes used in text sections addressing both children and adolescents.

Introductory comment

The summary that follows and the introductory chapter describe that the updated recommendations for puberty suppression with GnRH-analogues and gender-affirming hormonal treatment have become more restrictive compared to 2015, and the reasons that they have changed. The new recommendations entail that a larger

proportion than before, among adolescents with gender incongruence referred for diagnostic assessment of gender dysphoria, will need to be offered other care than hormonal treatments. Questions on how to ensure that all young people suffering from gender dysphoria be taken seriously and confirmed in their gender identity, well received and offered adequate care are becoming increasingly relevant, and will need to be answered during the ongoing restructuring of certain care for gender dysphoria into three national specialised medical care services (NBHW decision in December 2020). The care for children, adolescents and adults with gender dysphoria in these three national specialised units aims to improve equality in care, coordination and dialogue, and may enhance the implementation of national guidelines.

Recommendations and criteria for hormonal treatment

For adolescents with gender incongruence, the NBHW deems that the risks of puberty suppressing treatment with GnRH-analogues and gender-affirming hormonal treatment currently outweigh the possible benefits, and that the treatments should be offered only in exceptional cases. This judgement is based mainly on three factors: the continued lack of reliable scientific evidence concerning the efficacy and the safety of both treatments [2], the new knowledge that detransition occurs among young adults [3], and the uncertainty that follows from the yet unexplained increase in the number of care seekers, an increase particularly large among adolescents registered as females at birth [4].

A systematic review published in 2022 by the Swedish Agency for Health Technology Assessment and Assessment of Social Services [2] shows that the state of knowledge largely remains unchanged compared to 2015. High quality trials such as RCTs are still lacking and the evidence on treatment efficacy and safety is still insufficient and inconclusive for all reported outcomes. Further, it is not possible to determine how common it is for adolescents who undergo gender-affirming treatment to later change their perception of their gender identity or interrupt an ongoing treatment. An important difference compared to 2015 however, is that the occurrence of

detransition among young adults is now documented [3], meaning that the uncertain evidence that indicates a low prevalence of treatment interruptions or any aspects of regret is no longer unchallenged. Although the prevalence of detransition is still unknown, the knowledge that it occurs and that genderconfirming treatment thus may lead to a deteriorating of health and quality of life (i.e. harm), is important for the overall judgement and recommendation.

To minimize the risk that a young person with gender incongruence later will regret a gender-affirming treatment, the NBHW deems that the criteria for offering GnRH-analogue and gender-affirming hormones should link more closely to those used in the Dutch protocol, where the duration of gender incongruence over time is emphasized [5-7]. Accordingly, an early (childhood) onset of gender incongruence, persistence of gender incongruence until puberty and a marked psychological strain in response to pubertal development is among the recommended criteria. The publications that describe these criteria and the treatment outcomes when given in accordance [5, 6, 8] consitute the best available knowledge and should be used as guidance.

To ensure that new knowledge is gathered, the NBHW further deems that treatment with GnRH-analogues and sex hormones for young people should be provided within a research context, which does not necessarily imply the use of randomized controlled trials (RCTs). As in other healthcare areas where it is difficult to conduct RCTs while retaining sufficient internal validity, it is also important that other prospective study designs are considered for ethical review and that register studies are made possible. Until a research study is in place, the NBHW deems that treatment with GnRH-analogues and sex hormones may be given in exceptional cases, in accordance with the updated recommendations and criteria described in the guidelines. The complex multidisciplinary assessments will eventually be carried out in the three national units that are granted permission to provide highly specialized care services.

In accordance with the DSM-5, the recommendations in the guidelines from 2015 applied to young people with gender dysphoria in general, i.e. also young people with a non-binary gender identity. Another criterion within the Dutch protocol is that the child has had a binary ("cross-gender") gender identity since childhood [5, 6].

It has emerged during the review process, that the clinical experience and documentation of puberty-suppressing and hormonal treatment for young people with non-binary gender identity is lacking, and also that it is limited for adults. The NBHW still considers that gender dysphoria rather than gender identity should determine access to care and treatment. An urgent work thus remains, to clarify criteria under which adolescents with non-binary gender identity may be offered puberty-suppressing and gender-affirming hormonal treatment within a research framework.

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STM038:00/2020

Recommendation of the Council for Choices in Health Care in Finland (PALKO / COHERE Finland)

Medical Treatment Methods for Dysphoria Related to Gender Variance In Minors

Concepts

Suppression treatment	Pubertal suppression with GnRH analogues (drugs that inhibit gonadotropin-releasing hormone activity) to halt the development of secondary sex characteristics of the biological sex.
Cisgender/Cis person	A person whose gender identity matches the sex determined at birth (identifies, and is satisfied with, the sex determined at birth and generally expresses his/her gender accordingly).
Other gender identity	A person who does not identify as a man or a woman, but rather somewhere along the continuum or outside of it; genderless, nonbinary, or multigendered.
Transgender	A person whose gender identity differs from the legal and biological sex determined at birth but instead aligns with the opposite sex.

Content

1. Basis for Preparing These Recommendations

As the number of patients, including minors, referred to the Helsinki University Hospital (HUS) and the Tampere University Hospital (TAYS) multidisciplinary outpatient clinics for assessment and treatment of gender dysphoria has increased, PALKO (Council for Choices in Healthcare in Finland / COHERE Finland) decided to prepare recommendations for medical treatments of gender dysphoria, i.e., distress which is associated with a minor's gender variance and impairs function. Gender variance refers to a spectrum of gender experience anywhere on the male-female identity continuum or outside it, and is not exclusively confined to the dichotomized male/female conception of gender. Not all patients with gender variance experience significant suffering or functional impairments, and not all seek medical treatment.

These recommendations are based on the legislation in force at the time of the adoption of the recommendation, the available research evidence, and the clinical experience of multidisciplinary teams with expertise in gender dysphoria assessment and treatment at HUS and TAYS. The knowledge base supporting these recommendations is detailed in a separate Preparatory Memorandum and appendices and includes a description of planning and implementation of medical treatments, a literature review of medical treatments, an extensive ethical analysis, and feedback following meetings with patients and the advocacy groups who represent them.

Finnish legislation defines the requirements for the legal gender recognition of transsexuals (Act on Legal Recognition of the Gender of Transsexuals (Trans Act) 536/2002). The detailed requirements for providing the assessment and treatment to enable legal gender recognition are spelled out further in a Decree of the Ministry of Social Affairs and Health (1053/2002). The Trans Act and the related Decree apply to adults. For those who are not of legal age, there are no laws governing the provision and needs of transgender healthcare; however, these are subject to the Health Care Act of Finland (1326/2010), in particular section 7 (criteria for integrated care), section 7a (criteria for treatment options), section 8 (evidence-based, high quality, safe and appropriate care) and section 10 (rationale for centralization); and also to the Constitution of Finland (731/1999)'s section 6 on equality and section 19 on the right to adequate social and healthcare services. Finland's Act on the Status and Rights of Patients, (785/1992), and especially sections 5, 6, and 7, are also relevant.

2. Recommendations' Target Population

These recommendations apply to minors suffering from dysphoria related to gender variance who are seeking a consultation regarding an evaluation of medical examination and treatment needs; the children and adolescents may identify with the opposite sex (transgender), or may identify as genderless, non-binary, or anywhere along or outside the male/female gender identity continuum (other gender).

3. Procedures Assessed

These recommendations focus on medical treatment procedures that aim to decrease suffering and functional impairment of gender-dysphoric minors.

4. Current Care

Cross-sex identification in childhood, even in extreme cases, generally disappears during puberty. However, in some cases, it persists or even intensifies. Gender dysphoria may also emerge or intensify at the onset of puberty. There is considerable variation in the timing of the onset of puberty in both sexes. The first-line treatment for gender dysphoria is psychosocial support and, as necessary, psychotherapy and treatment of possible comorbid psychiatric disorders.

Consultation appointments (for parents / caregivers) regarding pre-pubescent children's cross-sex identification or gender dysphoria are provided by the research group on the gender identity of minors at TAYS or HUS. However, ongoing support or other treatment of psychiatric disorders are provided through the local municipal services.

In clear cases of pre-pubertal onset of gender dysphoria that intensified during puberty, a referral can be made for an assessment by the research group at TAYS or HUS regarding the appropriateness for puberty suppression. If no contraindications to early intervention are identified, pubertal suppression with GnRH analogues (to suppress the effect of gonadotropin-releasing hormone) may be considered to prevent further development of secondary sex characteristics of the biological sex.

Adolescents who have already undergone puberty, whose gender dysphoria occurs in the absence of co-occurring symptoms requiring psychiatric treatment, and whose experience of transgender identity failed to resolve following a period of reflection, can be referred for assessment by the research group on the gender identity of minors at TAYS or HUS. Hormone therapy (testosterone/estrogen and anti-androgen) can be started after the diagnostic evaluations, but no earlier than age 16. Additionally, patients under 18 receive three to six months of GnRH analogue treatment prior to the initiation of cross-sex hormones in order to suppress the hormonal activity of the gonads. No gender confirmation surgeries are performed on minors.

5. Risks, Benefits and Uncertainty

The literature review identified two studies with the total of 271 persons diagnosed with childhood-onset gender identity disorder and associated gender or body dysphoria that intensified after the onset of puberty (Preparatory Memorandum Appendix 1, Tables 15 and 16, pages 46-48).

In a smaller study of 70 adolescents, puberty was suppressed with the GnRH analogue at the average age of 14.8 (12-18 years) and puberty blockade continued for an average of 2 years. During the treatment period, the adolescents' mood improved, and the risk of behavioral disorders diminished, but gender dysphoria itself did not diminish, and there were no changes in body image. In a larger study consisting of 201 adolescents, 101 patients with the average age of 15.5 (12-18 years) started an 18-month psychological supportive intervention, and, additionally at six months, pubertal development was suppressed by starting GnRH analogue treatment. The other cohort of 100 only received psychological supportive intervention for 18 months. In both groups, statistically significant increases in global psychosocial functioning were found at 12 and 18 months; among those having received psychological intervention alone, the improvement in global functioning was already significant at the 6-month mark. Both studies lack long-term treatment follow-up into adulthood.

A recent Finnish study, published after the completion of this literature review, reported on the effect of initiating cross-sex hormone therapy on functioning, progression of developmental tasks of adolescence, and psychiatric symptoms. This study found that during cross-sex hormone therapy, problems in these areas did not decrease.

Potential risks of GnRH therapy include disruption in bone mineralization and the as yet unknown effects on the central nervous system. In trans girls, early pubertal suppression inhibits penile growth, requiring the use of alternative sources of tissue grafts for a potential future vaginoplasty. The effect of pubertal suppression and cross-sex hormones on fertility is not yet known.

6. Ethical Assessment

Although the ethics analysis did not systematically address the issues pertaining to children and adolescents, they have been discussed in several areas in the related documents (Preparatory Memorandum pages 52-62; Appendix 5).

According to the Health Care Act (section 8), healthcare services must be based on evidence and recognized treatment and operational practices. As far as minors are concerned, there are no medical treatment that can be considered evidence-based. At the same time, the numbers of minors developing gender dysphoria has increased. In this situation, it is vital to assure that children and young people are able to talk about their feelings, and that their feelings are acknowledged. The opportunity to reflect on one's experience should be easily accessible through the local health system (i.e., school or student health care, primary care). A young

person's feelings should not be interpreted as immediately requiring specialized medical examinations or treatments.

In cases of children and adolescents, ethical issues are concerned with the natural process of adolescent identity development, and the possibility that medical interventions may interfere with this process. It has been suggested that hormone therapy (e.g., pubertal suppression) alters the course of gender identity development; i.e., it may consolidate a gender identity that would have otherwise changed in some of the treated adolescents. The reliability of the existing studies with no control groups is highly uncertain, and because of this uncertainty, no decisions should be made that can permanently alter a still-maturing minor's mental and physical development.

From the point of view of patient advocacy groups, halting puberty is providing young people with a period of reflection, rather than consolidating their gender identity. This is based on the premise that halting the development of one's permanent sex characteristics will improve the minor's social interactions, while allowing more time for diagnostic evaluations. Additionally, patient advocacy groups assert that early intervention with hormonal treatments will lead to improved outcomes for the patients who do eventually pursue gender reassignment. Professionals, for their part, consider it important to ensure that irreversible interventions, which may also have significant adverse effects, both physical and mental, are only performed on individuals who are able to understand the permanence of the changes and the potential for harm, and who are unlikely to regret such interventions. It is not known how the hormonal suppression of puberty affects young people's judgement and decision-making.

The Act on the Status and Rights of Patients (1992/785) states that the patient shall be provided with information about his/her state of health, the significance of the treatment, various alternative forms of treatment and their effects, and about other factors concerning treatment that have an effect on treatment decision-making. In a situation where a minor's identification with the opposite sex causes long-term and severe dysphoria, it is important to make sure that he/she understands the realistic potential of gender reassignment treatments to alter secondary sex characteristics, the reality of a lifelong commitment to medical therapy, the permanence of the effects, and the possible physical and mental adverse effects of the treatments. Although patients may experience regret, after reassignment treatments, there is no going back to the non-reassigned body and its normal functions. Brain development continues until early adulthood – about age 25, which also affects young people's ability to assess the consequences of their decisions on their own future selves for rest of their lives.

A lack of recognition of comorbid psychiatric disorders common among gender-dysphoric adolescents can also be detrimental. Since reduction of psychiatric symptoms cannot be achieved with hormonal and surgical interventions, it is not a valid justification for gender reassignment. A young person's identity and personality development must be stable so that they can genuinely face and discuss their gender dysphoria, the significance of their own feelings, and the need for various treatment options.

For children and adolescents, these factors are key reasons for postponing any interventions until adulthood.

7. Conclusions

The first-line intervention for gender variance during childhood and adolescent years is psychosocial support and, as necessary, gender-explorative therapy and treatment for comorbid psychiatric disorders. Uncertainty related to gender identity should be dealt with according to the severity of symptoms and the need for treatment and should be handled at the school / student health care, primary health care at the local level, or in specialty care.

In adolescents, psychiatric disorders and developmental difficulties may predispose a young person to the onset of gender dysphoria. These young people should receive treatment for their mental and behavioral health issues, and their mental health must be stable prior to the determination of their gender identity.

Clinical experience reveals that autistic spectrum disorders (ASD) are overrepresented among adolescents suffering from gender dysphoria; even if such adolescents are presenting with gender dysphoria, rehabilitative interventions for ASD must be properly addressed.

In light of available evidence, gender reassignment of minors is an experimental practice. Based on studies examining gender identity in minors, hormonal interventions may be considered before reaching adulthood in those with firmly established transgender identities, but it must be done with a great deal of caution, and no irreversible treatment should be initiated. Information about the potential harms of hormone therapies is accumulating slowly and is not systematically reported. It is critical to obtain information on the benefits and risks of these treatments in rigorous research settings.

At a minimum, a consultation for a pre- pubescent child at the specialist setting at the TAYS includes an extensive assessment appointment costing EUR 369. If necessary, a day-long outpatient consultation can be arranged, costing EUR 1,408.

The consultation and assessment process for minors at the specialist settings of TAYS or HUS costs EUR 4,300. If it is determined that this process would be untimely, the minimum cost is EUR 640. An initial assessment / consultation by phone costs EUR 100.

The planning and monitoring costs for pubertal suppression are EUR 2,000 for the first year, and EUR 1,200 for subsequent years. The costs for the planning and monitoring of hormone treatments are a minimum of EUR 400 per year.

These costs do not take into account the additional costs of psychosocial support provided in the local level, the possible need for psychiatric treatment, or hormone treatment medication costs.

8. Summary of the Recommendations

PALKO / COHERE maintains the following:

1. For the treatment of gender dysphoria due to variations in gender identity in minors, psychosocial support should be provided in school and student healthcare and in primary healthcare, and there must be sufficient competency to provide such support.
2. Consultation with a child or youth psychiatrist and the necessary psychiatric treatment and psychotherapy should be arranged locally according to the level of treatment needed.
3. If a child or young person experiencing gender-related anxiety has other simultaneous psychiatric symptoms requiring specialised medical care, treatment according to the nature and severity of the disorder must be arranged within the services of their own region, as no conclusions can be drawn on the stability of gender identity during the period of disorder caused by a psychiatric illness with symptoms that hamper development.

PALKO / COHERE considers that the consultation, periods of assessment, and treatments by the research group on the gender identity of minors at TAYS or HUS must be carried out according to the following principles:

1. Children who have not started puberty and are experiencing persistent, severe anxiety related to gender conflict and/or identification as the other sex may be sent for a consultation visit to the research group on the gender identity of minors at TAYS or HUS. Any need for support beyond the consultation visit or need for other psychiatric treatment should be addressed by local services according to the nature and severity of the problem.

2. If a child is diagnosed prior to the onset of puberty with a persistent experience of identifying as the other sex and shows symptoms of gender-related anxiety, which increases in severity in puberty, the child can be guided at the onset of puberty to the research group on the gender identity of minors at TAYS or HUS for an assessment of the need for treatment to suppress puberty. Based on these assessments, puberty suppression treatment may be initiated on a case-by-case basis after careful consideration and appropriate diagnostic examinations if the medical indications for the treatment are present and there are no contraindications. Therapeutic amenorrhea, i.e. prevention of menstruation, is also medically possible.

3. A young person who has already undergone puberty can be sent to the research clinic on the gender identity of minors at TAYS or HUS for extensive gender identity studies if the variation in gender identity and related dysphoria do not reflect the temporary search for identity typical of the development stage of adolescence and do not subside once the young person has had the opportunity to reflect on their identity but rather their identity and personality development appear to be stable.

4. Based on thorough, case-by-case consideration, the initiation of hormonal interventions that alter sex characteristics may be considered before the person is 18 years of age only if it can be ascertained that their identity as the other sex is of a permanent nature and causes severe dysphoria. In addition, it must be confirmed that the young person is able to understand the significance of irreversible treatments and the

benefits and disadvantages associated with lifelong hormone therapy, and that no contraindications are present.

5. If a young person experiencing gender-related anxiety has experienced or is simultaneously experiencing psychiatric symptoms requiring specialized medical care, a gender identity assessment may be considered if the need for it continues after the other psychiatric symptoms have ceased and adolescent development is progressing normally. In this case, a young person can be sent by the specialized youth psychiatric care in their region for an extensive gender identity study by the TAYS or HUS research group on the gender identity of minors, which will begin the diagnostic studies. Based on the results of the studies, the need for and timeliness of medically justified treatments will be assessed individually.

Surgical treatments are not part of the treatment methods for dysphoria caused by gender-related conflicts in minors. The initiation and monitoring of hormonal treatments must be centralized at the research clinics on gender identity at HUS and TAYS.

9. Additional Evidence Gathering and Monitoring the Effectiveness of Recommendations

Moving forward, the following information must be obtained about the patients diagnosed and receiving treatments in Finland before re-evaluating these recommendations:

- Number of new patient referrals
- Number of patients starting the assessment period, and numbers of new transgender (F64.0) vs “other gender” (F64.8) diagnoses
- Whether the diagnosis remains stable or changes during the assessment phase
- Number of patients discontinuing the assessment period and the reasons for the discontinuation
- Adverse effects of treatments (especially long-term effects and effect on fertility)
- Number of patients regretting hormone therapy
- Analysis of the effects of the assessment and the treatment period on gender dysphoria outcomes, as measured by the Gender Congruence and Life Satisfaction Scale (GCLS)
- Analysis of the effects of the assessment and the treatment period on functional capacity and quality of life
- The prevalence of co-occurring psychiatric diagnoses (especially neurodevelopmental diagnoses F80-F90) among those diagnosed with / seeking treatment for gender dysphoria, and whether the presence of these co-occurring diagnoses impacts the ability to achieve the desired outcome (e.g. decreased dysphoria) in the assessment or the treatment phase.
- Whether the assessment and treatment periods lead to a reduction of suicide attempts
- Whether the assessment and treatment periods lead to a reduction in depression and distress

10. Appendices

Preparatory Memorandum, with Appendices 1-5.

DEFENDANT'S EXHIBIT 13

ACADÉMIE NATIONALE DE MÉDECINE

FONDÉE LE 20 DÉCEMBRE 1820

Medicine and gender transidentity in children and adolescents

Press release of the French National Academy of Medicine[1]

February 25, 2022

Gender transidentity is the strong sense, for more than 6 months, of identification with a gender different from that assigned at birth. This feeling can cause a significant and prolonged suffering, which can lead to a risk of suicide (a). No genetic predisposition has been found.

The recognition of this disharmony is not new, but a very strong increase in the demand for physicians for this reason has been observed (1, 2) in North America, then in the countries of northern Europe and, more recently, in France, particularly in children and adolescents. For example, a recent study within a dozen high schools in Pittsburgh revealed a prevalence that was much higher than previously estimated in the United States (3): 10% of students declared themselves to be transgender or non-binary or of uncertain gender (b). In 2003, the Royal Children's Hospital in Melbourne had diagnosed gender dysphoria in only one child, while today it treats nearly 200.

Whatever the mechanisms involved in the adolescent – overuse of social networks, greater social acceptability, or example in the entourage - this epidemic-like phenomenon results in the appearance of cases or even clusters in the immediate surroundings (4). This primarily social problem is based, in part, on a questioning of an excessively dichotomous vision of gender identity by some young people.

The medical demand is accompanied by an increasing supply of care, in the form of consultations or treatment in specialized clinics, because of the distress it causes rather than a mental illness per se. Many medical specialties in the field of pediatrics are concerned. First of all psychiatry, then, if the transidentity appears real or if the malaise persists, endocrinology gynecology and finally surgery are concerned.

However, a great medical caution must be taken in children and adolescents, given the vulnerability, particularly psychological, of this population and the many undesirable effects, and even serious complications, that some of the available therapies can cause. In this respect, it is important to recall the recent decision (May 2021) of the Karolinska University Hospital in Stockholm to ban the use of hormone blockers.

Although, in France, the use of hormone blockers or hormones of the opposite sex is possible with parental authorization at any age, the greatest reserve is required in their use, given the

[1] This Press release, adopted by the French Academy of Medicine on February 25, 2022, by 59 votes for, 20 against and 13 abstentions, was approved, in its revised version, by the Board of Directors on February 28, 2022.

side effects such as impact on growth, bone fragility, risk of sterility, emotional and intellectual consequences and, for girls, symptoms reminiscent of menopause.

As for surgical treatments, in particular mastectomy, which is authorized in France from the age of 14, and those involving the external genitalia (vulva, penis), their irreversible nature must be emphasized.

Therefore, faced with a request for care for this reason, it is essential to provide, first of all, a medical and psychological support to these children or adolescents, but also to their parents, especially since there is no test to distinguish a "structural" gender dysphoria from transient dysphoria in adolescence. Moreover, the risk of over-diagnosis is real, as shown by the increasing number of transgender young adults wishing to "detransition". It is therefore advisable to extend as much as possible the psychological support phase.

The National academy of medicine draws the attention of the medical community to the increasing demand for care in the context of gender transidentity in children and adolescents and recommends:

- A psychological support as long as possible for children and adolescents expressing a desire to transition and their parents;

- In the event of a persistent desire for transition, a careful decision about medical treatment with hormone blockers or hormones of the opposite sex within the framework of Multi-disciplinary Consultation Meetings;

- The introduction of an appropriate clinical training in medical studies to inform and guide young people and their families;

- The promotion of clinical and biological as well as ethical research, which is still too rare in France on this subject.

- The vigilance of parents in response to their children's questions on transidentity or their malaise, underlining the addictive character of excessive consultation of social networks which is both harmful to the psychological development of young people and responsible, for a very important part, of the growing sense of gender incongruence.

Glossary:

a. Gender dysphoria is the medical term used to describe the distress resulting from the incongruence between the felt gender and the gender assigned at birth (5).

b. A non-binary person is a person whose gender identity is neither male nor female.

c. A transgender person adopts the appearance and lifestyle of a sex different from that assigned at birth. Whether born male or female, the transgender persons changes, or even rejects, their original gender identity. The sex registered on his or her civil status does not correspond to the appearance he or she sends back. This does not necessarily lead to a therapeutic approach.

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DEFENDANT'S EXHIBIT 14

Recognising and addressing the mental health needs of people experiencing Gender Dysphoria / Gender Incongruence

August 2021

Position statement 103

Summary

This position statement developed by the Royal Australian and New Zealand College of Psychiatrists (RANZCP) provides an overview of Gender Dysphoria and highlights the importance of respecting an individual's gender identity.

Purpose

This position statement developed by the Royal Australian and New Zealand College of Psychiatrists (RANZCP) provides an overview of Gender Dysphoria and highlights the importance of respecting an individual's gender identity. This statement offers insight into the key issues relevant to the mental health needs of people experiencing Gender Dysphoria and guidance is provided on how psychiatrists and mental health services can support individuals constructively. People experiencing Gender Dysphoria may experience a disproportionate level of mental illness and psychological distress. This position statement makes recommendations for enhancing the mental health sector's responsiveness to these needs.

Key messages

- Gender Dysphoria is associated with significant distress.
- There are polarised views and mixed evidence regarding treatment options for people presenting with gender identity concerns, especially children and young people. It is important to understand the different factors, complexities, theories, and research relating to Gender Dysphoria.
- It is important that there is adequate, person-centred care, for the mental health needs of people experiencing Gender Dysphoria.
- Psychiatrists play a crucial role in caring for the mental health needs of people experiencing Gender Dysphoria.
- Psychiatrists should act in a manner which is supportive, ethical, and non-judgmental.
- Comprehensive assessment is crucial. Assessment and treatment should be evidence-informed, fully explore the patient's gender identity, the context in which this has arisen, other features of mental illness

and a thorough assessment of personal and family history. This should lead to a formulation. The assessment will be always responsive to and supportive of the person's needs.
- Psychiatrists must have regard to the relevant laws and professional standards in relation to assessing capacity and obtaining consent, including the RANZCP Code of Ethics.
- Gender Dysphoria is an emerging field of research and, at present, there is a paucity of evidence. Better evidence in relation to outcomes, especially for children and adolescents is required.

Definition

Gender Dysphoria, as defined in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), refers to marked incongruence between one's experienced or expressed gender and one's assigned gender, associated with clinically significant distress or impairment in functioning.[1] Gender Incongruence is defined in the International Classification of Diseases 11th revision (ICD-11) as is 'a marked and persistent incongruence between an individual's experienced gender and the assigned sex'.[2]

Terminology

The RANZCP acknowledges the importance of using appropriate terminology when discussing issues of sexual, sex and gender identity.[3] Inclusive language engenders respect and promotes visibility for important issues, and this is integral to improving the health of LGBTIQ+ people.[4] The key terminology section below provides an overview of some key terms used in Australia and New Zealand.

It is important to be mindful of the importance of individual terminology preferences when talking about someone's sexual orientation or gender identity. Using the individual's preferred terms, especially pronouns, is very important for trans, gender diverse and non-binary people. Healthcare providers should not refer to someone using terms or pronouns that are against the individual's wishes. For example, an individual may wish to be referred to by the pronouns 'they and them' so as to avoid the gendered pronouns 'she' and 'he', and this should be respected. It is important to also be aware of the rapidity with which language and terminology can change and develop in this area, and to consider additional research or inquiry with relevant organisations as appropriate (please refer to the list of resources below for more information).

Key Terminology

- **Transphobia** encompasses a range of negative attitudes and feelings such as hatred, disgust, contempt, prejudice and fear towards people who are gender variant.
- **Trans,** or **TGD (trans and gender diverse)** are commonly used to describe a broad range of non-conforming gender identities or expressions including **transgender, agender** (having no gender), **bigender** (identifying as both a woman and a man), or **non-binary** (neither woman nor man). Some people may describe themselves as **MTF/M2F** (male-to-female), **FTM/F2M** (female-to-male), **AFAB** (assigned female at birth) or **AMAB** (assigned male at birth). The term **genderqueer** is used to refer to gender identity that does not conform to sociocultural norms. **Gender fluid** is used to refer to gender identity which shifts over time.
- For **TGDNB** (trans, gender diverse and non-binary) people, preferred pronouns may include 'he/him', 'she/her', 'they/them' or neopronouns like 'zi/zim'.
- Some Aboriginal and Torres Strait Islander peoples use the term **sistergirl** to refer to sex assigned at birth males who live partly or fully as women and **brotherboy** to refer to sex assigned at birth females who live partly or fully as men.[3]
- **Takatāpui** as a self-descriptor is often used by Māori to describe non-binary gender and/or sexual identity. Specific meaning can vary depending on context.[5] There are several Māori words for transgender people, including whakawahine (trans woman) and **whakatāne** (trans man).[6]

- In Pacific Island cultures, there are a number of gender-diverse identities including the Samoan **fa'afafine** and Tongan **fakaleiti**.[7]

Background

People experiencing Gender Dysphoria should be supported by mental health services to navigate their experience in a constructive way. Gender Dysphoria can emerge in a variety of ways. Each case should be assessed by a mental health professional, which will frequently be a psychiatrist, with the person at the centre of care. It is important the psychological state and context in which Gender Dysphoria has arisen is explored to assess the most appropriate treatment.

The views about whether psychiatric diagnosis is warranted for people who experience incongruence of gender identity are changing.[8] While 'Gender Dysphoria' is classified as a mental disorder in DSM-5, ICD-11 classifies the condition 'Gender Incongruence' not as a 'mental, behavioural and neurodevelopmental disorder' but as a 'condition related to sexual health'.[1, 2] ICD-11 has undergone significant revisions to ensure that disorders relating to sexuality and gender identity reflect contemporary evidence while appropriately distinguishing between health conditions and private behaviours.[9]

Gender Dysphoria continues to be widely debated across jurisdictions in Australia and New Zealand. The RANZCP has developed this position statement from the perspective of psychiatry.

Supporting people experiencing Gender Dysphoria/Gender Incongruence

There is evidence that people who experience incongruence between their gender identity and assigned gender have higher levels of mental illness than the general population.[10] In a retrospective study, Reisner et al (2015) found higher rates of depression, anxiety, suicidal ideation and self-harm in youth who identified as transgender.[11]

Data suggest that the number of people seeking help for gender identity issues has increased worldwide, with referrals to gender clinics increasing across age groups, including amongst children and adolescents.[12, 13] Clinics seeing young people have also reported an increasing preponderance of sex assigned at birth females among those seeking intervention and a co-occurrence of autism spectrum disorder and Gender Dysphoria. [14, 15]

Gender Dysphoria emerges in many different ways and is associated with significant distress for those who experience it. However, Gender Incongruence is not in and of itself pathological. There are polarised views and mixed evidence regarding treatment options for people presenting with gender identity concerns, especially children and young people.

The World Professional Association for Transgender Health (WPATH) uses the terminology "real life experience" defining it as "the act of fully adopting a new or evolving gender role or gender presentation in everyday life".[16] Real life experience allows transgender individuals who wish to permanently change their gender role, to transition from imagined experience to a lived experience. This experience can differ between individuals, for some the experience is liberating, whereas others can experience disappointment due to transition not living up to the desired expectation.[17]

A major challenge for clinicians working with children and adolescents who present for treatment of Gender Dysphoria is the impact of polarised socio-political discourse on clinical assessment and decision-making. Polarised views can be unhelpful and can make the task of clinicians assisting young people presenting with complex presentations more difficult.[18] Whilst these debates must be acknowledged, the most important goal currently is to ensure that there is adequate care available to meet the mental health needs of people experiencing Gender Dysphoria.

Role of psychiatrists

There are a number of guidelines and resources available which relate to Gender Dysphoria. [19-27] The RANZCP does not preference any specific guidelines. The RANZCP encourages psychiatrists to be aware there are multiple perspectives and views.

There is some evidence to suggest positive psychosocial outcomes for those who are supported in their gender identity.[28] However, evidence and professional opinion is divided as to whether an affirmative approach should be taken in relation to treatment of transgender children or whether other approaches are more appropriate.[24]

A gender affirmative approach endorses the belief system that children should be able to 'live in the gender that feels most real or comfortable to that child and to express that gender with freedom from restriction, aspersion, or rejection' therefore the child's statements regarding their gender identity should not be questioned, but instead accepted.[29] Affirmative approaches may include consideration of the need for medical treatments including gender affirming hormones, gonadotrophin releasing hormone analogues (GnRH) (in children and adolescents) and surgery. Approaches which don't include medical treatments may focus on utilising psychotherapy to aid individuals with Gender Dysphoria in exploring their gender identity, and aid alleviation of any co-existing mental health concerns identified in screening and assessment.[24]

The RANZCP endorses practice which supports and validates the identity, strength, and experience of the individual, recognising that all experiences of gender are equally healthy and valuable. In all cases, clinicians have a crucial role in empathetically supporting the individual and family/whānau assertions and lived experiences. The RANZCP acknowledges the dynamic changes in a child or adolescent's identity and brain development, appreciating the inherent complexities in the clinical care and assessment of the individual.

Mental health professionals should acknowledge the concerns of children, adolescents, and their families whilst not expressing any negative attitudes towards experiences of Gender Dysphoria. Acceptance, and alleviation of secrecy can provide relief to individuals experiencing Gender Dysphoria as well as their families.[24]

Psychiatric assessment and treatment should be both based on available evidence and allow for full exploration of the person's gender identity.[20] The RANZCP emphasises the importance of the psychiatrist's role to undertake thorough assessment and evidence-based treatment ideally as part of a multidisciplinary team, especially highlighting co-existing issues which may need addressing and treating. Psychiatric assessment and treatment must also occur in accordance with professional standards, and in a way which is person-centred, responsive to and supportive of the person's needs. Psychosocial support should be continuously offered and provided to people and their families before, during and after any treatment to maximise positive mental health outcomes.[20] If appropriate, psychiatrists can additionally facilitate the assessment of eligibility, preparation and referral for treatment.[24]

Mental health professionals including psychiatrists should maintain a collaborative and multidisciplinary approach to the treatment of Gender Dysphoria. Psychiatrists should discuss progress and obtain peer consultation from other professionals competent in the assessment and treatment of Gender Dysphoria, within both mental health and other medical disciplines.[24]

Health professionals should also be aware of ethical and medicolegal dilemmas in relation to medical and surgical treatment for people experiencing Gender Dysphoria. Psychiatrists should practise within the relevant laws and accepted professional standards in relation to assessing capacity and obtaining consent, including the RANZCP Code of Ethics.[30] Consent and authorisation for children and adolescents to commence GnRH and gender affirming hormones are subject to specific legislation in Australia and New Zealand. The legal position is rapidly changing, with the implications for policy and practice differing by jurisdiction. It is important that psychiatrists are aware of the policies and practices within the jurisdiction in which they work.

Given the complexity of these issues, it is essential that sufficient information is provided to people (and their family/whānau, or carer where relevant) to enable informed consent.[31] Further, evidence for clinical decisions about whether a child or adolescent is capable and competent to consent to treatment should be clearly recorded. In all cases, the risks and benefits of different treatments must be carefully assessed and balanced by the multidisciplinary team providing care and support to the person experiencing Gender Dysphoria.

Research on Gender Dysphoria is still emerging. At present, there is a paucity of quality evidence on the outcomes of those presenting with Gender Dysphoria. In particular, there is a need for better evidence in relation to outcomes for children and young people.[20] The RANZCP supports further research being undertaken into the long-term effects of medical and surgical affirming treatment in all age groups, including children and adolescents. Findings from the

Australian Trans20 longitudinal cohort study and Gender identity Longitudinal Experience (GENTLE) cohort study are expected to improve our understanding.[32, 33] Such research is crucial in ensuring that individuals can safely access evidence-based therapies for Gender Dysphoria/Gender Incongruence as needed.[34, 35]

Recommendations

The RANZCP recommends the following actions to support the mental health needs of people experiencing Gender Dysphoria/Gender Incongruence:

- Psychiatrists should engage with people experiencing Gender Dysphoria in a way which is person-centred, non-judgmental and cares for their mental health needs.
- Assessment and treatment should be based on the best available evidence and fully explore the person's gender identity and the biopsychosocial context from which this has emerged.
- Health services should take steps to accommodate the needs and ensure the cultural safety of people experiencing Gender Dysphoria/Gender Incongruence.
- Further research should be supported and funded in relation to wellbeing and quality of life during and after medical and surgical interventions for Gender Dysphoria/Gender Incongruence.

Further reading

Royal Australian and New Zealand College of Psychiatrists Position Statement 83: Recognising and addressing the mental health needs of the LGBTIQ+ population

Responsible committee: Practice, Policy and Partnerships Committee

References ›

DEFENDANT'S EXHIBIT 15

Neutral Citation Number: [2020] EWHC 3274 (Admin)

Case No: CO/60/2020

IN THE HIGH COURT OF JUSTICE
ADMINISTRATIVE COURT
DIVISIONAL COURT

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 01/12/2020

Before :

THE PRESIDENT OF THE QUEEN'S BENCH DIVISION
LORD JUSTICE LEWIS
MRS JUSTICE LIEVEN

- -

Between :

(1) QUINCY BELL
(2) MRS A

Claimants

and

THE TAVISTOCK AND PORTMAN NHS FOUNDATION TRUST

Defendant

NATIONAL HEALTH SERVICE COMMISSIONING BOARD (NHS ENGLAND)

Interested Party

(1) UNIVERSITY COLLEGE LONDON HOSPITALS NHS FOUNDATION TRUST
(2) LEEDS TEACHING HOSPITALS NHS TRUST
(3) TRANSGENDER TREND LTD

Interveners

Mr Jeremy Hyam QC and Mr Alasdair Henderson (instructed by **Sinclairslaw**) for the **Claimants**
Ms Fenella Morris QC and Ms Nicola Kohn (instructed by **DAC Beachcroft**) for the **Defendant**
The Interested Party did not appear and was not represented
Mr John McKendrick QC (instructed by **Hempsons**) for the **First and Second Interveners**
Mr Paul Skinner and Mr Aidan Wills (instructed by **Ai Law)** for the **Third Intervener**
Hearing dates: **7 and 8 October 2020**

- -

Approved Judgment

I direct that pursuant to CPR PD 39A para 6.1 no official shorthand note shall be taken of this Judgment and that copies of this version as handed down may be treated as authentic.

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THE PRESIDENT OF THE QUEEN'S BENCH DIVISION
LORD JUSTICE LEWIS
MRS JUSTICE LIEVEN

Dame Victoria Sharp P., Lord Justice Lewis, Lieven J.

SECTION A: INTRODUCTION AND BACKGROUND

1. This is the judgment of the court.

2. This is a claim for judicial review of the practice of the defendant, the Tavistock and Portman NHS Foundation Trust, through its Gender Identity Development Service (GIDS) and the first and second Interveners (the Trusts) of prescribing puberty-suppressing drugs to persons under the age of 18 who experience gender dysphoria.

3. Gender dysphoria or GD is a condition where persons experience distress because of a mismatch between their perceived identity and their natal sex, that is, their sex at birth. Such persons have a strong desire to live according to their perceived identity rather than their natal sex.

4. Those with gender dysphoria may be referred to GIDS. GIDS may, in turn, refer them to one of two NHS Trusts (the first and second Interveners) whose clinicians may be prepared to undertake medical interventions in relation to those with gender dysphoria. We are concerned in this case with the administration of gonadotropin-releasing hormone agonists (GnRHa) which are hormone or puberty blocking drugs (also called PBs) to suppress the physical developments that would otherwise occur during puberty.

5. Puberty blocking drugs can in theory be, and have in practice been, prescribed for gender dysphoria through the services provided by the defendant to children as young as 10. It is the practice of the defendant, through GIDS, to require the informed consent of those children and young persons to whom such drugs are prescribed.

6. The issue at the heart of this claim is whether informed consent in the legal sense can be given by such children and young persons.

7. The claimants' case is that children and young persons under 18 are not competent to give consent to the administration of puberty blocking drugs. Further, they contend that the information given to those under 18 by the defendant is misleading and insufficient to ensure such children or young persons are able to give informed consent. They further contend that the absence of procedural safeguards, and the inadequacy of the information provided, results in an infringement of the rights of such children and young persons under Article 8 of the European Convention for the Protection of Human Rights and Fundamental Freedoms (the Convention).

8. In our view, it is appropriate to consider first, whether a child under 16, or a young person between 16 and 18, can give the requisite consent; and secondly, if, in principle, they can do so, whether the information provided by the defendant and the Trusts is adequate for achieving informed consent.

9. The court in this case is concerned with the legal requirements of the process of obtaining consent for the carrying out of medical treatment. In considering this issue the court has had to consider evidence on the use of PBs, their impact on the patients, both in the short and long term, and the evidence of the efficacy of their use. The court is not deciding on the benefits or disbenefits of treating children with GD with PBs, whether in the long or short term. The court has been given a great deal of evidence

about the nature of GD and the treatments that may or may not be appropriate. That is not a matter for us. The sole legal issue in the case is the circumstances in which a child or young person may be competent to give valid consent to treatment in law and the process by which consent to the treatment is obtained.

10. We have had placed before us written evidence from a wide variety of those engaged in issues surrounding GD and a number of individuals who have been treated or are still being treated with PBs.

11. On behalf of the defendant and the Trusts there are statements from Dr Polly Carmichael, Director of GIDS, Professor Gary Butler, Consultant in Paediatric Endocrinology at University College Hospital London, and Dr Nurus-Sabah Alvi, Consultant in Paediatric Endocrinology at Leeds General Infirmary and Clinical Lead for Endocrine Liaison Clinics of the GIDS, Leeds. These witnesses describe the process that the children and young people go through at GIDS and at the Trusts. The court has also had a wide range of evidence from a variety of people concerned with the treatment of those under 18 with PBs. We will refer to that evidence and its sources as appropriate below. Our references to a child or children will be to those under the age of 16, and to young person(s) to anyone under the age of 18, save where it is clear from the context that we are referring to anyone under the age of 18.

Gender Dysphoria

12. Gender dysphoria is defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) which provides for one overarching diagnosis of gender dysphoria with separate specific criteria for children and for adolescents and adults:

> "In adolescents and adults gender dysphoria diagnosis involves a difference between one's experienced gender and assigned gender, and significant distress or problems functioning. It lasts at least six months and is shown by at least two of the following:
>
> 1. A marked incongruence between one's experienced / expressed gender and primary and / or secondary sex characteristics
>
> 2. A strong desire to be rid of one's primary and / or secondary sex characteristics
>
> 3. A strong desire for the primary and / or secondary sex characteristics of the other gender
>
> 4. A strong desire to be of the other gender
>
> 5. A strong desire to be treated as the other gender
>
> 6. A strong conviction that one has the typical feelings and reactions of the other gender.
>
> In children, gender dysphoria diagnosis involves at least six of the following and an associated significant distress or impairment in function, lasting at least six months:

1. A strong desire to be of the other gender or an insistence that one is the other gender

2. A strong preference for wearing clothes typical of the other gender

3. A strong preference for cross-gender roles in make-believe play or fantasy play

4. A strong preference for toys, games or activities stereotypically used or engaged in by the other gender

5. A strong preference for playmates of the other gender

6. A strong rejection of toys, games and activities typical of one's assigned gender

7. A strong dislike of one's sexual anatomy

8. A strong desire for the physical sex characteristics that match one's experienced gender."

Gender Identity Development Service (GIDS)

13. The defendant is an NHS Foundation Trust employing specialist staff including child psychologists, psychotherapists, psychiatrists, social workers, family therapists and nurses. Since 1989 it has provided a gender identity development service, a specialised service providing care to patients up to the age of 18 suffering from GD. GIDS is commissioned by the National Health Service Commissioning Board. The statutory mechanism is that under section 3B of the NHS Act 2006, the Secretary of State has the power to require NHS England to arrange services or facilities as may be prescribed by regulations. The Secretary of State has exercised that power (pursuant to Regulation 11 of the National Health Service Commissioning Board and Clinical Commissioning Groups (Responsibilities and Standing Rules) Regulations 2012/2296, which concerns specified services for rare and very rare conditions) that NHS England must arrange for the provision of services including, pursuant to para 56 of Schedule 4, a gender identity development service specifically for children and adolescents in addition to gender dysphoria services more generally (para 57).

14. Schedule 2, Part A of the NHS Standard Contract, pursuant to which GIDS is provided, sets out the Service Specification which establishes the context of the service, its aims and objectives and the manner in which it will be delivered. As set out in the Service Specification, the service is commissioned to provide specialist assessment, consultation and care including psychological support and physical treatments. The purpose of the treatment is *"to help reduce the distressing feelings of a mismatch between their natal (assigned) sex and their gender identity."* The service also provides support to family and carers of children and young persons so affected.

15. GIDS recognises three stages of physical intervention that may be appropriate in cases of GD. Stage 1 is the administration of GnRHa (one form of puberty blocker). This is clinically appropriate for children and young people who have reached Tanner Stage 2

of puberty and above. Tanner Stage 2 marks the beginning of the physical development of puberty. In natal girls this is the start of development of the breasts, and in boys the testicles and scrotum begin to get larger. Stage 2 of the treatment is the administration of cross-sex hormones (CSH) which can only be prescribed from around the age of 16. Stage 3 is gender reassignment surgery which is only available via adult services to people aged over 18.

16. GIDS takes referrals from across England and Wales and from a wide range of professionals in the health, social services and education sectors, and the voluntary sectors. When a referral is made, the case will be discussed with the relevant regional team. If the intake is successful, then the child will then progress to the GIDS waiting list.

17. As at November 2019 the waiting time for a first assessment at GIDS was between 22-26 months. When a young person reaches the top of the waiting list, they will be invited to the first of a number of assessment appointments at GIDS. The assessment process laid out in the Service Specification anticipates that the assessment process will typically span three to six sessions over 6 months or longer. Most young people will have more sessions than this, and the younger the age the more sessions are likely.

18. Dr Carmichael said that during assessments young persons will be asked, for example, about: the onset of their gender dysphoria; the consistency of their feelings about their gender; how they identify (cross-gender, non-binary, etc); their relationships with peers and family members; their social functioning in general, thoughts about or experience of puberty; their relationship to their bodies; their attractions or romantic relationships as appropriate based on their age and maturity; and their hopes and expectations for the future.

19. As this case is brought by way of judicial review of the GIDS policy and practice, rather than a challenge to an individual treatment decision, it is not possible to give a detailed analysis of the facts of an individual case and the degree to which all the matters referred to by Dr Carmichael were explored in the particular case. We refer at paras 78 to 89 below to the evidence of the experience of the first claimant and some of the other patients of the GIDS service.

20. Dr Carmichael sets out the broad range of professionals who work within GIDS, their specialism in working with young people with GD and the care that is taken when discussing the young person's expression of their gender identity.

21. At the end of the assessment period the clinicians will agree a care plan with the young person and their family. Where the young person fulfils the criteria in the Service Specification and has reached at least Tanner Stage 2 of puberty, they will be referred by GIDS to the first and second Interveners for consultation and/or physical assessment with endocrinologists with a view to being prescribed PBs. Dr Carmichael explains that before any referral to the Trusts, GIDS clinicians discuss the treatment with the young person, including explaining side effects.

The Age and Patient Group for Puberty Blockers

22. Until 2011 PBs were only available at GIDS for those aged 16 or older. In 2011 PBs started to be prescribed for those aged 12-15 and in mid-puberty. This was first done between 2011-14 at University College London Hospital (UCLH) under an approved research study known as the Early Intervention Study. The Study took an uncontrolled treatment cohort of 12-15 year olds with established and persistent GD in England. The Study recruited children for 3 years, but there was then a period until February 2019 when the last cohort member began the next stage of therapy (cross-sex hormones).

23. One of the issues raised in these proceedings is the non-existent or poor evidence base, as it is said to be, for the efficacy of such treatment for children and young persons with GD.

24. In that context, we note that though this research study was commenced some 9 years ago, at the time of the hearing before us the results of this research had yet to be published. Dr Carmichael says in her witness statement dated 2 February 2020 that a paper is now being finalised for publication. At the hearing we were told that that this paper had been submitted for peer-review but that Professor Viner, one of the authors of it, had yet to respond to issues raised by the reviewers, as he has been otherwise engaged in working on issues relating to the coronavirus pandemic.

25. The court was however provided with a paper entitled *"The Early Intervention Study. An evaluation of early pubertal suppression in a carefully selected group of adolescents with "Gender Identity Disorder". A statement and update on the Early Intervention Study (dated 2020)".* We refer further to this paper at para 73 below.

26. There are now two types of endocrine clinic: a clinic for under 15s, referred to as the early intervention clinic, and a clinic for over 15s. The Service Specification states that the early intervention clinic will continue to follow the 2011 Protocol, save that PBs will now be considered for any children *under the age of 12* if they are in established puberty.

27. The age distribution of those treated with PBs in each year between 2011 and 2020 was not provided to the court. Although the defendant and the Trusts said that such data was available, in the sense that the ages of the children are known, the data has not been collated for each year. However, Ms Ailsa Swarbrick, the Divisional Director of Gender Services at the Trust, has presented evidence in relation to patients referred to endocrinology services in 2019-20 and those treated in earlier years but who were discharged from GIDS in 2019-2020. This work was done in response to recommendations in the GIDS Review Action Plan 2019 (a Review commissioned by the Trust following a report by Dr David Bell) that data would help to inform clinical and service developments and a process of continuous improvement.

28. We note here that we find it surprising that such data was not collated in previous years given the young age of the patient group, the experimental nature of the treatment and the profound impact that it has.

29. As it is, for the year 2019/2020, 161 children were referred by GIDS for puberty blockers (a further 10 were referred for other reasons). Of those 161, the age profile is as follows:

> 3 were 10 or 11 years old at the time of referral;
>
> 13 were 12 years old;
>
> 10 were 13 years old;
>
> 24 were 14 years old;
>
> 45 were 15 years old;
>
> 51 were 16 years old;
>
> 15 were 17 or 18 years old.

For the year 2019/20, therefore, 26 of the 161 children referred were 13 or younger; and 95 of the 161 (well over 50%) were under the age of 16.

30. It follows from the information that the court does have on age distribution that some young people could be on PBs for a number of years, in the most extreme case for 5 years between the age of 10 and when they start CSH at 16.

31. Apart from the age distribution, there are other aspects of the patient group which are relevant to this case. The number of referrals to GIDS has increased very significantly in recent years. In 2009, 97 children and young people were referred. In 2018 that number was 2519.

32. Further, in 2011 the gender split was roughly 50/50 between natal girls and boys. However, in 2019 the split had changed so that 76 per cent of referrals were natal females. That change in the proportion of natal girls to boys is reflected in the statistics from the Netherlands (Brik et al "*Trajectories of Adolescents Treated with Gonadotropin-Releasing Hormone Analogues for Gender Dysphoria"* 2018). The defendant did not put forward any clinical explanation as to why there had been this significant change in the patient group over a relatively short time.

33. It is recorded in the GIDS Service Specification and the wider literature that a significant proportion of those presenting with GD have a diagnosis of Autistic Spectrum Disorder (ASD). The Service Specification says:

> "There seems to be a higher prevalence of autistic spectrum disorder (ASD) conditions in clinically referred, gender dysphoric adolescents than in the general adolescent population. Holt, Skagerberg & Dunsford (2014) found that 13.3% of referrals to the service in 2012 mentioned comorbid ASD (although this is likely to be an underestimate). This compares with 9.4% in the Dutch service; whereas in the Finnish service, 26% of adolescents were diagnosed to be on the autism spectrum (Kaltiala-Heino et al. 2015)."

34. The court asked for statistics on the number or proportion of young people referred by GIDS for PBs who had a diagnosis of ASD. Ms Morris said that such data was not available, although it would have been recorded on individual patient records. We therefore do not know the proportion of those who were found by GIDS to be *Gillick* competent who had ASD, or indeed a mental health diagnosis.

35. Again, we have found this lack of data analysis – and the apparent lack of investigation of this issue - surprising.

The process of taking consent

36. The position taken by GIDS is that they will only refer a young person for PBs if they determine that person is competent to give consent, i.e. is *Gillick* competent within the meaning of competence identified in the decision of the House of Lords in *Gillick v West Norfolk and Wisbech Health Authority* [1986] AC 112.

37. Dr Carmichael explained that GIDS takes consent from the young person to their case being referred to the Trusts for treatment; however the consent for the actual prescription of the PBs is taken separately by the clinicians working for the Trusts. She set out the careful process by which GIDS gives information to the young persons and to their parents in order to seek to ensure that the young person is in a position to give valid consent. The court was taken through the statements of Dr Carmichael and Professor Butler and various documents to show the level of information and dialogue that was involved in achieving lawful consent to the treatment. The Service Specification includes Section 3.2 on "Informed Consent". This states *"The consequences of treatment decisions can be significant and life-changing"* and states:

> "All efforts will be made to ensure that clients are aware of the longer term consequences of the endocrine treatments, including implications for fertility, and the decision of the competence of the client will be jointly made by the endocrine and psychological members of the Service's integrated team.
>
> The current context of treatment decisions about cross sex hormones in adolescence is that there is limited scientific evidence for the long-term benefits versus the potential harms of the intervention. There are also concerns that it is uncertain whether or not a young person will continue to identify as transgender in the future, given that some subsequently identify in a different way."

38. The defendant has recently adopted a Standard Operating Procedure for the taking of consent in GIDS. This has taken 2 years to develop and is dated 31 January 2020. Dr Carmichael says at para 33 of her first statement:

> "In advance of any referral by the Trust of a young person for consideration by an endocrinologist for GnRHa treatment, GIDS clinicians discuss treatment with the young person. This includes, checking that the young person's hopes for treatment are realistic, explaining what the treatment can and cannot do, discussing any potential

> side-effects, discussing fertility and potential impact on genital development for birth registered males. We have developed visual aids to support this process.
>
> UCLH and LTH have collated extensive written information to help young people and their parents further understand the nature of the drugs, their limitations and the possible side effects. These written documents are given to young people at their first endocrine clinic visit. The written documents act as a reference point for patients with questions whilst they contemplate whether they would like to go ahead with the referral, and subsequently with treatment. In particular, informational slides titled "Have you thought about having children in the future?" explains the impact GnRHa treatment can have on fertility in explicit terms. Young people and their families are encouraged to raise any questions with their GIDS clinicians or at their next endocrine clinic visit."

39. Ms Morris emphasised that the process of ensuring that consent could validly be given was a discursive and iterative one that involved multiple discussions and answering any questions the young people or their parents might raise. Dr Carmichael said at para 35: "*The GIDS clinicians make it very clear to children and young people that there are both known and unknown risks associated with GnRHa treatment."* Further, she said at para 41: "*In my experience, those young people we see who are recommended for GnRHa treatment understand the implications and limitations of treatment with GnRHa treatment and are able to consent to this stage of treatment."*

40. Professor Butler described the approach to consent at the Trusts as follows:

> "For those under 15 years of age all the pre-assessment consultations are individual and occur with a consultant or senior clinical fellow on at least two visits. Parental support (or that of their guardian or social services where appropriate) is a pre-requisite for the under 15 year stream. On occasions, a young person is not deemed, on clinical examination, to be at an appropriate stage of puberty so further follow-up visits are arranged thereafter at 6-12 monthly intervals until a person is deemed at an appropriate physical stage for intervention and taking of consent. This also gives the opportunity to judge the level of emotional cognitive and psychosocial maturity, and capacity.
>
> The decisions at UCLH and Leeds do not automatically follow on from those made at the GIDS Tavistock. They are a reassessment of physical maturity and cognitive capacity in their own right. They may be at odds with the Tavistock formulation (an infrequent event) and thus would be returned to the Tavistock MDT for reconsideration."

41. Professor Butler said that in his clinic they are careful to ensure that the force behind the decision to seek treatment comes from the young person themselves and is not a consequence of pressure upon them from others around them. The Trusts work closely

with parents to reach a solution that is satisfactory to all and meets the best interests of the child. His clinic has never sought to apply to the Court under its inherent jurisdiction "against" parental opinions because he is concerned that would cause familial frictions. Equally, he suggested UCLH would not wish to have to apply to the court for consent on behalf of the child because it would delay treatment and put an additional burden on GIDS and the Trusts; and because "*it would also increase the distress suffered by the young people themselves, finding that their right to autonomous decision making had been removed from them.*"

42. Professor Butler said a full written information package is provided to older adolescents. For those under 15 there is an initial individual consultation because of the need for "*individualising the approach for very young people, taking special care to assess their level of knowledge and understanding and they are given the written information package then.*" In relation to impacts on fertility and sexual functioning he says:

> "It is also relevant for the consultation purposes that matters of fertility are discussed and counselling by the team takes place, and the option of meeting a fertility specialist is offered, and often taken up. The options of fertility preservation are discussed with all the young people and it is a requirement of the consent process that they fully understand this at an age appropriate level. This understanding must include that they are unable to have the typical sexual relationship of their identified gender with another person on account of their biological sex organ development, and that other surgical procedures may be necessary later on to achieve this possibility."

43. He then said: "*it is an absolute requirement before starting any treatment that a young person can fully understand this effect on fertility and sexual functioning according to their age and level of maturation.*"

44. The court asked for statistical material on the number, if any, of young people who had been assessed to be suitable for PBs but who were *not* prescribed them because the young person was considered not to be *Gillick* competent to make the decision, whether at GIDS or the Trusts. Ms Morris could not produce any statistics on whether this situation had ever arisen. She suggested that in the main, GIDS would work with the young person to give them further information, discuss the matter further and in some cases wait until they had achieved further maturity. The court gained the strong impression from the evidence and from those submissions that it was extremely unusual for either GIDS or the Trusts to refuse to give PBs on the ground that the young person was not competent to give consent. The approach adopted appears to be to continue giving the child more information and to have more discussions until s/he is considered *Gillick* competent or is discharged.

45. Relevant to the evidence of consent is the evidence of Professor Scott (Director of University College London's Institute of Cognitive Neuroscience). She *"seeks to explain, from a neuroscientific point of view, why I have significant doubts about the ability of young people under the age of 18 years old to adequately weigh and*

appreciate the significant consequences that will result from the decision to accept hormonal treatment for gender dysphoria."

46. She explained the neurological development of adolescents' brains that leads to teenagers making different, more risky decisions than adults. She said further that this is backed up by behavioural studies showing that when decision making is "hot" (i.e. more emotional), under 18 year olds make less rational decisions than when the responses are made in a colder, less emotional context. Her conclusion was that:

> "11. … given the risk of puberty blocking treatment, and the fact that these will have irreversible effects, that have life-long consequences, it is my view that even if the risks are well explained, that in the light of the scientific literature, that it is very possible for an adolescent to be unable to fully grasp the implications of puberty-blocking treatment. All the evidence we have suggests that the complex, emotionally charged decisions required to engage with this treatment are not yet acquired as a skill at this age, both in terms of brain maturation and in terms of behaviour."

Parental consent

47. If a child cannot give consent for treatment because they are not *Gillick* competent then the normal position in law would be that someone with parental responsibility could consent on their behalf. Mr Hyam sought at one point to argue that a decision as to giving PBs would fall outside the scope of parental responsibility because of the nature of the treatment concerned. However, the GIDS practice in relation to acting on parental consent alone is quite clear. In the response to the pre-action protocol letter the defendant said:

> "36. There is a fundamental misunderstanding in your letter, which states that parents can consent to pubertal suspension on behalf of a child who is not capable of doing so. This is not the case for this service, as is clear from the above. Although the general law would permit parent(s) to consent on behalf of their child, GIDS has never administered, nor can it conceive of any situation where it would be appropriate to administer blockers on a patient without their consent. The Service Specification confirms that this is the case."

It follows that is not necessary for us to consider whether parents could consent to the treatment if the child cannot lawfully do so because this is not the policy or practice of the defendant and such a case could not currently arise on the facts.

The effect of Puberty Blockers

48. PBs have been used for many years to stop precocious puberty. This is a condition experienced largely by children aged 7 or under when puberty commences at a very early age. This condition is seen more often in natal girls but sometimes in natal boys. PBs are used to stop this early onset of puberty and the use of them ceases when the child reaches an appropriate age for puberty. As can be seen from the evidence this use of PBs does not interfere with the onset of puberty at a normal biological age and, as such, will not interfere with normal development of puberty through adolescence.

49. The use of PBs in cases of GD is quite different. We have some evidence of the history of this treatment and the meaning of puberty from Professor Hruz (Associate Professor of Paediatrics, Endocrinology and Diabetes at Washington University, St Louis, USA) on behalf of the claimants.

50. In summary, PBs were first used for such treatment at a Dutch gender clinic in the late 1990s. That clinic developed a protocol, often referred to as the Dutch protocol. The Dutch protocol was published in the European Journal of Endocrinology in 2006 and called for puberty suppression to begin at the age of 12 after a diagnosis of GD. Puberty is understood in medicine or biology as a process of physiological change involving the process of maturation of the gonads. Hormones in a part of the brain secrete a gonadotropin-releasing hormone which, in turn, stimulates the pituitary gland to secrete other hormones. These stimulate the growth of the gonads, that is ovaries in females and testes in males. Further hormones are secreted which contribute to the further development of the primary sex characteristics, the uterus in females and the penis and scrotum in males. The hormones contribute to the development of secondary sex characteristics including breasts and wider hips in girls and wider shoulders, deeper voices and increased muscle mass in boys. Further growth hormones are released, which stimulate growth. With regular injection of the PBs there is no progression of puberty and some regression of the first stages of already developed sexual characteristics. This means that in girls *"breast tissue will become weak and may disappear completely"* and in boys *"testicular volume will regress to a lower volume."*

51. Under the Dutch protocol, the introduction of CSH starts at age 16. As Professor Hruz explained:

> "29. Then, starting at age 16, cross-sex hormones are administered while GnRH analogue treatment continues, in order to induce something like the process of puberty that would normally occur for members of the opposite sex. In female-to-male patients, testosterone administration leads to the development of "a low voice, facial and body hair growth, and a more masculine body shape" as well as to clitoral engagement and further atrophying of breast tissue. In patients seeking a male-to-female transition, the administration of estrogens will result in "breast development and a female-appearing body shape." Cross-sex hormone administration for these patients will be prescribed for the rest of their lives."

52. There is some dispute as to the purpose of prescribing PBs. According to Dr Carmichael, the primary purpose of PBs is to give the young person time to think about their gender identity. This is a phrase which is repeated on a number of the GIDS and Trust information documents. The Health Research Authority carried out an investigation into the Early Intervention Study in 2019. Its report was somewhat critical of the description of the purpose and said:

> "The research team described the purpose of pubertal suppression as 'to induce a sex hormone-neutral environment to provide young people with space to decide whether to progress further with gender reassignment treatment as an adult.' This phrase appears to have caused confusion as it has been interpreted by some that the puberty suppression was for use in

> any children presenting to the clinic, that there would be no change in the course of any gender identity dysphoria during this time, and that the child could then choose to progress to cross-sex hormone treatment or to stop treatment with subsequent onset of puberty in the birth gender. It has been noted that the participants in this study and other research involving early puberty suppression have progressed to cross-sex hormones. This has raised concerns that the treatment might be responsible for generating persistence, rather than 'creating space to decide'.
>
> It would have reduced confusion if the purpose of the treatment had been described as being offered specifically to children demonstrating a strong and persistent gender identity dysphoria at an early stage in puberty, such that the suppression of puberty would allow subsequent cross-sex hormone treatment without the need to surgically reverse or otherwise mask the unwanted physical effects of puberty in the birth gender. The present study was not designed to investigate the implications on persistence or desistence of offering puberty suppression to a wider range of patients, it was limited to a group that had already demonstrated persistence and were actively requesting puberty blockers."

53. Professor Butler said that PBs:

> "may have some help or advantage in the support of transgender adolescents in some aspects of mental health functioning, in particular with reducing the risk of reduction of suicidal ideation and actual suicidal actions themselves."

54. See further the reference at para 73 below to the paper presented by Dr Carmichael and Professor Viner in 2014, referring to the Early Intervention Study and the limited evidence of psychological benefit.

55. As is clear from the literature and referred to by the HRA, the other purpose of giving PBs is stopping the development of the physical effects of puberty (something that obviously varies depending on at what age and stage in pubertal development the PBs are commenced) because slowing or preventing the early development of secondary sex characteristics during puberty can make a later transition (both medical and social) to living as the opposite sex easier.

The relationship between Puberty Blockers and Cross-Sex Hormones (CSH)

56. GIDS and the Trust place reliance on the fact that Stage 1 treatment with PBs and Stage 2 treatment (CSH) are separate. Thus, so it is said, it is possible for a young person to come off the PBs at any point and not proceed to taking CSH. On one view, this is correct. However, the evidence that we have on this issue clearly shows that practically all children / young people who start PBs progress on to CSH.

57. No precise numbers are available from GIDS (as to the percentage of patients who proceed from PBs to CSH). There was some evidence based on a random sample of those who in 2019-2020 had been discharged or had what is described as a closing summary from GIDS. However the court did have the evidence of Dr de Vries. Dr de Vries is a founding board member of EPATH (European Professional Association for Transgender Health) and a member of the WPATH (World Professional Association for Transgender Health) Committee on Children and Adolescents and its Chair between 2010 and 2016, and leads the Centre of Expertise on Gender Dysphoria at the Amsterdam University Medical Centre in the Netherlands (CEGD). This is the institution which has led the way in the use of PBs for young people in the Netherlands; and is the sole source of published peer reviewed data (in respect of the treatment we are considering) produced to the court. She says that of the adolescents who started puberty suppression, only 1.9 per cent stopped the treatment and did not proceed to CSH.

58. We were told that the defendant did not have any data recording the proportion of those on puberty blockers who progress to cross-sex hormones. We were told that in part this resulted from the fact that some would have progressed to adult services and would not be recorded by the defendant. Ms Swarbrick had carried out an analysis of a random sample of 312 of 1648 files of patients discharged from GIDS from 1st March 2019 to 4th March 2020. Dr Carmichael summarised this as:

> "…based on a random sample of those referred to GIDS who had been discharged or had a closing summary from GIDS in 19-20 (analysis B) 16% of patients (49 individuals) had accessed the endocrinology service during their time with GIDS. Of those 16%, 55% (27 individuals) were subsequently approved for or accessed cross-sex hormones during their time with GIDS. This number represents 8.7% of all the patients discharged from GIDS that year. We also know that of the 49 patients who were referred to endocrinology for GnRHa whilst at GIDS, two did not commence GnRHa treatment, and a further five were discharged from GIDS without being referred on to another gender service."

59. We find it surprising that GIDS did not obtain full data showing the figures and the proportion of those on puberty blockers who remain within GIDS and move on to cross-sex hormones. Although neither Dr Carmichael nor Professor Butler could give the equivalent figures in the United Kingdom to those from the Netherlands, the language used in their witness statements suggests that a similarly high proportion of children and young people in the United Kingdom move from PBs onto CSH.

The impact of Puberty Blockers and their reversibility

60. Both WPATH and the Endocrine Society in their documentation describe PBs as fully reversible. Professor Butler says that "*we do not know everything about the blocker and as far as we know it is a safe reversible treatment with a well-established history.*" Dr Alvi also referred to the history of the use of PBs as showing that they are fully reversible. However, it is important to note that apart from the Amsterdam study, the history of the use of PBs relied upon in this context is *from the treatment of precocious*

puberty which is a different condition from GD, and where PBs are used in a very different way.

61. Dr de Vries was somewhat more nuanced in her evidence. She said:

> "Puberty blocking treatment is fully reversible (see for example section 2.0 of the Endocrine Society's Clinical Practice Guidelines…). By fully reversible I mean that the administration of puberty blockers in young people has no irreversible physical consequences, for example for fertility, voice deepening or breast growth".

62. At para 20 of her evidence she said:

> "Ethical dilemmas continue to exist around … the uncertainty of apparent long-term physical consequences of puberty blocking on bone density, fertility, brain development and surgical options."

63. The GIDS Early Intervention Young Person Information Sheet states:

> "What are the possible benefits of starting on hormone blockers?
>
> We have looked at other countries who have given this treatment **and the results** suggest that:
>
> - Hormone blockers which block the body's natural sex hormones may improve the way you feel about yourself.
> - If you decide to stop the hormone blockers early **your physical development** will return as usual in your natal gender. **As far as we are aware**, the hormone blockers will not harm your physical or psychological development.
> - Hormone blockers will make you feel less worried about growing up in the wrong body and will give you more time and space to think about your gender identity.
>
> What are the possible disadvantages and risks of the hormone blockers?
>
> - Possible side effects from the hormone blockers are hot flushes, headache, nausea and weight gain.
> - A short term effect is that your bone strength is shown not to grow as fast as it usually would whilst you are on hormone blockers. However, this will resume once your body is exposed to hormones again. That is why we have to do a bone scan every year to check the thickness of your bones. **We do not fully know how hormone blockers will affect bone strength, the development of your sexual organs, body shape or your final adult height. There**

> **could be other long-term effects of hormone blockers in early puberty that we don't yet know about.**
>
> - Hormone blockers could affect your memory, your concentration or the way you feel about your gender and how likely you are to change your mind about your gender identity.
>
> - Hormone blockers could affect your ability to have a baby. It could take 6 to 12 months longer after stopping the hormone blockers before natal boys start making sperm again or natal girls start maturing eggs in their ovaries. However, hormone blockers do not work as a contraceptive. If you are sexually active, please ask your doctor for advice about birth control." (emphasis added)

64. A number of aspects of this asserted reversibility are raised by the claimants. PBs stop the physical changes in the body when going through puberty. But in reliance on the evidence of Professor Levine (Clinical Professor of Psychiatry at Western Reserve University, Ohio) and Professor Hruz, the claimants assert that neurological and psychological changes occurring in puberty are less well understood than the physiological changes. Further, the degree to which neurological differences are caused by biological factors like hormones and genes are matters of debate. Professor Levine set out evidence on the degree to which young people mature through adolescence through both social and personal experiences. For young people on PBs that maturing process is stopped or delayed with potential social and psychological impacts which could be described as non-reversible.

65. Thus, the central point made by the claimants is that although most of the physical consequences of taking PBs may be reversible if such treatment is stopped, the child or young person will have missed a period, however long, of normal biological, psychological and social experience through adolescence; and that missed development and experience, during adolescence, can never be truly be recovered or "reversed".

66. It is to be noted that prior to June 2020, the NHS website on PBs said:

> "The effects of treatment with GnRH analogues are considered to be fully reversible, so treatment can usually be stopped at any time."

67. In June 2020 this section was updated to read as follows:

> "**Little is known about the long-term side effects of hormone or puberty blockers in children with gender dysphoria.**
>
> Although the Gender Identity Development Service (GIDS) advises that is a physically reversible treatment if stopped, **it is not known what the psychological effects may be.**

> **It's also not known whether hormone blockers affect the development of the teenage brain or children's bones**. Side effects may also include hot flushes, fatigue and mood alterations." (emphasis added)

68. A second key part of the argument about reversibility turns on the relationship between PBs and CSH and the degree to which commencing PBs in practice puts a young person on a virtually inexorable path to taking CSH. CSH are to a very significant degree not reversible. As is set out above at para 57 above, a very high proportion of those who start PBs move on to CSH and thus in statistical terms once a child or young person starts on PBs they are on a very clear clinical pathway to CSH.

Evidence base to support the use of Puberty Blockers for Gender Dysphoria

69. The claimants submit that the treatment of PBs for GD is properly described as (i) experimental (ii) a treatment with a very limited evidence base, and (iii) as a highly controversial treatment. The claimants rely on witness statements from a number of undoubted experts in various relevant fields and from academic institutions in the United Kingdom, the USA, Sweden and Australia who refer to the controversial nature of the treatment and its limited evidential support.

70. It is not however the court's role to judge the weight to be given to various different experts in a judicial review. In our view, more important is the evidence from the defendant and the evidence base *it* relies upon for the use of PBs. In the USA the treatment of GD is not an FDA approved use and as such PBs can only be used "off-label". That does not prevent clinicians, whether in the USA or the United Kingdom, from using PBs for this purpose, as long as their use falls within the clinician's professional expertise. Professor Butler explained that it is very common for paediatric medicines to be used off-label and that this factor does not render the treatment in any sense experimental.

71. However, the lack of a firm evidence base for their use is evident from the very limited published material as to the effectiveness of the treatment, however it is measured.

72. Paul Jenkins, Chief Executive of the defendant said:

> "…it is correct that in recent years, some clinicians [at the Trust] have raised their concerns about the use of GnRHa for young people presenting with gender dysphoria. Indeed, some have called for the Trust to alter its practices and have done so in a variety of ways. We are keenly aware that the subject of gender dysphoria raises complex issues and that many have strong opinions about it."

73. The Evaluation Paper on the Early Intervention Study at GIDS, referred to in para 25 above, gives some (albeit limited) material on the outcome of that study. It summarised a meeting paper presented by Dr Carmichael and Professor Viner in 2014 (but not published in a peer review journal) as follows:

> "The reported qualitative data on early outcomes of 44 young people who received early pubertal suppression. It noted that 100% of young people stated that they wished to continue on GnRHa, that 23 (52%) reported an improvement in mood since starting the blocker but that 27% reported a decrease in mood. **Noted that there was no overall improvement in mood or psychological wellbeing using standardized psychological measures**." (emphasis added)

74. Ms Morris submitted it is not for this court to determine clinical disagreements between experts about the efficacy of a treatment. We agree. That is a matter for the relevant NHS and regulatory bodies to oversee and to decide. However the degree to which the treatment is experimental and has, as yet, an unknown impact, does go to the critical issue of whether a young person can have sufficient understanding of the risks and benefits to be able lawfully to consent to that treatment.

Persistence

75. The claimants submit that there is good evidence that for a significant proportion of young people presenting with GD, the condition resolves itself through adolescence without treatment with PBs. Further, that PBs serve to increase the likelihood of GD, and, as such, can be positively harmful to the child or young person's long-term health. According to DSM5: "*in natal males, persistence of [gender dysphoria] has ranged from 2.2% to 30%. In natal females, persistence has ranged from 12% to 50%."* These figures need to be treated with some caution because it may be that the cohort whose persistence was being considered in these statistics was at a lower age and with less clearly established GD than the young people being treated at GIDS.

76. The Dutch study argued that adolescents who show established GD rarely identify as their biological sex. Professor Hruz suggested there may be two reasons for this. It may be that the clinicians made sound diagnoses of persistent GD. Alternatively, it may be that the very fact of the diagnosis and the course of treatment which affirmed that diagnosis (that is, both gender affirmative psychotherapy and the use of PBs) solidified the feeling of cross-gender identification and led the young people to commit to sex reassignment more strongly than they would have done if there had been a different diagnosis and treatment.

77. As already indicated, it is not our role to adjudicate on the reasons for persistence or otherwise of GD. However, the nature of this issue highlights the highly complex and unusual nature of this treatment and the great difficulty there is in fully understanding its implications for the individual young person. In short, the treatment may be supporting the persistence of GD in circumstances in which it is at least possible that without that treatment, the GD would resolve itself.

SECTION B: EVIDENCE OF THE CLAIMANTS AND OTHER INDIVIDUALS

78. The first claimant was born a female. In her witness statement in these proceedings she set out her experience of being prescribed PBs and then CSH. It should be noted that some of the details relating to her treatment and the information she was given (at GIDS and the first defendant) is disputed. This case is a judicial review of the GIDS policy,

not a tort action relating to the specific facts surrounding the first claimant's treatment and it is not necessary therefore to resolve any factual dispute. We simply record the first claimant's account. She describes a highly traumatic childhood. From the age of 4 or 5 she displayed gender non-conformity, associating more with male games and clothes. She felt highly alienated at secondary school and took birth control pills to stop her periods. She felt disgusted by her body and became depressed and highly anxious. From the age of 14 she began actively to question her gender identity and started to look at YouTube videos and do research on the internet about gender identity disorder and the transition process. She said: "*I thought I had finally found the answer as to why I felt so masculine, uncomfortable with my female body and why I was so much more similar to a stereotypical boy than to a stereotypical girl in physical expression and interests.*"

79. When she was 15, the first claimant was referred to GIDS. When she was at the local Children and Adolescent Mental Health Services clinic she remembered: *"the psychiatrist attempted to talk of the gender spectrum as a way of persuading me to not pursue medical transition. I took this as a challenge to how serious I was about my feelings and what I wanted to do and it made me want to transition more. Now I wish I had listened to her."* She was first seen at GIDS aged 16 and had a number of appointments spread out over 1 year and 9 months. She was referred to UCLH in June 2013 and after three appointments commenced PBs. She was given advice about the impact on her fertility, but her priority was to move on to testosterone. She said that at 16, she was not thinking about children and, in any event, egg storage was not available on the NHS.

80. In April 2014 she was referred to an adult Gender Identity Clinic to discuss surgery. She "*was visualising myself becoming a tall, physically strong young man where there was virtually no difference between me and a biological boy.*" After commencing testosterone at 17, changes to her body commenced rapidly: these changes included genital changes, her voice dropping and the growth of facial and body hair. She was on testosterone for 3 years but increasingly began to doubt the process of transition:

> "27. I started to have my first serious doubts about transition. These doubts were brought on by for the first time really noticing how physically different I am to men as a biological female, despite having testosterone running through my body. There were also a lot of experiences I could not relate to when having conversations with men due to being biologically female and socialised in society as a girl. There was an unspoken "code" a lot of the time that I felt I was missing. I remember telling a close male friend at the time about these transition doubts, who responded by telling me that I was being silly and I believed him. This was reinforced by the online forums that I browsed where the consensus was that most transsexual people have doubts and that that is a normal part of transitioning, so the doubts should be ignored. I continued on, pushing the doubts in the far back of my mind and no more doubts creeped in for a while."

81. Despite these doubts, when she was 20, she had a double mastectomy. In the year following this:

> "31. … I started to realise that the vision I had as a teenager of becoming male was strictly a fantasy and that it was not possible. My biological make-up was still female and it showed, no matter how much testosterone was in my system or how much I would go to the gym. I was being perceived as a man by society, but it was not enough. I started to just see a woman with a beard, which is what I was. I felt like a fraud and I began to feel more lost, isolated and confused than I did when I was pre-transition."

82. She described facing the reality of taking a regular dose of drugs for the rest of her life to maintain her male appearance; and the need to have a hysterectomy if she remained a man because of the atrophy of her reproductive organs if she continued to take testosterone.

83. From January 2019 the first claimant stopped taking testosterone. She now wishes to identify as a woman and is seeking to change her legal sex back to that on her original birth certificate. She said:

> "39. … It is only until recently that I have started to think about having children and if that is ever a possibility, I have to live with the fact that I will not be able to breastfeed my children. I still do not believe that I have fully processed the surgical procedure that I had to remove my breasts and how major it really was. I made a brash decision as a teenager, (as a lot of teenagers do) trying to find confidence and happiness, except now the rest of my life will be negatively affected. I cannot reverse any of the physical, mental or legal changes that I went through. Transition was a very temporary, superficial fix for a very complex identity issue."

84. The defendant submits the first claimant was given the fullest possible information after a large number of consultations (at least 10) and that she was *Gillick* competent to make the decision to take PBs. Further, the defendant produced witness statements from a number of children and young people who are strongly supportive of the treatment they have received.

85. J is a 20 year old transgender man who received PBs in 2012 at the age of 12 followed by CSH in 2015. He described how he felt a strong need to become a boy from an early age and how he was bullied at school for his behaviour. He found the onset of female puberty horrifying and unbearable. After a number of sessions at GIDS he was prescribed PBs from the age of 12.

86. According to J he was given the fullest possible information from the clinicians at GIDS as to the benefits and disbenefits of the treatment. The clinicians strongly challenged his desire to transition and why he had chosen to express his gender identity as male. He was advised as to the impact on fertility if he chose to go on to CSH and surgery. He said: "*I made the decision to proceed with pubertal suppression without pursuing egg preservation. It was a difficult decision to make because I did not know whether I would want biological children in adulthood, but I was certain I would never want to*

carry a child and give birth. Ultimately, I made the decision because I had a poor quality of life and without immediate treatment I did not feel I had a future at all." He says: "*We discussed sex and I told them the idea of it disgusted me. I knew I would be unable to consider having a sexual relationship as an adult with my body so wrongly formed."* He ended his witness statement by saying that he is thankful that his pubertal development was halted as it removed the distress caused by continued development, but he wishes that the PBs were started earlier which would have prevented the need for breast surgery later.

87. S is a 13 year old trans boy who is on the waiting list at GIDS. He was told that he would have to wait for approximately 24 months to be seen and with his parents decided to see a private provider, GenderGP, where he has been prescribed PBs. We note at this point that the GP in question was removed from the professional register and now operates from outside the United Kingdom. S in his witness statement said:

> "13. … I haven't really thought about parenthood – I have been asked about it by the gender identity specialist I have mentioned but I just have no idea what me in the future is going to think. I haven't had a romantic relationship and it's just not a thing that is really on my radar at the moment."

88. N, an 18 year old trans woman, who was prescribed PBs when she was 17 years old said:

> "12. The treatment of hormone blockers may very well have saved my life. In the period of my life that I was prescribed them my mental health was spiralling due to my dysphoria and this impacting on my daily life, learning and social interactions. While the first injections of gonapeptyl were slow to take effect they eventually began to alleviate my dysphoria in very real ways. I had to shave less and I didn't have to fear pubertal development anymore. I had the time necessary to think about my situation and decide on further courses of action. This also helped my mental health as it gave me significantly less issues overall allowing me to focus and concentrate on aspects in my life alongside my gender identity rather than my fears of puberty and development overtaking everything else in my life."

89. The second claimant, Mrs A, is the mother of a 15 year old girl who has ASD. The daughter has a history of mental health and behavioural problems. She "*is desperate to run away from all that made her female"* and has been referred to CAMHS (Child and Adolescent Mental Health Services). Mrs A is very concerned that her daughter would be referred to GIDS and prescribed PBs. However the daughter has not currently been referred to GIDS and having regard to the defendant's current practice, would not meet the criteria for PBs because her parents would not support that treatment. Mrs A's interest in this action is therefore largely theoretical.

SECTION C: SUBMISSIONS

90. The claimants' primary case is that children or young persons under the age of 18 are not capable of giving consent to the administration of PBs. Their secondary case is that the information given by the defendant and the Interested Party is misleading and inadequate to form the basis for informed consent to be given. In their statement of issues, the claimants put issue one as the adequacy of the information and issue two whether children and young people are capable of giving consent. In our view, the first issue must be whether *Gillick* competence can be achieved, and the secondary or alternative issue, whether the information being given is adequate. We deal with the arguments in that order.

91. Mr Hyam also raised a third issue (at least in writing). This was a submission that if any young person under the age of 18 is prescribed PBs, their case should be referred to the Court of Protection. In oral argument he accepted that the Court of Protection, being a creature of statute, would have no jurisdiction to consider such referrals. We think that the substance of issue three falls within the terms of issue one.

92. Mr Hyam stressed that the claimants were not calling into question that GD existed. Nor were they questioning that it could cause extreme distress or that PBs should never be given to people under 18 or that it was never in their best interests for it to be prescribed. The central issue was whether those under 18 could give informed consent.

93. Mr Hyam submitted that a child still going through puberty is not capable of properly understanding the nature and effect of PBs and weighing the consequences and side effects properly. He pointed to the evidence of the individuals, including that put forward on behalf of the defendant, to show that children of this age cannot understand the implications of matters such as the loss of the ability to orgasm, the potential need to construct a neo-vagina, or the loss of fertility. He argued that the use of PBs to address GD does not have an adequate evidence base to support it and thus should properly be described as experimental treatment. There is evidence that PBs can have significant side effects and there is strong evidence that once a child commences on PBs they will progress to CSH which will cause irreversible changes to the child's body with lifelong medical, psychological and emotional implications for the child. He relies on the harm potentially caused to these vulnerable young people as evidenced by the witness statement of the first claimant.

94. He submitted that the advice given to the children and young persons is misleading because they are told that the PBs are fully reversible when the current evidence on reversibility or the long term implications of the treatment is limited and unclear. He said further, that the reality is that PBs pave the way for CSH which do have irreversible impacts. Further, the information provided by GIDS fails to tell the child that there are no proven benefits to this treatment in either physical or psychological terms. The information is misleading as to the reversibility of PBs, their purpose and their benefits.

95. In those circumstances he submitted that the court should be guided by the approach of the Court of Protection in its *Practice Guidance (Court of Protection: Serious Medical Treatment)* [2020] 1 WLR 641 which sets out those decisions relating to medical treatment where an application should be made to the Court of Protection.

96. Paras 10 and 11 of that Guidance state:

> "10. In any case which is not about the provision of life-sustaining treatment, but involves the serious interference with the person's rights under the ECHR, it is:
>
> "highly probable that, in most, if not all, professionals faced with a decision whether to take that step will conclude that it is appropriate to apply to the court to facilitate a comprehensive analysis of [capacity and] best interests, with [the person] having the benefit of legal representation and independent expert advice."
>
> This will be so even where there is agreement between all those with an interest in the person's welfare.
>
> 11. Examples of cases which may fall into paragraph 10 above will include, but are not limited to: (a) where a medical procedure or treatment is for the primary purpose of sterilisation; (b) where a medical procedure is proposed to be performed on a person who lacks capacity to consent to it, where the procedure is for the purpose of a donation of an organ, bone marrow, stem cells, tissue or bodily fluid to another person; (c) a procedure for the covert insertion of a contraceptive device or other means of contraception; (d) where it is proposed that an experimental or innovative treatment to be carried out; (e) a case involving a significant ethical question in an untested or controversial area of medicine."

97. The defendant and the first and second Interveners make common cause. Ms Morris argued that the care and treatment provided at GIDS fell within the terms of the Service Specification laid down by NHS England (NHSE) as required in accordance with the international frameworks of WPATH and the Endocrine Society and by the domestic regulatory frameworks of the General Medical Council and the Care Quality Commission. The NHSE is currently undertaking a review of the efficacy of treatment for GD (the Cass Review) which will report in due course, and its findings will be reflected in the Service Specification.

98. She argued that the process at GIDS was "deeply *Montgomery* compliant" (i.e. it met the requirements for informed consent identified by the Supreme Court in *Montgomery v Lanarkshire Health Board* [2015] AC 1430) having regard to the frequent consultations, discussions and the provision of detailed, but age appropriate, information. The "vast majority" of the children referred for PBs are 15 or older she said, and the information given is varied depending on the age and maturity of the child or young person. Where the assessment is that the individual is not initially *Gillick* competent, time is taken to see if their understanding develops and competency can be achieved. The information that is given is what is salient for that individual at that age.

99. As to those between the ages of 16-18, if the young person, the parents and the clinicians are agreed then she submitted there is no justiciable issue and the court has no jurisdiction.

100. Mr McKendrick for the first and second Interveners argued that the child or young person did not need to understand the impact of CSH on their fertility because that did

not fall to be decided at the stage of prescribing PBs. The PBs provided the space for the person to think about further stages. In appropriate cases, a natal girl or young person's eggs could be harvested and preserved in order to preserve their fertility. The critical thing for the child was that s/he had GD and that there was no alternative physical treatment to PBs. Once the child or young person had reached the Endocrine Clinic at the Trust, there was no alternative psychological treatment available because that was a matter within the purview of GIDS and GIDS had referred the child for PBs, although ongoing psychological treatment is provided at GIDS alongside treatment with PBs. Therefore, the Trust clinicians were faced with a child in acute distress with no alternative treatment options. The purpose of the treatment was to alleviate distress and that, according to Mr McKendrick, had been achieved.

101. When asked by the court what evidence there was that the PBs did achieve the purpose of alleviating distress, in the light of the lack of published research, Mr McKendrick pointed to the evidence of experienced endocrinologists in both Trusts who could see the real benefits of the treatment.

102. Like Ms Morris, Mr McKendrick said the current practice was not to proceed only on parental consent. However, he did argue that if the child's consent was rendered invalid, the treatment would continue to be lawful if the parents had consented.

103. The third Intervener is Transgender Trend Ltd., an organisation that provides evidence-based information and resources for parents and schools concerning children with GD. Ms Davies-Arai is the director of that organisation and she has filed a witness statement in these proceedings. She set out concerns about the lack of evidence as to the impacts and effectiveness of PBs and in relation to which patients it is most likely to help. Much of her evidence focused on the increase of referrals to GIDS of teenage natal girls and the cultural factors, including material on the internet and social media, which may play a part in this. She said that GIDS does not offer young people with GD a range of ways to interpret their experience, and the GIDS pathway offers a minimal challenge to the beliefs and ideas of the young person.

104. Mr Skinner on behalf of Transgender Trend said the case was particularly important because it concerned the deliberate provision by the State of medical treatment to children and young people which may cause harm. The court should be anxious to ensure that vulnerable children, for example those with ASD, are provided with the full protection of the law.

SECTION D: THE LAW

105. In *Gillick v West Norfolk and Wisbech Health Authority* [1986] AC 112, the House of Lords considered the lawfulness of the Secretary of State's policy on giving contraceptive advice to children without parental consent. The House of Lords held by a majority that a doctor could lawfully give contraceptive advice and treatment to a girl aged under 16 if she had sufficient maturity and intelligence to understand that nature and implications of the proposed treatment and provided that certain conditions were satisfied.

106. Lord Fraser at p. 169B-E said:

> "It seems to me verging on the absurd to suggest that a girl or boy aged 15 could not effectively consent, for example, to have a medical examination of some trivial injury to his body or even to have a broken arm set. Of course the consent of the parents should normally be asked, but they may not be immediately available. Provided the patient, whether the boy or a girl, is capable of understanding what is proposed, and of expressing his or her own wishes, I see no good reason for holding that he or she lacks the capacity to express them validly and effectively and to authorise the medical man to make the examination or give the treatment which he advises. After all, a minor under the age of 16 can, with certain limits, enter into a contract. He or she can also sue and be sued, and can give evidence on oath. …."
>
> Accordingly, I am not disposed to hold now, for the first time, that a girl less than 16 lacks the power to give valid consent to contraceptive advice or treatment, merely on account of her age."

107. Lord Scarman at p. 186A-D said:

> "The law relating to parent and child is concerned with the problems of the growth and maturity of the human personality. If the law should impose upon the process of "growing up" fixed limits where nature knows only a continuous process, the price would be artificiality and a lack of realism in an area where the law must be sensitive to human development and social change. If certainty be thought desirable, it is better that the rigid demarcations necessary to achieve it should be laid down by legislation after a full consideration of all the relevant factors than by the courts confined as they are by the forensic process to the evidenced adduced by the parties and to whatever may properly fall within the judicial notice of judges. Unless and until Parliament should think fit to intervene, the courts should establish a principle flexible enough to enable justice to be achieved by its application to the particular circumstances proved by the evidence placed before them."

And at p.189C-E:

> "When applying these conclusions to contraceptive advice and treatment it has to be borne in mind there is much that has to be understood by a girl under the age of 16 if she is to have legal capacity to consent to such treatment. It is not enough that she should understand the nature of the advice which is being given: she must also have a sufficient maturity to understand what is involved. There are moral and family questions, especially her relationship with her parents; long-term problems associated with the emotional impact of pregnancy and its termination; and there are the risks to health of sexual intercourse at her age, risks which contraception may diminish but cannot eliminate. It follows that a doctor will have to satisfy himself that she is able to appraise these factors

> before he can safely proceed upon the basis that she has at law capacity to consent to contraceptive treatment. And it further follows that ordinarily the proper course will be for him, as the guidance lays down, first to seek to persuade the girl to bring her parents into consultation and, if she refuses, not to prescribe contraceptive treatment unless he is satisfied that her circumstances are such that he ought to proceed without parental knowledge and consent."

And p. 191C-D:

> "The truth may well be that the rights of parents and children in this sensitive area are better protected by the professional standards of the medical profession than by "a priori" legal lines of division between capacity and the lack of capacity to consent since any such general dividing line is sure to produce in some cases injustice, hardship, and injury to health."

108. In *R (Axon) v Secretary of State for Health (Family Planning Association Intervening)* [2006] QB 539 Silber J considered *Gillick* in the context of Article 8 of the Convention, the United Nations Convention on the Rights of the Child (UNCRC) and the increasing emphasis on the autonomy of the child. He held that the principles set out in *Gillick* continued to apply, see para 152.

109. There are two cases dealing with children aged 16 or over who refused medical treatment in circumstances where clinicians considered it was clinically indicated. The issue in each was whether the court could nevertheless, authorise the treatment. *Re W (a Minor) (Medical Treatment: Court's Jurisdiction)* [1993] Fam. 64, concerned the case of a 16 year old girl with anorexia nervosa. The local authority applied under the inherent jurisdiction of the High Court to give medical treatment to W without her consent and against her wishes. W relied on section 8 of the Family Law Reform Act 1969, which states:

> "Section 8 is in these terms:
>
> (1) The consent of a minor who has attained the age of 16 years to any surgical, medical or dental treatment which, in the absence of consent, would constitute a trespass to his person, shall be as effective as it would be if he were of full age; and where a minor has by virtue of this section given an effective consent to any treatment it shall not be necessary to obtain any consent for it from his parent or guardian. (2) In this section 'surgical, medical or dental treatment' includes any procedure undertaken for the purposes of diagnosis, and this section applies to any procedure which is ancillary to any treatment as it applies to that treatment. (3) Nothing in this section shall be construed

> as making ineffective any consent which would have been effective if this section had not been enacted."

110. The Court of Appeal held that section 8 did not confer on a minor an absolute right to determine whether or not she received medical treatment but protected the medical practitioner from an action in trespass. Lord Donaldson analysed *Gillick* and said that Lord Scarman would necessarily have considered that the purpose of section 8 was to provide the medical practitioners treating the child with a defence to either criminal assault or a civil claim for trespass, see pages 76G-H and 78D-F. Lord Donaldson described the effect of the section as being a *"legal flak jacket",* whereby the 16-17 year old is conclusively proved to be *Gillick* competent but this did not mean that someone else who has parental responsibility cannot give consent for the treatment.

111. When applying his analysis to the facts of W's case, Lord Donaldson said at p. 80G-81B:

> "I have no doubt that the wishes of a 16 or 17-year-old child or indeed of a younger child who is "Gillick competent" are of the greatest importance both legally and clinically, but I do doubt whether Thorpe J was right to conclude that W was of sufficient understanding to make an informed decision. I do not say this on the basis that I consider her approach irrational. I personally consider that religious or other beliefs which bar any medical treatment or treatment of particular kinds are irrational, but that does not make minors who hold those beliefs any the less "Gillick competent". They may well have sufficient intelligence and understanding fully to appreciate the treatment proposed and the consequences of their refusal to accept that treatment. What distinguishes W from them, and what with all respect I do not think that Thorpe J took sufficiently into account (perhaps because the point did not emerge as clearly before him as it did before us), is that it is a feature of anorexia nervosa that it is capable of destroying the ability to make an informed choice. It creates a compulsion to refuse treatment or only to accept treatment which is likely to be ineffective. This attitude is part and parcel of the disease and the more advanced the illness, the more compelling it may become. Where the wishes of the minor are themselves something which the doctors reasonably consider need to be treated in the minor's own best interests, those wishes clearly have a much reduced significance."

112. Lord Donaldson concluded at p. 84A-B that:

> "No minor of whatever age has power by refusing consent to treatment to override a consent to treatment by someone who has parental responsibility for the minor and a fortiori a consent by the court. Nevertheless such a refusal is a very important consideration in making clinical judgments and for parents and the courts in deciding whether themselves to give consent. Its importance increases with the age and maturity of the minor."

113. Balcombe LJ at p. 87G-H agreed with Lord Donaldson that the parents of a 16 and 17 year old retained the right to consent to treatment even if she did not consent, and that the court could continue to exercise its inherent jurisdiction. Nolan LJ did not express a view as to whether parents could consent to treatment where the child had refused, but considered that the court under its inherent jurisdiction could continue to do so. He said, at p. 94D-E:

> "To take it a stage further, if the child's welfare is threatened by a serious or imminent risk that the child will suffer grave and irreversible mental or physical harm, then once again the court when called upon has a duty to intervene. It makes no difference whether the risk arises from the action or inaction of others, or from the action or inaction of the child. Due weight must be given to the child's wishes, but the court is not bound by them. In the present case, Thorpe J was apparently satisfied on the evidence before him that such a risk existed. In my judgment, he was fully entitled to take this view. By the time the matter came to this court, it was impossible to take any other view. For these reasons, I would dismiss the appeal save to the extent of making the necessary variation of the order of Thorpe J."

114. We were taken to two cases concerning the application of *Gillick* in particularly difficult medical and ethical situations, which are of some assistance in the present case. In *Re L (Medical Treatment: Gillick Competency*) [1998] 2 F.L.R. 810 Sir Stephen Brown P. considered the case of a 14 year old girl with a life threatening condition involving the possibility of a blood transfusion. L was a Jehovah's Witness and would not consent to the blood transfusion. The court ordered that the medical treatment should take place without her consent. The expert clinician appointed by the Official Solicitor is recorded as giving the following evidence:

> "He makes the point that the girl's view as to having no blood transfusion is based on a very sincerely, strongly held religious belief which does not in fact lend itself in her mind to discussion. It is one that has been formed by her in the context of her own family experience and the Jehovah's Witness meetings where they all support this view. He makes the point that there is a distinction between a view of this kind and the constructive formulation of an opinion which occurs with adult experience. That has not happened of course in the case of this young girl."

115. Sir Stephen Brown then concluded at p. 813:

> "It is, therefore, a limited experience of life which she has – inevitably so – but this is in no sense a criticism of her or of her upbringing. It is indeed refreshing to hear of children being brought up with the sensible disciplines of a well-conducted family. But it does necessarily limit her understanding of matters which are as grave as her own present situation. It may be that because of her belief she is willing to say, and to mean it, 'I am willing to accept death rather than to have a blood transfusion', but it is quite clear in this case that she has not been able to be given all the

> details which it would be right and appropriate to have in mind when making such a decision.
>
> I do not think that in this case this young girl is 'Gillick competent'. I base that upon all the evidence that I have heard. She is certainly not 'Gillick competent' in the context of all the necessary details which it would be appropriate for her to be able to form a view about."

116. *Re S (A Child) (Child Parent: Adoption Consent)* [2019] 2 Fam 177 also concerned a child under 16. In that case Cobb J considered the competence of a mother under the age of 16 to consent to her baby being placed for adoption. Cobb J held that it was appropriate and helpful in determining *Gillick* competence to read across and borrow from the relevant concepts and language in the Mental Capacity Act 2005 but cognisant of some fundamental differences, in particular that the assumption of capacity in section 1(2) of that Act did not apply and there was no requirement for any diagnostic characteristic as there is in section 2(1) of the Mental Capacity Act 2005, see paras 15,16 and 60.

117. At paras 34 to 37 Cobb J considered what test he should apply to the information that S needed to understand and then set out the information that would be relevant for the decision in question:

> "34. Macur J in *LBL v RYJ and VJ* [2011] 1 FLR 1279, para 24 held that it would not be necessary for a decision-maker to be able to comprehend "all the peripheral detail" in the assessment of capacity to make the relevant decision; in a case concerning residence and the provision of education, Macur J went on to say, at para 58:
>
> "In [the expert's] view it is unnecessary for his determination of RYJ's capacity that she should understand all the details within the statement of special educational needs. It is unnecessary that she should be able to give weight to every consideration that would otherwise be utilised in formulating a decision objectively in her 'best interests'. I agree with his interpretation of the test in section 3 which is to the effect that the person under review must comprehend and weigh the salient details relevant to the decision to be made. To hold otherwise would place greater demands upon RYJ than others of her chronological age/commensurate maturity and unchallenged capacity."
>
> 35. In the same vein, Baker J remarked in *H v A Local Authority* [2011] EWHC 1704 at [16(xi)]: "[the] courts must guard against imposing too high a test of capacity to decide issues such as residence because to do so would run the risk of discriminating against persons suffering from a mental disability."
>
> 36. Although not cited in argument, I further remind myself of the comments of Chadwick LJ in the Court of Appeal in *Masterman-Lister v Brutton & Co (Nos 1 and 2)* [2003] 1 WLR 1511, para 79: "a person should not be held unable to understand the information relevant to a

> decision if he can understand the explanation of that information in broad terms and simple language…" So, says Ms Dolan, it is not necessary for S to understand all the peripheral and non-salient information in the adoption consent form in order to be declared capacitous. Nor does she even need to fully understand the legal distinctions between placement for adoption under a placement order and not under a placement order. Indeed, Ms Dolan herself relies in this regard on *In re A (Adoption: Agreement: Procedure)* [2001] 2 FLR 455, para 43 where Thorpe LJ observes that the differences between freeing and adoption are "complex in their inter-relationship and it is not to be expected that social workers should have a complete grasp of the distinction between the two, or always to signify the distinction in their discussion with the clients" (my emphasis)." If social workers are not expected to understand the complexities of the legislation (or its predecessor) or explain the distinction accurately to the parents with whom they are working asks Ms Dolan, why should a person under the age of 16 be expected to be able to grasp them in order to be able to be declared capacitous?
>
> 37. Accordingly, argues the local authority, the salient or "sufficient" information which is required to be understood by the child parent regarding extra-familial adoption is limited to the fundamental legal consequences of the same. The factors discussed at the hearing include: (i) your child will have new legal parents, and will no longer be your son or daughter in law, (ii) adoption is final, and non-reversible; (iii) during the process, other people (including social workers from the adoption agency) will be making decisions for the child, including who can see the child, and with whom the child will live; (iv) you may obtain legal advice if you wish before taking the decision; (v) the child will live with a different family forever; you will (probably) not be able to choose the adopters; (vi) you will have no right to see your child or have contact with your child; it is highly likely that direct contact with your child will cease, and any indirect contact will be limited; (vii) the child may later trace you, but contact will only be re-established if the child wants this; (viii) there are generally two stages to adoption; the child being placed with another family for adoption, and being formally adopted; (ix) for a limited period of time you may change your mind; once placed for adoption, your right to change your mind is limited, and is lost when an adoption order is made."

118. Cobb J's conclusions were these:

> "60… It follows that in order to satisfy the Gillick test in this context the child parent should be able to demonstrate "sufficient" understanding of the "salient" facts around adoption; she should understand the essential "nature and quality of the transaction" (per Munby J in *Sheffield City Council v E* [2005] Fam 326, para 19) and should not need to be concerned with the peripheral.

> 61. It will, however, be necessary for the competent child decision-maker to demonstrate a "full understanding" of the essential implications of adoption when exercising her decision-making, for the independent CAFCASS officer to be satisfied that the consent is valid. If consent is offered under section 19 and/or section 20 of the 2002 Act, it will be necessary for a form to be signed, even if not in the precise format of that identified by Practice Direction 5A. I accept that on an issue as significant and life-changing as adoption, there is a greater onus on ensuring that the child understands and is able to weigh the information than if the decision was of a lesser magnitude: see Baker J in *CC v KK and STCC* [2012] COPLR 627, para 69. This view is consistent with the Mental Capacity Act 2005 Code of Practice, which provides, at paragraph 4.19:
>
> "a person might need more detailed information or access to advice, depending on the decision that needs to be made. If a decision could have serious or grave consequences, it is even more important that a person understands the information relevant to that decision.""

119. In determining the level of understanding that the child needs to have to consent to PBs, Mr Hyam attached considerable importance to the decision of the Supreme Court in *Montgomery v Lancashire Health Board*. That case concerned an action in negligence brought by a mother on behalf of her child. The child was disabled as a result of complications during delivery and the mother argued that she should have been advised as to the possibility of delivery by elective caesarean. The central issue for present purposes was the information that the doctor needed to have given the patient in order to establish that she had given informed consent for the treatment.

120. Lord Kerr set out the requirements placed on a doctor in providing information on risks of injury from treatment in the following terms at para 87:

> "An adult person of sound mind is entitled to decide which, if any, of the available forms of treatment to undergo, and her consent must be obtained before treatment interfering with her bodily integrity is undertaken. The doctor is therefore under a duty to take reasonable care to ensure that the patient is aware of any material risks involved in any recommended treatment, and of any reasonable alternative or variant treatments. The test of materiality is whether, in the circumstances of the particular case, a reasonable person in the patient's position would be likely to attach significance to the risk, or the doctor is or should reasonably be aware that the particular patient would be likely to attach significance to it."

121. Mr Hyam submitted that in determining whether a child is *Gillick* competent the court should consider what would a *"reasonable person in the patient's position understand",* and in asking that question, he submitted that the "reasonable person" is one with adult knowledge.

122. Ms Morris went to the opposite extreme. She submitted that when deciding what information needs to be given to the patient and understood by them, the test is a reasonable person in that individual's position, i.e. a reasonable 12 year old (or other

age) with GD. She said that the "salient" information that needs to be provided is what that reasonable patient would attach importance to. She said that seeking consent, certainly for treatment with lifelong implications such as sterilisation will always involve some *"act of imagination"*. Many patients facing life changing treatment, such as the loss of fertility in cancer treatment or endometriosis, will not have had experience of what they are foregoing, for example, fertility. She submitted that the court ought not to be pronouncing on hypothetical cases: rather, it should or could consider the facts of one specific case as and when it arises.

123. Mr McKendrick submitted that the correct approach in deciding what information was material was to assume a reasonable child of the individual's age.

124. Mr Skinner pointed out that *Montgomery* concerned an adult and therefore the presumption of capacity in the Mental Capacity Act 2005 applied. That presumption is inapplicable in a case concerning *Gillick* competency where the very issue is whether the child is competent to make the decision. The decision in *Montgomery* was of limited assistance, therefore, in the present case. In determining competence, the child must have sufficient understanding of the factors that are not just relevant to him or her now but which on an objective basis ought to be given weight in the future.

125. In our view, the following principles can be derived from the cases to which we have referred:

126. First, the question as to whether a person under the age of 16 is *Gillick* competent to make the relevant decision will depend on the nature of the treatment proposed as well as that person's individual characteristics. The assessment is necessarily an individual one. Where the decision is significant and life changing then there is a greater onus to ensure that the child understands and is able to weigh the information, see *Re S* at para 60.

127. Secondly, however, that does not mean that it is not possible for the court to draw some lines. The Trusts themselves accept that a 7 year old being treated with PBs for precocious puberty cannot give informed consent and his or her parents must give that consent because of the young age of the child concerned and the nature of the treatment.

128. Thirdly, efforts should be made to allow the child or young person to achieve *Gillick* competency where that is possible. Clinicians should therefore work with the individual to help them understand the treatment proposed and its potential implications in order to help them achieve competence.

129. Fourthly, however, that does not mean that every individual under 16 can achieve *Gillick* competence in relation to the treatment proposed. As we discuss below, where the consequences of the treatment are profound, the benefits unclear and the long-term consequences to a material degree unknown, it may be that *Gillick* competence cannot be achieved, however much information and supportive discussion is undertaken.

130. Fifthly, in order to achieve *Gillick* competence it is important not to set the bar too high. It is not appropriate to equate the matters that a clinician needs to explain, as set out in *Montgomery*, to the matters that a child needs to understand to achieve *Gillick* competence. The consequence of Mr Hyam's approach would be significantly to raise

the bar for competence and capacity, which would be contrary both to the common law and to a child's Article 8 rights and the importance of supporting individual autonomy.

131. We adopt the language of Chadwick LJ in *Masterman-Lister v Brutton and Co (Nos 1 and 2)* [2003] 1 WLR 151: a person should be able to "*understand an explanation of that information in broad terms and simple language"*, see *Re S* at para 36. Although this was said in a case that concerned an adult's capacity, in our judgment the same approach should be applied to a case concerning *Gillick* competence. The child or young person needs to be able to demonstrate sufficient understanding of the salient facts, see *Re S* at para 60.

132. Sixthly, we agree with Mr Skinner, that in deciding what facts are salient and what level of understanding is sufficient, it is necessary to have regard to matters which are those which objectively ought to be given weight in the future although the child might be unconcerned about them now. On the facts of this case there are some obvious examples, including the impact on fertility and on future sexual functioning.

SECTION E: CONCLUSIONS

133. The principal issue before this court is in some ways a narrow one. Can a child or young person under the age of 16 achieve *Gillick* competence in respect of the decision to take PBs for GD? The legal position of 16 and 17 year olds is different, and we deal with that below.

134. The starting point is to consider the nature of the treatment proposed. The administration of PBs to people going through puberty is a very unusual treatment for the following reasons. Firstly, there is real uncertainty over the short and long-term consequences of the treatment with very limited evidence as to its efficacy, or indeed quite what it is seeking to achieve. This means it is, in our view, properly described as experimental treatment. Secondly, there is a lack of clarity over the purpose of the treatment: in particular, whether it provides a "pause to think" in a "hormone neutral" state or is a treatment to limit the effects of puberty, and thus the need for greater surgical and chemical intervention later, as referred to in the Health Research Authority report. Thirdly, the consequences of the treatment are highly complex and potentially lifelong and life changing in the most fundamental way imaginable. The treatment goes to the heart of an individual's identity, and is thus, quite possibly, unique as a medical treatment.

135. Furthermore, the nature and the purpose of the medical intervention must be considered. The condition being treated, GD, has no direct physical manifestation. In contrast, the treatment provided for that condition has direct physical consequences, as the medication is intended to and does prevent the physical changes that would otherwise occur within the body, in particular by stopping the biological and physical development that would otherwise take place at that age. There is also an issue as to whether GD is properly categorised as a psychological condition, as the DSM-5 appears to do, although we recognise there are those who would not wish to see the condition categorised in that way. Be that as it may, in our judgment for the reasons already identified, the clinical intervention we are concerned with here is different in kind to other treatments or clinical interventions. In other cases, medical treatment is used to remedy, or alleviate the symptoms of, a diagnosed physical or mental condition, and

the effects of that treatment are direct and usually apparent. The position in relation to puberty blockers would not seem to reflect that description.

136. Indeed the consequences which flow from taking PBs for GD and which must be considered in the context of informed consent, fall into two (interlinking) categories. Those that are a direct result of taking the PBs themselves, and those that follow on from progression to Stage 2, that is taking cross-sex hormones. The defendant and the Trusts argue that Stage 1 and 2 are entirely separate; a child can stop taking PBs at any time and that Stage 1 is fully reversible. It is said therefore the child needs only to understand the implications of taking PBs alone to be *Gillick* competent. In our view this does not reflect the reality. The evidence shows that the vast majority of children who take PBs move on to take cross-sex hormones, that Stages 1 and 2 are two stages of one clinical pathway and once on that pathway it is extremely rare for a child to get off it.

137. The defendant argues that PBs give the child "time to think", that is, to decide whether or not to proceed to cross-sex hormones or to revert to development in the natal sex. But the use of puberty blockers is not itself a neutral process by which time stands still for the child on PBs, whether physically or psychologically. PBs prevent the child going through puberty in the normal biological process. As a minimum it seems to us that this means that the child is not undergoing the physical and consequential psychological changes which would contribute to the understanding of a person's identity. There is an argument that for some children at least, this may confirm the child's chosen gender identity at the time they begin the use of puberty blockers and to that extent, confirm their GD and increase the likelihood of some children moving on to cross-sex hormones. Indeed, the statistical correlation between the use of puberty blockers and cross-sex hormones supports the case that it is appropriate to view PBs as a stepping stone to cross-sex hormones.

138. It follows that to achieve *Gillick* competence the child or young person would have to understand not simply the implications of taking PBs but those of progressing to cross-sex hormones. The relevant information therefore that a child would have to understand, retain and weigh up in order to have the requisite competence in relation to PBs, would be as follows: (i) the immediate consequences of the treatment in physical and psychological terms; (ii) the fact that the vast majority of patients taking PBs go on to CSH and therefore that s/he is on a pathway to much greater medical interventions; (iii) the relationship between taking CSH and subsequent surgery, with the implications of such surgery; (iv) the fact that CSH may well lead to a loss of fertility; (v) the impact of CSH on sexual function; (vi) the impact that taking this step on this treatment pathway may have on future and life-long relationships; (vii) the unknown physical consequences of taking PBs; and (viii) the fact that the evidence base for this treatment is as yet highly uncertain.

139. It will obviously be difficult for a child under 16 to understand and weigh up such information. Although a child may understand the concept of the loss of fertility for example, this is not the same as understanding how this will affect their adult life. A child's attitude to having biological children and their understanding of what this really means, is likely to change between childhood and adulthood. For many children, certainly younger children, and some as young as 10 and just entering puberty, it will not be possible to conceptualise what not being able to give birth to children (or conceive children with their own sperm) would mean in adult life. Similarly, the

meaning of sexual fulfilment, and what the implications of treatment may be for this in the future, will be impossible for many children to comprehend.

140. Ms Morris submitted that many decisions about complex and long-lasting medical treatment will involve the patient having, to some degree, to imagine themselves into an uncertain future of which they have no experience. However, for the reasons that we have explained in para 135 above we consider the treatment in this case to be in entirely different territory from the type of medical treatment which is normally being considered.

141. Some of the children and young people who have been treated at GIDS say in their witness statements that the thought of sex disgusted them, or they did not really think about fertility. These normal reactions do not detract from the difficulties surrounding consent and treatment with PBs. That adolescents find it difficult to contemplate or comprehend what their life will be like as adults and that they do not always consider the longer-term consequences of their actions is perhaps a statement of the obvious.

142. These various difficulties are compounded by the particular difficulties prevalent in the cohort of children treated at GIDS. On the defendant's case, they suffer considerable psychological distress by reason of their GD and are highly vulnerable. In those circumstances, the consequences of taking PBs on their fertility for example, or on their sexual life, may be viewed as a relatively small price to pay for what may be perceived as a solution to their immediate and real psychological distress. It would not follow however that their weighing of risks and benefits when they might start taking PBs would prevail in the longer-term.

143. The difficulty of achieving informed consent in these circumstances is further exacerbated by the lack of evidence as to the efficacy of PBs in treating GD and the long-term outcomes of taking it. We entirely accept that the fact that a treatment is experimental, or that the long-term outcomes are not yet known, does not of itself prevent informed consent being given. Otherwise no experimental treatment could ever be consented to. However, the combination here of lifelong and life changing treatment being given to children, with very limited knowledge of the degree to which it will or will not benefit them, is one that gives significant grounds for concern.

144. We do not think that the answer to this case is simply to give the child more, and more detailed, information. The issue in our view is that in many cases, however much information the child is given as to long-term consequences, s/he will not be able to weigh up the implications of the treatment to a sufficient degree. There is no age appropriate way to explain to many of these children what losing their fertility or full sexual function may mean to them in later years.

145. *Gillick* makes clear that any decision is treatment and person specific. However, for the reasons that we have set out above, we think that it is appropriate in this case to give clear guidance as to the application of the *Gillick* tests to the treatment and cohort of children in question. The conclusion we have reached is that it is highly unlikely that a child aged 13 or under would ever be *Gillick* competent to give consent to being treated with PBs. In respect of children aged 14 and 15, we are also very doubtful that a child of this age could understand the long-term risks and consequences of treatment in such a way as to have sufficient understanding to give consent. However, plainly the

increased maturity of the child means that there is more possibility of achieving competence at the older age.

146. In respect of a young person aged 16 or over, the legal position is different. There is a presumption of capacity under section 8 of the Family Law Reform Act 1969. As is explained in *Re W*, that does not mean that a court cannot protect the child under its inherent jurisdiction if it considers the treatment not to be in the child's best interests. However, so long as the young person has mental capacity and the clinicians consider the treatment is in his/her best interests, then absent a possible dispute with the parents, the court generally has no role. We do not consider that the court can somehow adopt an intrusive jurisdiction in relation to one form of clinical intervention for which no clear legal basis has been established.

147. We do however recognise that in the light of the evidence that has emerged, and the terms of this judgment, clinicians may well consider that it is not appropriate to move to treatment, such as PBs or CSH, without the involvement of the court. We consider that it would be appropriate for clinicians to involve the court in any case where there may be any doubt as to whether the long-term best interests of a 16 or 17 year old would be served by the clinical interventions at issue in this case.

148. We express that view for these reasons. First, the clinical interventions involve significant, long-term and, in part, potentially irreversible long-term physical, and psychological consequences for young persons. The treatment involved is truly life changing, going as it does to the very heart of an individual's identity. Secondly, at present, it is right to call the treatment experimental or innovative in the sense that there are currently limited studies/evidence of the efficacy or long-term effects of the treatment.

149. The position of the defendant and the Trusts is that they consider it would be an intrusion into the child or young person's autonomy if a decision about treatment with PBs were to be made by the court not by the patient. They are concerned about the use of NHS and court resources if these decisions have to be made by the court. We do not consider that this is the correct approach. In principle, a young person's autonomy should be protected and supported; however, it is the role of the court to protect children, and particularly a vulnerable child's best interests. The decisions in respect of PBs have lifelong and life-changing consequences for the children. Apart perhaps from life-saving treatment, there will be no more profound medical decisions for children than whether to start on this treatment pathway. In those circumstances we consider that it is appropriate that the court should determine whether it is in the child's best interests to take PBs. There is a real benefit in the court, almost certainly with a child's guardian appointed, having oversight over the decision. In any case, under the inherent jurisdiction concerning medical treatment for those under the age of 18, there is likely to be a conflict between the support of autonomy and the protective role of the court. As we have explained above, we consider this treatment to be one where the protective role of the court is appropriate.

150. The claimants' alternative ground is that the information provided by the defendant and the Trusts is inadequate to form the basis of informed consent. We accept that the defendant and the Trusts have in their written information, to children, young people and their parents and carers, tried hard to explain the potential consequences of PBs, including that of moving on to CSH, and to give full information. They have also

attempted to do this in an age appropriate manner. The problem is not the information given, but the ability of the children and young people, to understand and most importantly weigh up that information. The approach of the defendant appears to have been to work on the assumption that if they give enough information and discuss it sufficiently often with the children, they will be able to achieve *Gillick* competency. As we have explained above, we do not think that this assumption is correct.

OVERALL CONCLUSION

151. A child under 16 may only consent to the use of medication intended to suppress puberty where he or she is competent to understand the nature of the treatment. That includes an understanding of the immediate and long-term consequences of the treatment, the limited evidence available as to its efficacy or purpose, the fact that the vast majority of patients proceed to the use of cross-sex hormones, and its potential life changing consequences for a child. There will be enormous difficulties in a child under 16 understanding and weighing up this information and deciding whether to consent to the use of puberty blocking medication. It is highly unlikely that a child aged 13 or under would be competent to give consent to the administration of puberty blockers. It is doubtful that a child aged 14 or 15 could understand and weigh the long-term risks and consequences of the administration of puberty blockers.

152. In respect of young persons aged 16 and over, the legal position is that there is a presumption that they have the ability to consent to medical treatment. Given the long-term consequences of the clinical interventions at issue in this case, and given that the treatment is as yet innovative and experimental, we recognise that clinicians may well regard these as cases where the authorisation of the court should be sought prior to commencing the clinical treatment.

153. We have granted a declaration to reflect the terms of this judgment.

Decision Memo for GENDER Dysphoria and GENDER REASSIGNMENT SURGERY (CAG-00446N)

Links in PDF documents are not guaranteed to work. To follow a web link, please use the MCD Website.

Decision Summary

DEFENDANT'S EXHIBIT 16

Currently, the local Medicare Administrative Contractors (MACs) determine coverage of gender reassignment surgery on a case-by-case basis. We received a complete, formal request to make a national coverage determination on surgical remedies for gender identity disorder (GID), now known as gender dysphoria. The Centers for Medicare & Medicaid Services (CMS) is not issuing a National Coverage Determination (NCD) at this time on gender reassignment surgery for Medicare beneficiaries with gender dysphoria because the clinical evidence is inconclusive for the Medicare population.

In the absence of a NCD, coverage determinations for gender reassignment surgery, under section 1862(a)(1)(A) of the Social Security Act (the Act) and any other relevant statutory requirements, will continue to be made by the local MACs on a case-by-case basis. To clarify further, the result of this decision is not national non-coverage rather it is that no national policy will be put in place for the Medicare program. In the absence of a national policy, MACs will make the determination of whether or not to cover gender reassignment surgery based on whether gender reassignment surgery is reasonable and necessary for the individual beneficiary after considering the individual's specific circumstances. For Medicare beneficiaries enrolled in Medicare Advantage (MA) plans, the initial determination of whether or not surgery is reasonable and necessary will be made by the MA plans.

Consistent with the request CMS received, the focus of this National Coverage Analysis (NCA) was gender reassignment surgery. Specific types of surgeries were not individually assessed. We did not analyze the clinical evidence for counseling or hormone therapy treatments for gender dysphoria. As requested by several public commenters, we have modified our final decision memorandum to remove language that was beyond the scope of the specific request. We are not making a national coverage determination related to counseling, hormone therapy treatments, or any other potential treatment for gender dysphoria.

While we are not issuing a NCD, CMS encourages robust clinical studies that will fill the evidence gaps and help inform which patients are most likely to achieve improved health outcomes with gender reassignment surgery, which types of surgery are most appropriate, and what types of physician criteria and care setting(s) are needed to ensure that patients achieve improved health outcomes.

Decision Memo

To: Administrative File: CAG #00446N

From: Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group

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Analyst

Subject: Final Decision Memorandum on Gender Reassignment Surgery for Medicare Beneficiaries with Gender Dysphoria

Date: August 30, 2016

I. Decision

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II. Background

Below is a list of acronyms used throughout this document.

AHRQ - Agency for Healthcare Research and Quality
AIDS - Acquired Immune Deficiency Syndrome
ANOVA - Analysis of Variance

APA - American Psychiatric Association
APGAR - Adaptability, Partnership Growth, Affection, and Resolve test
BIQ - Body Image Questionnaire
BSRI - Bem Sex Role Inventory
CCEI - Crown Crips Experimental Index
CDC – Centers for Disease Control
CHIS - California Health Interview Survey
CI - Confidence Interval
CMS - Centers for Medicare & Medicaid Services
DAB - Departmental Appeals Board
DSM - Diagnostic and Statistical Manual of Mental Disorders
EMBASE - Exerpta Medica dataBASE
FBeK - Fragebogen zur Beurteilung des eigenen Korpers
FDA - Food and Drug Administration
FPI-R - Freiburg Personality Inventory
FSFI - Female Sexual Function Index
GAF - Global Assessment of Functioning
GID - Gender Identity Disorder
GIS - Gender Identity Trait Scale
GRS - Gender Reassignment Surgery
GSI - Global Severity Indices
HADS - Hospital Anxiety Depression Scale
HHS - U.S. Department of Health and Human Services
HIV - Human Immunodeficiency Virus
IIP - Inventory of Interpersonal Problems
IOM - Institute of Medicine
KHQ - King's Health Questionnaire
LGB - Lesbian, Gay, and Bisexual
LGBT - Lesbian, Gay, Bisexual, and Transgender
MAC - Medicare Administrative Contractor
MMPI - Minnesota Multiphasic Personality Inventory
NCA - National Coverage Analysis
NCD - National Coverage Determination
NICE - National Institute for Health Care Excellence
NIH - National Institutes of Health
NZHTA - New Zealand Health Technology Assessment
PIT - Psychological Integration of Trans-sexuals
QOL - Quality of Life
S.D. - Standard Deviation
SADS - Social Anxiety Depression Scale
SCL-90R - Symptom Check List 90-Revised
SDPE - Scale for Depersonalization Experiences
SES - Self Esteem Scale
SF - Short Form
SMR - Standardized Mortality Ratio SOC – Standards of Care
STAI-X1 - Spielberger State and Trait Anxiety Questionnaire
STAI-X2 - Spielberger State and Trait Anxiety Questionnaire
TSCS - Tennessee Self-Concept Scale
U.S. - United States
VAS - Visual Analog Scale
WHOQOL-BREF - World Health Organization Quality of Life - Abbreviated version of the WHOQOL-100
WPATH - World Professional Association for Transgender Health

A. Diagnostic Criteria

The criteria for gender dysphoria or spectrum of related conditions as defined by the American Psychiatric Association (APA) in the Diagnostic and Statistical Manual of Mental Disorders (DSM) has changed over time (See Appendix A).

Gender dysphoria (previously known as gender identity disorder) is a classification used to describe persons who experience significant discontent with their biological sex and/or gender assigned at birth. Although there are other therapeutic options for gender dysphoria, consistent with the NCA request, this decision only focuses on gender reassignment surgery.

B. Prevalence of Transgender Individuals

For estimates of transgender individuals in the U.S., we looked at several studies.

The Massachusetts Behavior Risk Factor Surveillance Survey (via telephone) (2007 and 2009) identified 0.5% individuals as transgender (Conron et al., 2012).

Derivative data obtained from the 2004 California Lesbian Gay Bisexual and Transgender (LGBT) Tobacco Survey (via telephone) and the 2009 California Health Interview Survey (CHIS) (via telephone) suggested the LGB population constitutes 3.2% of the California population and that transgender subjects constitute approximately 2% of the California LGBT population and 0.06% of the overall California population (Bye et al., 2005; CHIS 2009; Gates, 2011).

Most recently, the Williams Institute published a report that utilized data from the Centers for Disease Control's (CDC) Behavioral Risk Factor Surveillance System (BRFSS). Overall, they found that 0.6% or 1.4 million U.S. adults identify as transgender. The report further estimated 0.7% of adults between the ages of 18-25 identify as transgender, 0.6% of adults between the ages of 25-65 identify as transgender, and 0.5% of adults age 65 or older identify as transgender (Flores et al., 2016).

In a recent review of Medicare claims data, CMS estimated that in calendar year 2013 there were at least 4,098 transgender beneficiaries (less than 1% of the Medicare population) who utilized services paid for by Medicare, of which 90% had confirmatory diagnosis, billing codes, or evidence of a hormone therapy prescription. The Medicare transgender population is racially and ethnically diverse (e.g., 74% White, 15% African American) and spans the entire country. Nearly 80% of transgender beneficiaries are under age 65, including approximately 23% ages 45-54. (CMS Office of Minority Health 2015).

For international comparison purposes, recent estimates of transgender populations in other countries are similar to those in the United States. New Zealand researchers, using passport data, reported a prevalence of 0.0275% for male-to-female adults and 0.0044% female-to-male adults (6:1 ratio) (Veale, 2008). Researchers from a centers of transgender treatment and reassignment surgery in Belgium conducted a survey of regional plastic surgeons and reported a prevalence of 0.008% male-to-female and 0.003% female-to-male (ratio 2.7:1) surgically reassigned transsexuals in Belgium (De Cuypere et al., 2007). Swedish researchers, using national mandatory reporting data on those requesting reassignment surgery, reported secular changes over time in that the number of completed reassignment surgeries per application increased markedly in the 1990s; the male-to- female/female-to-male sex ratio changed from 1:1 to 2:1; the age of male-to-female and female-to-male applicants was initially similar, but increased by eight years for male-to-female applicants; and the proportion of foreign born applicants increased (Olsson and Moller 2003).

III. History of Medicare Coverage

Date	Action
August 1, 1989	CMS published the initial NCD, titled "140.3, Transsexual Surgery" in the Federal Register. (54 Fed. Reg. 34,555, 34,572)
May 30, 2014	The HHS Departmental Appeals Board (DAB) determined that the NCD denying coverage for all transsexual surgery was not valid. As a result, MACs determined coverage on a case-by-case basis.

CMS does not currently have a NCD on gender reassignment surgery.

A. Current Request

On December 3, 2015, CMS accepted a formal complete request from a beneficiary to initiate a NCA for gender reassignment surgery.

CMS opened this National Coverage Analysis (NCA) to thoroughly review the evidence to determine whether or not gender reassignment surgery may be covered nationally under the Medicare program.

B. Benefit Category

Medicare is a defined benefit program. For an item or service to be covered by the Medicare program, it must fall within one of the statutorily defined benefit categories as outlined in the Act. For gender reassignment surgery, the following are statutes are applicable to coverage:

Under §1812 (Scope of Part A) Under §1832 (Scope of Part B)
Under §1861(s) (Definition of Medical and Other Health Services)
Under §1861(s)(1) (Physicians' Services)

This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

IV. Timeline of Recent Activities

Timeline of Medicare Coverage Policy Actions for Gender Reassignment Surgery

Date	Action
December 3, 2015	CMS accepts an external request to open a NCD. A tracking sheet was posted on the web site and the initial 30 day public comment period commenced.
January 2, 2016	Initial comment period closed. CMS received 103 comments.
June 2, 2016	Proposed Decision Memorandum posted on the web site and the final 30 day public comment period commenced.
July 2, 2016	Final comment period closed. CMS received 45 comments.

V. FDA Status

Surgical procedures per se are not subject to the Food and Drug Administration's (FDA) approval.

Inflatable penile prosthetic devices, rigid penile implants, testicular prosthetic implants, and breast implants have been approved and/or cleared by the FDA.

VI. General Methodological Principles

In general, when making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. (§ 1862 (a)(1)(A)). The evidence may consist of external technology assessments, internal review of published and unpublished studies, recommendations from the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC), evidence-based guidelines, professional society position statements, expert opinion, and public comments.

The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) specific clinical question relevant to the coverage request can be answered conclusively; and 2) the extent to which we are confident that the intervention will improve health outcomes for patients.

A detailed account of the methodological principles of study design the agency staff utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix B. In general, features of clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, blinding of readers of the index test, and reference test results.

VII. Evidence

A. Introduction

Below is a summary of the evidence we considered during our review, primarily articles about clinical trials published in peer- reviewed medical journals. We also considered articles cited by the requestor, articles identified in public comments, as well as those found by a CMS literature review. Citations are detailed below.

B. Literature Search Methods

CMS staff extensively searched for primary studies for gender dysphoria. The emphasis focused less on specific surgical techniques and more on functional outcomes unless specific techniques altered those types of outcomes.

The reviewed evidence included articles obtained by searching literature databases and technology review databases from PubMed (1965 to current date), EMBASE, the Agency for Healthcare Research and Quality (AHRQ), the Blue Cross/Blue Shield Technology Evaluation Center, the Cochrane Collection, the Institute of Medicine, and the National Institute for Health and Care Excellence (NICE) as well as the source material for commentary, guidelines, and formal evidence-based documents published by professional societies. Systematic reviews were used to help locate some of the more obscure publications and abstracts.

Keywords used in the search included: Trans-sexual, transgender, gender identity disorder (syndrome), gender

dysphoria and/or hormone therapy, gender surgery, genital surgery, gender reassignment (surgery), sex reassignment (surgery) and/or quality of life, satisfaction-regret, psychological function (diagnosis of mood disorders, psychopathology, personality disorders), suicide (attempts), mortality, and adverse events-reoperations. After the identification of germane publications, CMS also conducted searches on the specific psychometric instruments used by investigators.

Psychometric instruments are scientific tools used to measure individuals' mental capabilities and behavioral style. They are usually in the form of questionnaires that numerically capture responses. These tools are used to create a psychological profile that can address questions about a person's knowledge, abilities, attitudes and personality traits. In the evaluation of patients with gender dysphoria, it is important that both validity and reliability be assured in the construction of the tool (validity refers to how well the tool actually measures what it was designed to measure, or how well it reflects the reality it claims to represent, while reliability refers to how accurately results of the tool would be replicated in a second identical piece of research). Reliability and validity are important because when evaluating patients with gender dysphoria most of the variables of interest (e.g., satisfaction, anxiety, depression) are latent in nature (not directly observed but are rather inferred) and difficult to quantify objectively.

Studies with robust study designs and larger, defined patient populations assessed with objective endpoints or validated test instruments were given greater weight than small, pilot studies. Reduced consideration was given to studies that were underpowered for the assessment of differences or changes known to be clinically important. Studies with fewer than 30 patients were reviewed and delineated, but excluded from the major analytic framework. Oral presentations, unpublished white papers, and case reports were excluded. Publications in languages other than English were excluded. The CMS initial internal search for the proposed decision memorandum was limited to articles published prior to March 21, 2016. The CMS internal search for the final decision memorandum continued through articles published prior to July 22, 2016.

Included studies were limited to those with adult subjects. Review and discussion of the management of children and adolescents with the additional considerations of induced pubertal delay are outside the scope of this NCD. In cases where the same population was studied for multiple reasons or where the patient population was expanded over time, the latest and/or most germane sections of the publications were analyzed. The excluded duplicative publications are delineated.

CMS also searched Clinicaltrials.gov to identify relevant clinical trials. CMS looked at trial status including early termination, completed, ongoing with sponsor update, and ongoing with estimated date of completion. Publications on completed trials were sought. For this final decision, CMS also reviewed all evidence submitted via public comment.

C. Discussion of Evidence

The development of an assessment in support of Medicare coverage determinations is based on the same general question for almost all national coverage analyses (NCAs): "Is the evidence sufficient to conclude that the application of the item or service under study will improve health outcomes for Medicare patients?" For this specific NCA, CMS is interested in answering the following question:

Is there sufficient evidence to conclude that gender reassignment surgery improves health outcomes for Medicare beneficiaries with gender dysphoria?

The evidence reviewed is directed towards answering this question.

1. Internal Technology Assessment

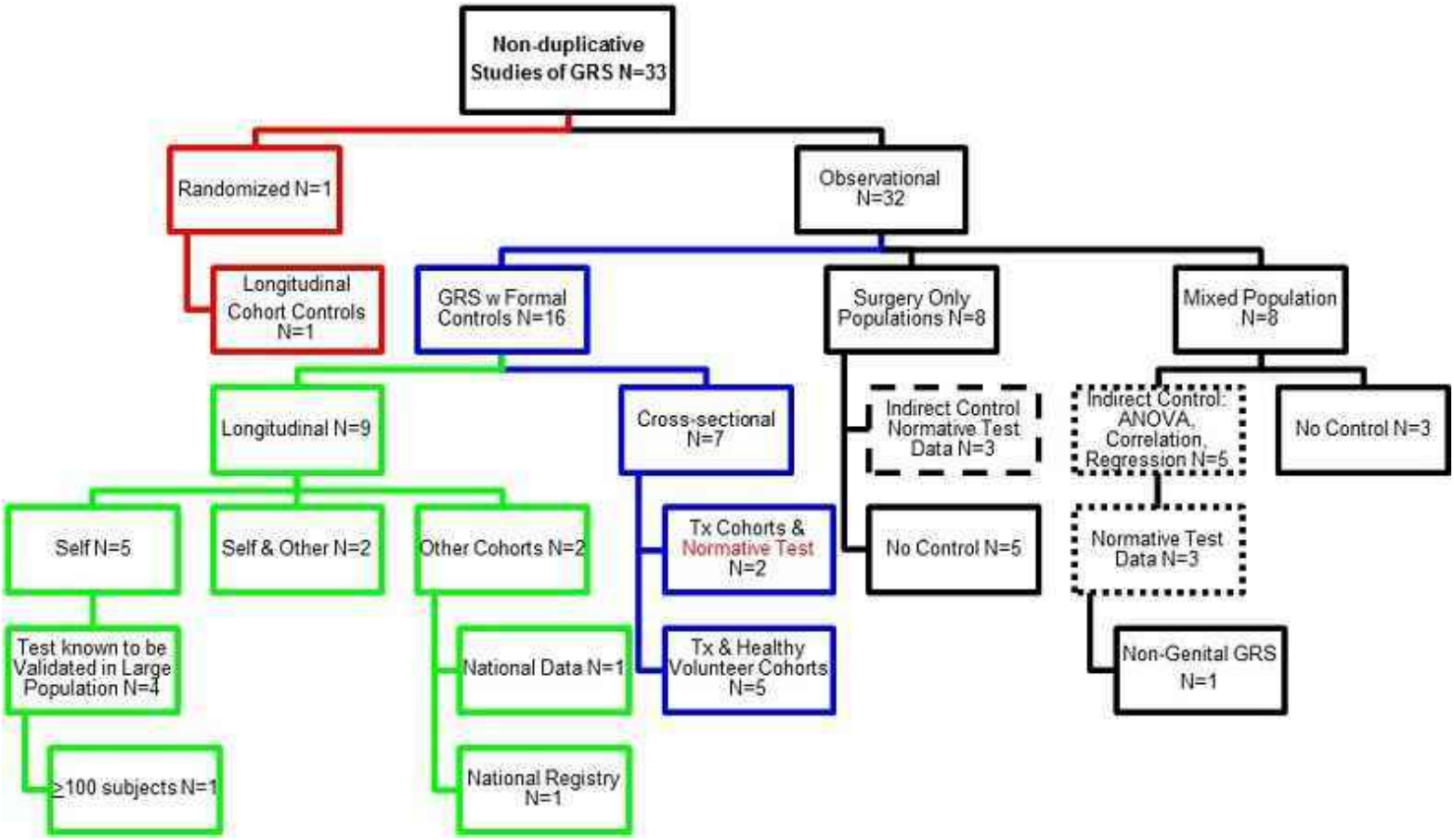
CMS conducted an extensive literature search on gender reassignment related surgical procedures and on facets of gender dysphoria that provide context for this analysis. The latter includes medical and environmental conditions.

CMS identified numerous publications related to gender reassignment surgery. A large number of these were case reports, case series with or without descriptive statistics, or studies with population sizes too small to conduct standard parametric statistical analyses. Others addressed issues of surgical technique.

CMS identified and described 36 publications on gender reassignment surgery that included health outcomes. Because the various investigators at a site sometimes conducted serial studies on ever-enlarging cohort populations, studied sub-populations, studied different outcomes, or used different tools to study the same outcomes, not all study populations were unique. To reduce bias from over-lapping populations, only the latest or most germane publication(s) were described. Subsumed publications were delineated.

Of these 36 publications, two publications used different assessment tools on the same population, and, so for the purposes of evaluation, were classified as one study (Udeze et al., 2008; Megeri and Khoosal, 2007). A total of 33 studies were reviewed (See Figure 1). Appendices C, D, and F include more detail of each study. The publications covered a time span from 1979 to 2015. Over half of the studies were published after 2005.

Figure 1. Studies of Gender Reassignment Surgery (GRS)



ANOVA=Analysis of Variance Normative=Psychometric Tests with known normative for large populations

Figure 1 Legend: The studies in Figure 1 are categorized into three groups. The first group, depicted by the colored

boxes (red, blue, and green), had explicit controls. There was a single randomized study. The remainder in the first group were observational studies. These were subdivided into longitudinal studies and cross-sectional studies. The second group, depicted by black boxes (starting with the surgery only population box) consisted of surgical series. The third group, depicted by black boxes (starting with mixed population), was composed of patients whose treatment could involve a variety of therapeutic interventions, but who were not stratified by that treatment.

When looking at the totality of studies, the 33 studies could be characterized by the following research design groups:

a. Observational, mixed population of surgical and non-surgical patients without stratification

Asscheman H, Giltay EJ, Megens JA, de Ronde WP, van Trotsenburg MA, Gooren LJ. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. Eur J Endocrinol. 2011 Apr;164(4):635-42. Epub 2011 Jan 25.

Asscheman et al. conducted a retrospective, non-blinded, observational study of mortality using a longitudinal design to assess a mixed population treated with hormones, as well as, reassignment surgery in comparison to a population-based cohort. The study was not designed to assess the specific impact of gender reassignment surgery on clinical outcomes.

The investigators assessed mortality in patients who (a) were from a single-center, unspecified, Dutch university specialty clinic, (b) had initiated cross-sex hormone treatment prior to July 1, 1997, and (c) had been followed (with or without continued hormone treatment) by the clinic for at least one year or had expired during the first year of treatment. The National Civil Record Registry (Gemeentelijke Basis Administratie) was used to identify/confirm deaths of clinic patients. Information on the types or hormones used was extracted from clinic records, and information on the causation of death was extracted from medical records or obtained from family physicians. Mortality data for the general population were obtained through the Central Bureau of Statistics of the Netherlands (Centraal Bureau voor Statistiek). Mortality data from Acquired Immune Deficiency Syndrome (AIDS) and substance abuse were extracted from selected Statistics Netherlands reports. The gender of the general Dutch population comparator group was the natal sex of the respective gender dysphoric patient groups.

A total of 1,331 patients who met the hormone treatment requirements were identified (365 female-to-male [27.4%]; 966 male- to-female [72.6%]; ratio 1:2.6). Of these, 1,177 (88.4%) underwent reassignment surgery (343 [94.0% of female-to-male entrants]; 834 [86.3% of male-to-female entrants]; ratio difference 1:2.4 with a p-value $p<0.0001$). Later calculations did not distinguish between those with hormone therapy alone versus those with hormone therapy plus reassignment surgery. The mean age at the time of hormone initiation in female-to-male and male-to-female patients was 26.1±7.6 (range 16–56) years and 31.4±11.4 (range 16–76) years respectively, although the male-to-female subjects were relatively older ($p<0.001$). The mean duration of hormone therapy in female-to-male and male-to-female patients was 18.8±6.3 and 19.4±7.7 years respectively.

There were a total of 134 deaths in the clinic population using hormone therapy with or without surgical reassignment. Of these patients, 12 (3.3%) of the 365 female-to-male patients and 122 (12.6%) of the 966 male-to-female patients died. All-cause mortality for this mixed population was 51% higher and statistically significant (Standardized Mortality Ratio [SMR] 95% confidence interval [CI]) 1.47-1.55) for males-to-females when compared to males in the general Dutch population. The increase in all-cause mortality (12%) for females-to-males when compared to females in the general Dutch population was not statistically significant (95% CI 0.87-1.42).

Ischemic heart disease was a major disparate contributor to excess mortality in male-to-female patients but only in older patients (n=18, SMR 1.64 [95% CI 1.43-1.87]), mean age [range]: 59.7 [42-79] years. Current use of a

particular type of estrogen, ethinyl estradiol, was found to contribute to death from myocardial infarction or stroke (Adjusted Hazard Ratio 3.12 [95% CI 1.28-7.63], p=0.01). There was a small, but statistically significant increase in lung cancer that was thought to possibly be related to higher rates of smoking in this cohort.

Other contributors to the mortality difference between male-to-female patients and the Dutch population at large were completed suicide (n=17, SMR 5.70 [95% CI 4.93-6.54]), AIDS (n=16, SMR 30.20 [95% CI 26.0-34.7]), and illicit drug use (n=5, SMR 13.20 [95% CI 9.70-17.6]). An additional major contributor was "unknown cause" (n=21, SMR 4.00 [95% CI 3.52-4.51]). Of the 17 male-to-female hormone treated patients who committed suicide, 13 (76.5%) had received prior psychiatric treatment and six (35.3%) had not undergone reassignment surgery because of concerns about mental health stability.

Overall mortality, and specifically breast cancer and cardiovascular disease, were not increased in the hormone-treated female-to-male patients. Asscheman et al. reported an elevated SMR for illicit drug use (n=1, SMR 25 [6.00-32.5]). This was the cause of one of the 12 deaths in the cohort.

This study subsumes earlier publications on mortality (Asscheman et al. 1989 [n=425]; Van Kesteren et al. 1997 [n=816]).

Gómez-Gil E, Zubiaurre-Elorza L, Esteva I, Guillamon A, Godás T, Cruz Almaraz M, Halperin I, Salamero M. Hormone-treated transsexuals report less social distress, anxiety and depression. Psychoneuroendocrinology. 2012 May;37(5):662-70. Epub 2011 Sep 19.

Gómez-Gil et al. conducted a prospective, non-blinded observational study using a cross-sectional design and non-specific psychiatric distress tools in Spain. The investigators assessed anxiety and depression in patients with gender dysphoria who attended a single-center specialty clinic with comprehensive endocrine, psychological, psychiatric, and surgical care. The clinic employed World Professional Association for Transgender Health (WPATH) guidelines. Patients were required to have met diagnostic criteria during evaluations by 2 experts. Investigators used the Hospital Anxiety and Depression Scale (HADS) and the Social Anxiety and Distress Scale (SADS) instruments. The SADS total score ranges from 0 to 28, with higher scores indicative of more anxiety. English language normative values are 9.1±8.0. HAD-anxiety and HAD-depression total score ranges from 0 to 21, with higher scores indicative of more pathology. Scores less than 8 are normal. ANOVA was used to explore effects of hormone and surgical treatment.

Of the 200 consecutively selected patients recruited, 187 (93.5% of recruited) were included in the final study population. Of the final study population, 74 (39.6%) were female-to-male patients; 113 (60.4%) were male-to-female patients (ratio 1:1.5); and 120 (64.2%) were using hormones. Of those using hormones, 36 (30.0%) were female-to-male; 84 (70.0%) were male-to-female (ratio 1:2.3). The mean age was 29.87±9.15 years (range 15-61). The current age of patients using hormones was 33.6±9.1 years (n=120) and older than the age of patients without hormone treatment (25.9±7.5) (p=0.001). The age at hormone initiation, however, was 24.6±8.1 years.

Of those who had undergone reassignment surgery, 29 (36.7%) were female-to-male; 50 (63.3%) were male-to-female (ratio 1:1.7). The number of patients not on hormones and who had undergone at least one gender-related surgical procedure (genital or non-genital) was small (n=2). The number of female-to-male patients on hormones who had undergone such surgery (mastectomy, hysterectomy, and/or phalloplasty) was 28 (77.8%). The number of male-to-female patients on hormones who had undergone such surgery (mammoplasty, facial feminization, buttock feminization, vaginoplasty, orchiectomy, and/or vocal feminization (thyroid chondroplasty) was 49 (58.3%).

Analysis of the data revealed that although the mean scores HAD-Anxiety, HAD-Depression, and SADS were statistically lower (better) in those on hormone therapy than in those not on hormone therapy, the mean scores for

HAD-Depression and SADS were in the normal range for gender dysphoric patients not using hormones. The HAD-Anxiety score was 9 in transsexuals without hormone treatment and 6.4 in transsexuals with hormone treatment. The mean scores for HAD-Anxiety, HAD- Depression, and SADS were in the normal range for gender dysphoric patients using hormones. ANOVA revealed that results did not differ by whether the patient had undergone a gender related surgical procedure or not.

Gómez-Gil E, Zubiaurre-Elorza L, de Antonio I, Guillamon A, Salamero M. Determinants of quality of life in Spanish transsexuals attending a gender unit before genital sex reassignment surgery. Qual Life Res. 2014 Mar;23(2):669-76. Epub 2013 Aug 13.

Gómez-Gil et al. conducted a prospective, non-blinded observational study using a non-specific quality of life tool. There were no formal controls for this mixed population ± non-genital reassignment surgery undergoing various stages of treatment.

The investigators assessed quality of life in the context of culture in patients with gender dysphoria who were from a single-center (Barcelona, Spain), specialty and gender identity clinic. The clinic used WPATH guidelines. Patients were required to have met diagnostic criteria during evaluations by both a psychologist and psychiatrist. Patients could have undergone non-genital surgeries, but not genital reassignment surgeries (e.g., orchiectomy, vaginoplasty, or phalloplasty). The Spanish version of the World Health Organization Quality of Life-Abbreviated version of the WHOQOL-100 (WHOQOL- BREF) was used to evaluate quality of life, which has 4 domains (environmental, physical, psychological, and social) and 2 general questions. Family dynamics were assessed with the Spanish version of the Family Adaptability, Partnership Growth, Affection, and Resolve (APGAR) test. Regression analysis was used to explore effects of surgical treatment.

All consecutive patients presenting at the clinic (277) were recruited and, 260 (93.9%) agreed to participate. Of this number, 59 of these were excluded for incomplete questionnaires, 8 were excluded for prior genital reassignment surgery, and 193 were included in the study (the mean age of this group was 31.2±9.9 years (range 16-67). Of these, 74 (38.3%) were female-to-male patients; 119 (61.7%) were male-to-female patients (ratio1:1.6). Of these, 120 (62.2%) were on hormone therapy; 29 (39.2%) of female-to-male patients had undergone at least 1 non-genital, surgical procedure (hysterectomy n=19 (25.7%); mastectomy n=29 (39.2%)); 51 (42.9%) of male-to-female patients had undergone at least one non-genital surgical procedure with mammoplasty augmentation being the most common procedure, n=47 (39.5%), followed by facial feminization, n=11 (9.2%), buttocks feminization, n=9 (7.6%), and vocal feminization (thyroid chondroplasty), n=2 (1.7%).

WHOQOL-BREF domain scores for gender dysphoric patients with and without non-genital surgery were: “Environmental” 58.81±14.89 (range 12.50-96.88), “Physical” 63.51±17.79 (range 14.29-100), “Psychological” 56.09+16.27 (range 16.67- 56.09), “Social” 60.35±21.88 (range 8.33-100), and “Global QOL and Health” 55.44+27.18 (range 0-100 with higher score representing better QOL). The mean APGAR family score was 7.23±2.86 (range 0-10 with a score of 7 or greater indicative of family functionality).

Regression analysis, which was used to assess the relative importance of various factors to WHOQOL-BREF domains and general questions, revealed that family support was an important element for all four domains and the general health and quality- of-life questions. Hormone therapy was an important element for the general questions and for all of the domains except “Environmental.” Having undergone non-genital reassignment surgery, age, educational levels, and partnership status, did not impact domain and general question results related to quality of life.

Hepp U, Kraemer B, Schnyder U, Miller N, Delsignore A. Psychiatric comorbidity in gender identity disorder. J Psychosom Res. 2005 Mar;58(3):259-61.

Hepp et al. conducted a single-site (Zurich, Switzerland) prospective, non-blinded, observational study using a cross-sectional design. There was some acquisition of retrospective data. The investigators assessed current and lifetime psychiatry co-morbidity using structured interviews for diagnosis of Axis 1 disorders (clinical syndromes) and Axis 2 disorders (developmental or personality disorders) and HADS for dimensional evaluation of anxiety and depression. Statistical description of the cohort and intra-group comparisons was performed. Continuous variables were compared using t-tests and ANOVA.

A total of 31 patients with gender dysphoria participated in the study: 11 (35.5%) female-to-male; 20 (64.5%) male-to-female (ratio 1:1.8). The overall mean age was 32.2±10.3 years. Of the participants, seven had undergone reassignment surgery, 10 pre- surgical patients had been prescribed hormone therapy, and 14 pre-surgical patients had not been prescribed hormone therapy. Forty five and one half percent of female-to-male and 20% of male-to-female patients did not carry a lifetime diagnosis of an Axis 1 condition. Sixty three and six tenths percent of female-to-male and 60% of male-to-female patients did not carry a current diagnosis of an Axis 1 condition. Lifetime diagnosis of substance abuse and mood disorder were more common in male-to-female patients (50% and 55% respectively) than female-to-male patients (36.4% and 27.3% respectively). Current diagnosis of substance abuse and mood disorder were present in male-to-female patients (15% and 20% respectively) and absent in female-to-male patients. One or more personality disorders were identified 41.9%, but whether this was a current or lifetime condition was not specified. Of the patients, five (16.1%) had a Cluster A personality disorder (paranoid-schizoid), seven (22.6%) had a Cluster B personality disorder (borderline, anti-social, histrionic, narcissistic), six (19.4%) had a Cluster C personality disorder (avoidant, dependent, obsessive-compulsive), and two (6.5%) were not otherwise classified.

HADS scores were missing for at least one person. The HADS test revealed non-pathologic results for depression (female-to-male: 6.64±5.03; male-to-female: 6.58±4.21) and borderline results for anxiety (female-to-male: 7.09±5.11; male-to-female: 7.74±6.13, where a result of 7-10 = possible disorder). There were no differences by natal gender. The investigators reported a trend for less anxiety and depression as measured by HADS in the patients who had undergone surgery.

Johansson A, Sundbom E, Höjerback T, Bodlund O. A five-year follow-up study of Swedish adults with gender identity disorder. Arch Sex Behav. 2010 Dec;39(6):1429-37. Epub 2009 Oct 9.

Johansson et al. conducted a two center (Lund and Umeå, Sweden) non-blinded, observational study using a semi-cross-sectional design (albeit over an extended time interval) using a self-designed tool and Axis V assessment. The study was prospective except for the acquisition of baseline Axis V data. There were no formal controls in this mixed population with and without surgery.

The investigators assessed satisfaction with the reassignment process, employment, partnership, sexual function, mental health, and global satisfaction in gender-reassigned persons from two disparate geographic regions. Surgical candidates were required to have met National Board of Health and Welfare criteria including initial and periodic psychiatric assessment, ≥1 year of real-life experience in preferred gender, and ≥1 year of subsequent hormone treatment. In addition, participants were required to have been approved for reassignment five or more years prior and/or to have completed surgical reassignment (e.g., sterilization, genital surgery) two or more years prior. The investigators employed semi-structured interviews covering a self-designed list of 55 pre-formulated questions with a three or five point ordinal scale. Clinician assessment of Global Assessment of Functioning (GAF; Axis V) was also conducted and compared to initial finding during the study. Changes or differences considered to be biologically significant were not pre- specified except for GAF, which pre-specified a difference to mean change ≥5 points. Statistical corrections for multiple comparisons were not included. There was no stratification by treatment.

Of the pool of 60 eligible patients, 42 (70.0% of eligible) (17 [40.5 %] female-to-male; 25 [59.5%] male-to-female;

ratio 1:1.5) were available for follow-up. Of these, 32 (53.3% of eligible) (14 [43.8%] female-to-male; 18 [56.2%] male-to-female [ratio 1:1.3]) had completed genital gender reassignment surgery (not including one post mastectomy), five were still in the process of completing surgery, and five (one female-to-male; four male- to-female; ratio 1:4) had discontinued the surgical process prior to castration and genital surgery.

The age (ranges) of the patients at entry into the program, reassignment surgery, and follow-up were 27.8 (18-46), 31.4 (22- 49), and 38.9 (28-53) years in the female-to-male group respectively and 37.3 (21-60), 38.2 (22-57), and 46.0 (25.0-69.0) years in the male- to-female group respectively. The differences in age by cohort group were statistically significant. Of participants, 88.2% of all enrolled female-to-male versus 44.0% of all enrolled female-to-male patients had cross-gender identification in childhood (versus during or after puberty) ($p<0.01$).

Although 95.2% of all enrolled patients self-reported improvement in GAF, in contrast, clinicians determined GAF improved in 61.9% of patients. Clinicians observed improvement in 47% of female-to-male patients and 72% of male-to- female patients. A ≥5 point improvement in the GAF score was present in 18 (42.9%). Of note, three of the five patients who were in the process of reassignment and five of the five who had discontinued the process were rated by clinicians as having improved.

Of all enrolled 95.2% (with and without surgery) reported satisfaction with the reassignment process. Of these 42 patients, 33 (79%) identified themselves by their preferred gender and nine (21%) identified themselves as transgender. None of these nine (eight male-to-female) had completed reassignment surgery because of ambivalence secondary to lack of acceptance by others and dissatisfaction with their appearance. Of the patients who underwent genital surgery (n=32) and mastectomy only (n=one), 22 (66.7%) were satisfied while four (three female-to-male) were dissatisfied with the surgical treatment.

Regarding relationships after surgery, 16 (38.1%) (41.2% of female- to-male; 36.0% of male-to-female patients) were reported to have a partner. Yet more than that number commented on partner relationships: (a) 62.2 % of the 37 who answered (50.0% of female- to- male; 69.6% of male-to-female patients) reported improved partner relationships (five [11.9%] declined to answer.); (b) 70.0% of the 40 who answered (75.0% of female-to-male; 66.7% of male-to-female patients) reported an improved sex life. Investigators observed that reported post-operative satisfaction with sex life was statistically more likely in those with early rather than late cross-gender identification. In addition 55.4% self-reported improved general health; 16.1% reported impaired general health; 11.9% were currently being treated with anti-depressants or tranquilizers.

This study subsumes earlier work by Bodlund et al. (1994, 1996). The nationwide mortality studies by Dhejne et al. (2011) may include all or part of this patient population.

Leinung M, Urizar M, Patel N, Sood S. Endocrine treatment of transsexual persons: extensive personal experience. Endocr Pract. 2013 Jul-Aug;19(4):644-50. (United States study)

Leinung et al. conducted a single-center (Albany, New York) a partially prospective, non-blinded, observational study using a cross-sectional design and descriptive statistics. There were no formal controls. The investigators assessed employment, substance abuse, psychiatric disease, mood disorders, Human Immunodeficiency Virus (HIV) status in patients who had met WPATH guidelines for therapy, and who had initiated cross-sex hormone treatment.

A total of 242 patients treated for gender identity disorder in the clinic from 1992 through 2009 inclusive were identified. The number of those presenting for therapy almost tripled over time. Of these patients, 50 (20.7%) were female-to-male; 192 (79.3%) male-to-female (ratio 1:3.8).

The age of female-to-male and male-to-female patients with gender dysphoria at the time of clinic presentation was 29.0 and 38.0 years respectively.

The female-to-male and male-to-female patients with gender dysphoria at the time of hormone initiation were young: 27.5 and 35.5 years old respectively ($p<0.5$). Of the male-to-female cohort, 19 (7.8%) had received hormone therapy in the absence of physician supervision; Of the patient population, 91 (37.6%) had undergone gender-reassignment surgery (32 female-to-male [64.0% of all female-to- male; 35.2% of all surgical patients]; 59 male-to-female [30.7% of all male-to-female; 64.8% of all surgical patients]; ratio 1:1.8).

Psychiatric disease was more common in those who initiated hormone therapy at an older age (>32 years) 63.9% versus 48.9% at a younger age and by natal gender (48.0% of female-to-male; 58.3% male-to-female). Mood disorders were more common in those who initiated hormone therapy at an older age (>32 years) 52.1% versus 36.0% at a younger age and this finding did not differ by natal gender (40.0% of female-to-male; 44.8% male-to-female). The presence of mood disorders increased the time to reassignment surgery in male-to-female patients.

Motmans J , Meier P, Ponnet K, T'Sjoen G. Female and male transgender quality of life: socioeconomic and medical differences. J Sex Med. 2012 Mar;9(3):743-50. Epub 2011 Dec 21.

Motmans et al., conducted a prospective, non-blinded, observational study using a cross-sectional design and a non-specific quality of life tool. No concurrent controls were used in this study. Quality of life in this Dutch-speaking population was assessed using the Dutch version of a SF-36 (normative data was used). Participants included subjects who were living in accordance with the preferred gender and who were from a single Belgian university specialty clinic at Ghent. The Dutch version of the SF-36 questionnaire along with its normative data were used. Variables explored included employment, pension status, ability to work, being involved in a relationship. Also explored, was surgical reassignment surgery and the types of surgical interventions. Intragroup comparisons by transgender category were conducted, and the relationships between variables were assessed by analysis of variance (ANOVA) and correlations.

The age of the entire cohort (n=140) was 39.89±10.21 years (female-to-male: 37.03±8.51; male-to-female: 42.26±10.39). Results of the analysis revealed that not all female-to-male patients underwent surgical reassignment surgery and, of those who did, not all underwent complete surgical reassignment. The numbers of female-to-male surgical interventions were: mastectomy 55, hysterectomy 55, metaoidplasty eight (with five of these later having phalloplasty), phalloplasty 40, and implantation of a prosthetic erectile device 20. The frequencies of various male-to-female surgical interventions were: vaginoplasty 48, breast augmentation 39, thyroid cartilage reduction 17, facial feminization 14, and hair transplantation three.

The final number of subjects with SF-36 scores was 103 (49 [47.6%] female-to-male; 54 [52.4%] male-to-female; ratio 1:1.1). For this measure, the scores for the vitality and mental health domains for the final female-to-male cohort (n= 49 and not limited to those having undergone some element of reassignment surgery) were statistically lower: 60.61±18.16 versus 71.9±18.31 and 71.51±16.40 versus 79.3±16.4 respectively. Scores were not different from the normative data for Dutch women: vitality: 64.3±19.7 or mental health 73.7±18.2. None of the domains of the SF-36 for the final male-to-female cohort (n=54 and not limited to those having undergone some element of reassignment surgery) were statistically different from the normative data for Dutch women.

Analysis of variance indicated that quality of life as measured by the SF-36 did not differ by whether female-to-male patients had undergone genital surgery (metaoidoplasty or phalloplasty) or not. Also, ANOVA indicated that quality of life as measured by the SF-36 did not differ by whether male-to-female patients had undergone either breast augmentation or genital surgery (vaginoplasty) or not.

Whether there is overlap with the Ghent populations studied by Heylens et al. or Weyers et al. is unknown.

Newfield E, Hart S, Dibble S, Kohler L. Female-to-male transgender quality of life. Qual Life Res. 2006 Nov;15(9):1447-57. Epub 2006 Jun 7. (United States study)

Newfield et al. conducted a prospective, observational internet self-report survey of unknown blinding status using a cross- sectional design and a non-specific quality of life tool in a mixed population with and without hormone therapy and/or reassignment surgery. There were no formal controls.

The investigators recruited natal female participants identifying as male using email, internet bulletin boards, and flyers/postcards distributed in the San Francisco Bay Area. Reduction of duplicate entries by the same participant was limited to the use of a unique user name and password.

The investigators employed the Short-Form 36 (SF-36) Version 2 using U.S. normative data. They reported using both male and female normative data for the comparator SF-36 cohort. Data for the eight domains were expressed as normative scoring. The Bonferroni correction was used to adjust for the risk of a Type 1 error with analyses using multiple comparisons.

A total of 379 U.S. respondents classified themselves as males-or-females to males with or without therapeutic intervention. The mean age of the respondents who classified themselves as male or female-to-male was 32.6±10.8 years. Of these 89% were Caucasian, 3.6% Latino, 1.8% African American, 1.8% Asian, and 3.8% other. Of these, 254 (67.0%) reported prior or current testosterone use while 242 (63.8%) reported current testosterone use. In addition, 136 (36.7%) reported having had “top” surgery and 11 (2.9%) reported having “bottom” surgery.

Complete SF-36 data were available for 376 U.S. respondents. For the complete, non-stratified U.S. cohort the Physical Summary Score (53.45±9.42) was statistically higher (better) than the natal gender unspecified SF-36 normative score (50±10) (p=<0.001), but was within one standard deviation of the normative mean. The Mental Summary Score (39.63±12.2) was statistically lower (worse) than the natal gender unspecified SF-36 normative score (50±10) (p<0.001), but was well within two standard deviations of the normative mean. Subcomponents of this score: Mental Health (42.12±10.2), Role Emotional (42.42±11.6), Social Functioning (43.14±10.9), and Vitality (46.22±9.9) were statistically lower (worse) than the SF-36 normative sub-scores, but well within one standard deviation of the normative sub- score means. Interpretive information for these small biologic differences in a proprietary assessment tool was not provided.

Additional intragroup analyses were conducted, although the data were not stratified by type of therapeutic intervention (hormonal, as well as, surgical). Outcomes of hormone therapy were considered separately and dichotomously from reassignment surgery. The Mental Summary Score was statistically higher (better) in those who had “Ever Received Testosterone” (41.22±11.9) than those with “No Testosterone Usage” (36.08±12.6) (p=0.001). The Mental Summary Scores showed a trend towards statistical difference between those who “Ever Received Top Surgery” (41.21±11.6) and those without “Top Surgery” (38.01±12.5) (p=0.067). These differences were well within one standard deviation of the normative mean. Interpretive information for these small biologic differences in a proprietary assessment tool was not provided.

b. Observational, surgical series, without concurrent controls

Blanchard R, Steiner BW, Clemmensen LH. Gender dysphoria, gender reorientation, and the clinical management of transsexualism. J Consult Clin Psychol. 1985 Jun; 53(3):295-304.

Blanchard et al. conducted a single-center (Ontario, Canada), prospective, non-blinded, cross-sectional study using a self-designed questionnaire and a non- specific psychological symptom assessment with normative data. The investigators assessed social adjustment and psychopathology in patients with gender dysphoria and who were at least one year post gender reassignment surgery. Reassignment surgery was defined as either vaginoplasty or mastectomy/construction of male chest contour with or without nipple transplants, but did not preclude additional procedures. Partner preference was determined using Blanchard's Modified Androphilia-Gynephilia Index, and the nature and extent of any psychopathology was determined with the Symptom Check List 90-Revised (SCL-90R). Differences in test scores considered to be biologically significant were not pre-specified in the methods.

Of the 294 patients (111 natal females and 183 natal males, ratio: 1:1.65) initially evaluated, 263 were diagnosed with gender dysphoria. Of these 79 patients participated in the study (38 female-to-male; 32 male-to-female with male partner preference; 9 male-to-female with female partner preference). The respective mean ages for these 3 groups were 32.6, 33.2, and 47.7 years with the last group being older statistically (p=0.01).

Additional surgical procedures in female-to-male patients included: oophorectomy/hysterectomy (92.1%) and phalloplasty (7.9%). Additional surgical procedures in male-to-female patients with male partner preference included facial hair electrolysis 62.5% and breast implantation (53.1%). Additional procedures in male-to-female patients with female partner preference included facial hair electrolysis (100%) and breast implantation (33.3%). The time between reassignment surgery and questionnaire completion did not differ by group.

Psychopathology as measured by the Global Severity Index of the SCL-90R was absent in all three patient groups. Interpretation did not differ by the sex of the normative cohort.

Of participants, 63.2% of female-to-male patients cohabitated with partners of their natal gender; 46.9% of male-to-female patients with male partner preference cohabitated with partners of their natal gender; and no male-to-female patients with female partner preference cohabitated with partners of their natal gender.

Of participants, 93.7% reported that they would definitely undergo reassignment surgery again. The remaining 6.3% (one female-to-male; one male-to-female with male partner preference; three male-to-female with female partner preference) indicated that they probably would undertake the surgery again. Post hoc analysis suggested that the more ambivalent responders had more recently undergone surgery. Of responders, 98.7% indicated that they preferred life in the reassigned gender. The one ambivalent subject was a skilled and well compensated tradesperson who was unable to return to work in her male dominated occupation.

Eldh J, Berg A, Gustafsson M. Long-term follow up after sex reassignment surgery. Scand J Plast Reconstr Surg Hand Surg. 1997 Mar;31(1):39-45.

Eldh et al. conducted a non-blinded, observational study using a prospective cross-sectional design with an investigator designed questionnaire and retrospective acquisition of pre-operative data. The investigators assessed economic circumstances, family status, satisfaction with surgical results, and sexual function in patients who had undergone gender reassignment surgery.

Of the 175 patients who underwent reassignment surgery in Sweden, 90 responded. Of this number, 50 were female-to-male and 40 were male-to-female (ratio: 1:0.8). Patients reportedly were generally satisfied with the appearance of the reconstructed genitalia (no numbers provided). Of the patients who had undergone surgery prior to 1986, seven (14%) were dissatisfied with shape or size of the neo-phallus; eight (16%) declined comment. There were 14 (35%), with 12 having surgery prior to 1986 and two between 1986 and 1995 inclusive, were moderately satisfied because of insufficient vaginal volume; 8 (20%) declined comment. A neo-clitoris was not constructed until the later surgical cohort. Three of 33 reported no sensation or no sexual sensation. Eight had difficulties

comprehending the question and did not respond.

A total of nine (18%) patients had doubts about their sexual orientation; 13 (26%) declined to answer the question. The study found that two female-to- male patients and two male-to-female patients regretted their reassignment surgery and continued to live as the natal gender, and two patients attempted suicide.

Hess J, Rossi Neto R, Panic L, Rübben H, Senf W. Satisfaction with male-to-female gender reassignment surgery. Dtsch Arztebl Int. 2014 Nov 21;111(47):795-801.

Hess at al. conducted a prospective, blinded, observational study using a cross-sectional design and a self-designed anonymous questionnaire. The investigators assessed post-operative satisfaction in male-to-female patients with gender dysphoria who were followed in a urology specialty clinic (Essen, Germany). Patients had met the ICD-10 diagnostic criteria, undergone gender reassignment surgeries including penile inversion vaginoplasty, and a Likert-style questionnaire with 11 elements. Descriptive statistics were provided.

There were 254 consecutive eligible patients who had undergone surgery between 2004 and 2010 identified and sent surveys, of whom 119 (46.9%) responded anonymously. Of the participants, 13 (10.9%) reported dissatisfaction with outward appearance and 16 (13.4%) did not respond; three (2.5%) reported dissatisfaction with surgical aesthetics and 25 (21.0%) did not respond; eight (6.7%) reported dissatisfaction with functional outcomes of the surgery and 26 (21.8%) did not respond; 16 (13.4%) reported they could not achieve orgasm and 28 (23.5%) did not respond; four (3.4%) reported feeling completely male/more male than female and 28 (23.5%) did not respond; six (5.0%) reported not feeling accepted as a woman, two (1.7%) did not understand the question, and 17 (14.3%) did not respond; and 16 (13.4%) reported that life was harder and 24 (20.2%) did not respond.

Lawrence A. Patient-reported complications and functional outcomes of male-to-female sex reassignment surgery. Arch Sex Behav. 2006 Dec;35(6):717-27. Epub 2006 Nov 16. (United States study)

Lawrence conducted a prospective, blinded observational study using a cross-sectional design and a partially self-designed quality of life tool using yes/no questions or Likert scales. The investigator assessed sexual function, urinary function, and other pre/post-operative complications in patients who underwent male-to-female gender reassignment surgery. Questions addressed core reassignment surgery (neo-vagina and sensate neo-clitoris) and related reassignment surgery (labiaplasty, urethral meatus revision, vaginal deepening/widening, and other procedures), use of electrolysis, and use of hormones.

Questionnaires were designed to be completed anonymously and mailed to 727 eligible patients. Of those eligible, 232 (32%) returned valid questionnaires. The age at the time reassignment surgery was 44±9 (range 18-70) years and mean duration after surgery was 3±1 (range 1-7) years.

Happiness with sexual function and the reassignment surgery was reported to be lower when permanent vaginal stenosis, clitoral necrosis, pain in the vagina or genitals, or other complications such as infection, bleeding, poor healing, other tissue loss, other tissue necrosis, urinary incontinence, and genital numbness were present. Quality of life was impaired when pain in the vagina or genitals was present.

Satisfaction with sexual function, gender reassignment surgery, and overall QOL was lower when genital sensation was impaired and when vaginal architecture and lubrication were perceived to be unsatisfactory. Intermittent regret regarding reassignment surgery was associated with vaginal hair and clitoral pain. Vaginal stenosis was associated with surgeries performed in the more distant past; whereas, more satisfaction with vaginal depth and width was present in more recent surgical treatment.

Salvador J, Massuda R, Andreazza T, Koff WJ, Silveira E, Kreische F, de Souza L, de Oliveira MH, Rosito T, Fernandes BS, Lobato MI. Minimum 2-year follow up of sex reassignment surgery in Brazilian male-to-female transsexuals. Psychiatry Clin Neurosci. 2012 Jun; 66(4):371-2. PMID: 22624747.

Salvador et al. conducted a single center (Port Alegre, Brazil) prospective, non-blinded, observational study using a cross-sectional design (albeit over an extended time interval) and a self-designed quality of life tool. The investigators assessed regret, sexual function, partnerships, and family relationships in patients who had undergone gender reassignment surgery at least 24 months prior.

Out of the 243 enrolled in the clinic over a 10 year interval, 82 underwent sex reassignment surgery. There were 69 participants with a minimum 2-year follow up, of whom 52 patients agreed to participate in the study. The age at follow-up was 36.3±8.9 (range 15-58) years with the time to follow-up being 3.8±1.7 (2-7) years. A total of 46 participants reported pleasurable neo-vaginal sex and post-surgical improvement in the quality of their sexual experience. The quality of sexual intercourse was rated as satisfactory to excellent, average, unsatisfactory, or not applicable in the absence of sexual contact by 84.6%, 9.6%, 1.9%, and 3.8% respectively. Of the participants, 78.8% reported greater ease in initiating and maintaining relationships; 65.4% reported having a partner; 67.3% reported increased frequency of intercourse; 36.8% reported improved familial relationships. No patient reported regret over reassignment surgery. The authors did not provide information about incomplete questionnaires.

Tsoi WF. Follow-up study of transsexuals after sex-reassignment surgery. Singapore Med J. 1993 Dec; 34(6):515-7.

Tsoi conducted a single-center (Singapore) prospective, non-blinded, observational study using a cross-sectional design and a self-designed quality of life tool. The investigator assessed overall life satisfaction, employment, partner status, and sexual function in gender-reassigned persons who had undergone gender reassignment surgery between 1972 and 1988 inclusive and who were approximately 2 to 5 years post-surgery. Acceptance criteria for surgery included good physical health, good mental health, absence of heterosexual tendencies, willingness to undergo hormonal therapy for ≥6 months, and willingness to function in the life of the desired gender for ≥6 months. Tsoi also undertook retrospective identification of variables that could predict outcomes.

The size of the pool of available patients was not identified. Of the 81 participants, 36 (44.4%) were female-to-male and 45 (55.6%) were male-to-female (ratio 1:1.25).

The mean ages at the time of the initial visit and operation were: female-to-male 25.4±4.4 (range 14-36) and 27.4 ±4.0; (range 14-36); male-to-female 22.9±4.6 (range 14-36) and 24.7±4.3 (14-36) years respectively. Of all participants, 14.8% were under age 20 at the time of the initial visit. All were at least 20 at the time of gender reassignment surgery. The reported age of onset was 8.6 years for female-to-male patients and 8.7 years for male-to-female patients.

All participants reported dressing without difficulty in the reassigned gender; 95% of patients reported good or satisfactory adjustment in employment and income status; 72% reported good or satisfactory adjustment in relationships with partners. Although the quality of life tool was self-designed, 81% reported good or satisfactory adjustment to their new gender, and 63% reported good or acceptable satisfaction with sexual activity. Of the female-to-male patients, 39% reported good or acceptable satisfaction with sex organ function in comparison to 91% of male-to-female patients ($p<0.001$). (The author reported that a fully functioning neo-phallus could not be constructed at the time.) The age of non-intercourse sexual activity was the only predictor of an improved outcome.

Weyers S, Elaut E, De Sutter P, Gerris J, T'Sjoen G, Heylens G, De Cuypere G, Verstraelen H. Long-term assessment of the physical, mental, and sexual health among transsexual women. J Sex Med. 2009 Mar;6(3):752-60. Epub 2008 Nov 17.

Weyers at al. (2009) conducted a prospective, non-blinded, observational study using a cross-sectional design and several measurement instruments including a non-specific quality of life tool and a semi-specific quality of life tool (using normative data) along with two self-designed tools.

The investigators assessed general quality of life, sexual function, and body image from the prior four weeks in Dutch-speaking male-to-female patients with gender dysphoria who attended a single-center (Ghent, Belgium), specialized, comprehensive care university clinic. Investigators used the Dutch version of the SF-36 and results were compared to normative data from Dutch women and U.S. women. The 19 items of the Dutch version of the Female Sexual Function Index (FSFI) were used to measure sexual desire, function, and satisfaction. A self-designed seven question visual analog scale (VAS) was used to measure satisfaction with gender related body traits and appearance perception by self and others. A self-designed survey measured a broad variety of questions regarding personal medical history, familial medical history, relationships, importance of sex, sexual orientation, gynecologic care, level of regret, and other health concerns. For this study, hormone levels were also obtained.

The study consisted of 50 (71.5% of the eligible recruits) participants. Analysis of the data revealed that the patient's average age was 43.1 ±10.4 years, and all of the patients had vaginoplasty. This same population also had undergone additional feminization surgical procedures (breast augmentation 96.0%, facial feminization 36.0%, vocal cord surgery 40.0%, and cricoid cartilage reduction 30.0%). A total of two (4.0%) participants reported "sometimes" regretting reassignment surgery and 23 (46.0%) were not in a relationship. For the cohort, estradiol, testosterone, and sex hormone binding globulin levels were in the expected range for the reassigned gender. The SF-36 survey revealed that the subscale scores of the participants did not differ substantively from those of Dutch and U.S. women. VAS scores of body image were highest for self-image, appearance to others, breasts, and vulva/vagina (approximately 7 to 8 of 10). Scores were lowest for body hair, facial hair, and voice characteristics (approximately 6 to 7 of 10).

The total FSFI score was 16.95±10.04 out of a maximal 36. The FSFI scores averaged 2.8 (6 point maximum): satisfaction 3.46±1.57, desire 3.12+1.47, arousal 2.95±2.17, lubrication 2.39±2.29, orgasm 2.82±2.29, and pain 2.21±2.46. Though these numbers were reported in the study, data on test population controls were not provided.

A post hoc exploration of the data suggested the following: perceived improvement in general health status was greater in the subset that had undergone reassignment surgery within the last year; sexual orientation impacted the likelihood of being in a relationship; SF-36 scores for vitality, social functioning, and mental health were nominally better for those in relationships, but that overall SF-36 scores did not differ by relationship status; sexual orientation and being in a relationship impacted FSFI scores; and reported sexual function was higher in those with higher satisfaction with regards to their appearance.

Wierckx K, Van Caenegem E, Elaut E, Dedecker D, Van de Peer F, Toye K, Weyers S, Hoebeke P, Monstrey S, De Cuypere G, T'Sjoen G. Quality of life and sexual health after sex reassignment surgery in transsexual men. J Sex Med. 2011 Dec;8 (12):3379-88. Epub 2011 Jun 23.

Wierckx at al. conducted a prospective, non-blinded, observational study using a cross-sectional design and several measurement instruments (a non-specific quality of life tool with reported normative data along with three self-designed tools). The investigators assessed general quality of life, sexual relationships, and surgical complications in Dutch-speaking female-to-male patients with gender dysphoria who attended a single-center, specialized, comprehensive care, university clinic (Ghent, Belgium). Investigators used the Dutch version of the SF-36 with 36 questions, eight subscales, and two domains evaluating physical and mental health. Results were compared to normative data from Dutch women and Dutch men. Self -designed questionnaires to evaluate aspects of medical history, sexual functioning (there were separate versions for those with and without partners), and surgical results were also used. The Likert-style format was used for many of the questions.

A total of 79 female-to-male patients with gender dysphoria had undergone reassignment surgery were recruited; ultimately, 47 (59.5%) chose to participate. Three additional patients were recruited by other patients. One of the 50 participants was later excluded for undergoing reassignment surgery within the one year window. The age of patients was: 30±8.2 years (range 16 to 49) at the time of reassignment surgery and 37.1 ±8.2 years (range 22 to 54) at the time of follow-up. The time since hysterectomy, oopherectomy, and mastectomy was 8 years (range 2 to 22). The patient population had undergone additional surgical procedures: metaidoiplasty (n=9; 18.4%), phalloplasty (n=8 after metaidoiplasty, 38 directly; 93.9% total), and implantation of erectile prosthetic device (n=32; 65.3%). All had started hormonal therapy at least two years prior to surgery and continued to use androgens.

The SF-36 survey was completed by 47 (95.9%) participants. The "Vitality" and the "Mental Health" scales were lower than the Dutch male population: 62.1±20.7 versus 71.9±18.3 and 72.6±19.2 versus 79.3±16.4 respectively. These subscale scores were equivalent to the mean scores of the Dutch women.

None of the participants were dissatisfied with their hysterectomy-oopherectomy procedures; 4.1% were dissatisfied with their mastectomies because of extensive scarring; and 2.2% were dissatisfied with their phalloplasties. Of the participants, 17.9% were dissatisfied with the implantation of an erectile prosthetic device; 25 (51.0%) reported at least one post-operative complication associated with phalloplasty (e.g., infection, urethrostenosis, or fistula formation); 16 (50.0% of the 32 with an erectile prosthetic device) reported at least one post-operative complication associated with implantation of an erectile prosthetic (e.g., infection, leakage, incorrect positioning, or lack of function).

A total of 18 (36.7%) participants were not in a relationship; 12.2% reported the inability to achieve orgasm with self-stimulation less than half the time; 12.2% did not respond to the question. Of those participants with partners, 28.5% reported the inability to achieve orgasm with intercourse less than half the time and 9.7% did not respond to this question. Also, 61.3% of those with partners reported (a) no sexual activities (19.4%) or (b) activities once or twice monthly (41.9%), and there were 12.9% who declined to answer.

c. Observational, surgical patients, cross-sectional, with controls

Ainsworth TA, Spiegel JH. Quality of life of individuals with and without facial feminization surgery or gender reassignment surgery. Qual Life Res. 2010 Sep;19(7):1019-24.

Ainsworth and Spiegel conducted a prospective, observational study using a cross-sectional design and a partially self-designed survey tool. The blind status is unknown. Treatment types served as the basis for controls.

The investigators, head and neck surgeons who provided facial feminization services, assessed perception of appearance and quality of life in male-to-female subjects with self-reported gender dysphoria. Patients could have received no therapeutic intervention, hormone therapy, reassignment surgery, and/or facial feminization surgery and an unrestricted length of transition. (Transition refers to the time when a transgender person begins to live as the gender with which they identify rather than the gender assigned at birth.) Criteria for the various types of interventions were not available because of the survey design of the study. Patients were recruited via website or at a 2007 health conference. Pre-specified controls to eliminate duplicate responders were not provided. The investigators employed a self-designed Likert-style facial feminization outcomes evaluation questionnaire and a "San Francisco 36" health questionnaire. No citations were provided for the latter. It appears to be the Short-form (SF) 36-version 2. Changes or differences considered to be biologically significant were not pre-specified. Power corrections for multiple comparisons were not provided.

The investigators reported that there were 247 participants. (The numbers of incomplete questionnaires was not reported.) Of the 247 participants, 25 (10.1%) received only primary sex trait reassignment surgery, 28 (11.3%)

received facial surgery without primary sex trait reassignment surgery, 47 (19.0%) received both facial and primary sex trait reassignment surgery, and 147 (59.5%) received neither facial nor reassignment surgery.

The mean age for each of these cohorts was: 50 years (no standard deviation [S.D.]) only reassignment surgery, 51 years (no S.D.) only facial surgery, 49 years (no S.D.) both types of surgery, and 46 years (no S.D.) (neither surgery). Of the surgical cohorts: 100% of those who had undergone primary sex trait reassignment surgery alone used hormone therapy, 86% of those who had undergone facial feminization used hormone therapy, and 98% of those who had undergone both primary sex trait reassignment surgery and facial feminization used hormone therapy. In contrast to the surgical cohorts, 66% of the "no surgery" cohort used hormonal therapy, and a large proportion (27%) had been in transition for less than one year.

The investigators reported higher scores on the facial outcomes evaluation in those who had undergone facial feminization. Scores of the surgical cohorts for the presumptive SF-36 comprehensive mental health domain did not differ from the general U.S. female population. Scores of the "no surgery" cohort for the comprehensive mental health domain were statistically lower than those of the general U.S. female population, but within one standard deviation of the normative mean. Mean scores of all the gender dysphoric cohorts for the comprehensive physical domain were statistically higher than those of the general female U.S. population, but were well within one standard deviation of the normative mean. Analyses of inter-cohort differences for the SF-36 results were not conducted. Although the investigators commented on the potential disproportionate impact of hormone therapy on outcomes and differences in the time in "transition", they did not conduct any statistical analyses to correct for putative confounding variables.

Kraemer B, Delsignore A, Schnyder U, Hepp U. Body image and transsexualism. Psychopathology. 2008;41(2):96-100. Epub 2007 Nov 23.

Kraemer et al. conducted a single center (Zurich, Switzerland) prospective, non-blinded, observational study using a cross-sectional design comparing pre-and post- surgical cohorts. Patients were required to meet DSM III or DSM IV criteria as applicable to the time of entry into the clinic. Post-surgical patients were from a long-term study group (Hepp et al., 2002). Pre-surgical patients were recent consecutive referrals. The assessment tool was the Fragebogen zur Beurteilung des eigenen Korpers (FBeK) which contained three domains.

There were 23 pre-operative patients: 7 (30.4%) female-to-male and 16 (69.6%) male-to-female (ratio 1:2.3). There were 22 post-operative patients: 8 (36.4 %) female-to-male and 14 (63.6%) male-to-female (ratio 1:1.8). The mean ages of the cohorts were as follows: pre-operative 33.0±11.3 years; post-operative 38.2±9.0 years. The mean duration after reassignment surgery was 51±25 months (range 5-96).

The pre-operative groups had statistically higher insecurity scores compared to normative data for the natal sex: female-to-male 9.0±3.8 versus 5.1±3.7; male-to-female 8.1±4.5 versus 4.7±3.1 as well as statistically lower self-confidence in one's attractiveness: female-to-male 3.1±2.9 versus 8.9±3.1; male-to-female 7.0±2.9 vs 9.5±2.6.

Mate-Kole C, Freschi M, Robin A. Aspects of psychiatric symptoms at different stages in the treatment of transsexualism. Br J Psychiatry. 1988 Apr;152: 550-3.

Mate-Kole at al. conducted a single site (London, United Kingdom) prospective non-blinded, observational study using a cross-sectional design and two psychological tests (one with some normative data). Concurrent controls were used in this study design. The investigators assessed neuroticism and sex role in natal males with gender dysphoria. Patients at various stages of management, (i.e., under evaluation, using cross-sex hormones, or post reassignment surgery [6 months to 2 years]) were matched by age of cross-dressing onset, childhood neuroticism, personal psychiatric history, and family psychiatric history. Both a psychologist and psychiatrist conducted assessments. The

instruments used were the Crown Crisp Experiential Index (CCEI) for psychoneurotic symptoms and the Bem Sex Role Inventory. ANOVA was used to identify differences between the three treatment cohorts.

For each cohort, investigators recruited 50 male-to-female patients from Charing Cross Hospital. The mean ages of the three cohorts were as follows: 34 years for patients undergoing evaluation; 35 years for wait-listed patients; and 37 years for post-operative patients. For the cohorts, 22% of those under evaluation, 24% of those on hormone treatment only, and 30% of those post-surgery had prior psychiatric histories, and 24%, 24%, while 14% in each cohort, respectively, had a history of attempted suicide. More than 30% of patients in each cohort had a first degree relative with a history of psychiatric disease.

The scores for the individual CCEI domains for depression and somatic anxiety were statistically higher (worse) for patients under evaluation than those on hormone treatment alone. The scores for all of the individual CCEI domains (free floating anxiety, phobic anxiety, somatic anxiety, depression, hysteria, and obsessionality) were statistically lower in the post-operative cohort than in the other two cohorts.

The Bem Sex Role Inventory masculinity score for the combined cohorts was lower than for North American norms for either men or women. The Bem Sex Role Inventory femininity score for the combined cohorts was higher than for North American norms for either men or women. Those who were undergoing evaluation had the most divergent scores from North American norms and from the other treatment cohorts. Absolute differences were small. All scores of gender dysphoric patients averaged between 3.95 and 5.33 on a 7 point scale while the normative scores averaged between 4.59 and 5.12.

Wolfradt U, Neumann K. Depersonalization, self-esteem and body image in male-to-female transsexuals compared to male and female controls. Arch Sex Behav. 2001 Jun;30(3):301-10.

Wolfradt and Neumann conducted a controlled, prospective, non-blinded, observational study using a cross-sectional design. The investigators assessed aspects of personality in male-to-female patients who had undergone vocal cord surgery for voice feminization and in healthy non-transgender volunteers from the region. The patients had undergone gender reassignment surgery 1 to 5 years prior to voice surgery. The volunteers were matched by age and occupation.

The primary hypothesis was that depersonalization, with the sense of being detached from one’s body or mental processes, would be more common in male-to- female patients with gender dysphoria. German versions of the Scale for Depersonalization Experiences (SDPE), the Body Image Questionnaire (BIQ), a Gender Identity Trait Scale (GIS), and the Self-Esteem Scale (SES) were used in addition to a question regarding global satisfaction. Three of the assessments used a 5 point scale (BIQ, GIS, and SDPE) for questions. One used a 4 point scale (SES). Another used a 7 point scale (global satisfaction). The study consisted of 30 male-to-female patients, 30 healthy female volunteers, and 30 healthy male volunteers. The mean age of study participants was 43 years (range 29- 67).

Results of the study revealed that there were no differences between the three groups for the mean scores of measures assessing depersonalization, global satisfaction, the integration of masculine traits, and body-image-rejected (subset). Also, the sense of femininity was equivalent for male-to-female patients and female controls and higher than that in male controls. The levels of self-esteem and body image-dynamic (subset) were equivalent for male-to-female patients and male controls and higher than that in female controls, and none of the numeric differences between means exceeded 0.61 units.

Kuhn A, Bodmer C, Stadlmayr W, Kuhn P, Mueller M, Birkhäuser M. Quality of life 15 years after sex reassignment surgery for transsexualism. Fertil Steril. 2009 Nov;92(5):1685-1689.e3. Epub 2008 Nov 6.

Kuhn et al. conducted a prospective, non-blinded, observational study using a cross-sectional design and semi-matched control cohort. The investigators assessed global satisfaction in patients who were from gynecology and endocrinology clinic (Bern, Switzerland), and who had undergone some aspect of gender reassignment surgery in the distant past, but were still receiving cross-sex hormones from the clinic. The quality of life assessment tools included a VAS and the King's Health Questionnaire (KHQ), which consists of eight domains with scores between zero and five or one and five, with lower scores indicating higher preference. The KHQ and the numerical change/difference required for clinical significance (≥5 points in a given domain, with higher scores being more pathologic) were included in the publication. Twenty healthy female controls from the medical staff who had previously undergone an abdominal or pelvic surgery were partially matched by age and body mass index (BMI), but not sex. No corroborative gynecologic or urologic evaluations were undertaken.

Of the 55 participants, three (5.4%) were female-to-male and 52 (94.5%) were male-to-female (ratio 1:17.3). Reassignment surgery had been conducted 8 to 23 years earlier (median 15 years). The median age of the patients at the time of this study was 51 years (range 39-62 years). The patients had undergone a median of nine surgical procedures in comparison to the two undergone by controls. Reassignment patients were less likely to be married (23.6% versus 65%; p=0.002); partnership status was unknown in five patients. The scores of VAS global satisfaction (maximal score eight) were lower for surgically reassigned patients (4.49±0.1 SEM) than controls (7.35±0.26 SEM) (p<0.0001).

The abstract stated that quality of life was lower in reassignment patients 15 years after surgery relative to controls. One table in the study, Table 2, delineated statistically and biologically significant differences for four of the eight KHQ domains between the patients and controls: physical limitation: 37.6±2.3 versus 20.9±1.9 (p<0.0001), personal limitation: 20.9±1.9 versus 11.6±0.4 (p<0.001), role limitation: 27.8+2.4 versus 34.6+1.7 (p=0.046), and general health: 31.7±2.2 versus 41.0±2.3 (p<0.02). There is a related paper by Kuhn et al. 2006.

Haraldsen IR, Dahl AA. Symptom profiles of gender dysphoric patients of transsexual type compared to patients with personality disorders and healthy adults. Acta Psychiatr Scand. 2000 Oct;102(4):276-81.

Haraldsen and Dahl conducted a single-center (Oslo, Norway) partially prospective, non-blinded, observational study using a cross-sectional design and a non-specific psychometric test. There was a control group, but it was not concurrent.

In the germane sub-study, the investigator assessed psychopathology in patients with gender dysphoria. Patients, who were independently evaluated by two senior psychiatrists, were required to meet DSM III-R or DSM IV diagnostic criteria and the Swedish criteria for reassignment surgery. The Norwegian version of the SCL-90 was used. The testing was conducted from 1987 to 1989 for those who had undergone reassignment surgery between 1963 and 1987 and from 1996 to 1998 for pre- surgical patients who had applied for reassignment surgery between 1996 and 1998. In addition, Axis I, Axis II, and Axis V (Global Functioning) was assessed.

Of 65 post–surgical and 34 pre-surgical patients, 59 post-surgical and 27 pre-surgical patients ultimately entered the study. The combined cohorts consisted of 35 (40.7%) female-to-male patients and 51 (59.3%) male-to-female patients (ratio 1:1.5). The ages were female-to-male 34±9.5 years and female-to-male 33.3±10.0 years. The other control group consisted of patients with personality disorder. Of these, 101 (27 men (33.9±7.3 years) and 74 women (31.6±8.2) were tested during a treatment program. One year later, 98% were evaluated. A total of 28 (32.5%) of the pre- and post- reassignment surgery patients had an Axis I diagnosis compared to 100 (99.0%) of those with personality disorders. Depression and anxiety were the most common diagnoses in both groups, but were approximately three to four times more common in the personality disorder cohort. Seventeen (19.8%) of the pre- and post-reassignment surgery patients had an Axis II diagnosis whereas the mean number of personality disorders in the personality disorder cohort was 1.7±1. The Global Assessment of Function was higher (better) in the gender

dysphoric groups (78.0±8.9) than in the personality disorder cohort (53.0±9.0).

Global Severity Indices (GSI) were highest for those with personality disorder regardless of gender and exceeded the cut-point score of 1.0. The GSI scores for females-to-males and males-to-females were 0.67±57 and 0.56±0.45. Although they were nominally higher than the healthy normative controls (males: 0.32±0.36 and females 0.41±0.43), they were well within the non- pathologic range. The same was true for the subscales.

SCL-90 GSI scores did not differ substantively between pre- and post-surgical patients, nor did the SCI subscale scores differ substantively between pre- and post-surgical patients. Any small non-significant differences tracked with the age and sex differences.

Beatrice J. A psychological comparison of heterosexuals, transvestites, preoperative transsexuals, and postoperative transsexuals. J Nerv Ment Dis. 1985 Jun;173(6):358-65. (United States study)

Beatrice conducted a prospective, non-blinded, observational study using a cross-sectional design and control cohorts in the U.S. The investigator assessed psychological adjustment and functioning (self-acceptance) in male-to-female patients with gender dysphoria (with and without GRS), transvestites from two university specialty clinics, and self-identified heterosexual males recruited from the same two universities. The criteria to qualify for the study included being known to the clinic for at least one year, cross-dressing for at least one year without arrest, attendance at 10 or more therapy sessions, emotionally self-supporting, and financially capable of payment for reassignment surgery, and all of these criteria were met by the pre-operative cohort as well as the post-operative cohort. The cohorts were matched to the post-operative cohort (age, educational level, income, ethnicity, and prior heterosexual object choice). The post-operative cohort was selected not on the basis of population representation, but on the basis of demographic feasibility for a small study. The instruments used were the Minnesota Multiphasic Personality Inventory (MMPI) and the Tennessee Self-Concept Scale (TSCS). Changes or differences considered to be biologically significant were not pre-specified.

Of the initial 54 recruits, ten subjects were left in each of the cohorts because of exclusions identified due to demographic factors. The mean age of each cohort were as follows: pre-operative gender dysphoric patients 32.5 (range 27-42) years, postoperative patients 35.1 (30-43) years old, transvestite 32.5 (29-37) years old, and heterosexual male 32.9 (28-38) years old. All were Caucasian. The mean age for cross-dressing in pre-operative patients (6.4 years) and post-operative patients (5.8 years) was significantly lower than for transvestites (11.8 years).

The scores for self-acceptance did not differ by diagnostic category or surgical status as measured by the TSCS instrument. As measured by the T-scored MMPI instrument (50±10), levels of paranoia and schizophrenia were higher for post-operative (GRS) patients (63.0 and 68.8) than transvestites (55.6 and 59.6) and heterosexual males (56.2 and 51.6). Levels of schizophrenia were higher for pre-operative patients (65.1) than heterosexual males (51.6). There were no differences between patients with gender dysphoria. Scores for the Masculine-Feminine domain were equivalent in those with transvestitism and gender dysphoria with or without surgery, but higher than in heterosexual males. The analysis revealed that despite the high level of socio-economic functioning in these highly selected subjects, the MMPI profiles based on the categories with the highest scores were notable for antisocial personality, emotionally unstable personality, and possible manic psychosis in the pre-operative GRS patients and for paranoid personality, paranoid schizophrenia, and schizoid personality in the post-operative GRS patients. By contrast, the same MMPI profiling in heterosexual males and transvestites was notable for the absence of psychological dysfunction.

d. Observational, surgical patients, longitudinal, with controls

Dhejne C, Lichtenstein P, Boman M, Johansson A, Långström N, Landén M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. PLoS One. 2011;6(2):e16885. Epub 2011 Feb 22.

Dhejne et al. conducted a retrospective, non-blinded, observational study of nation-wide mortality using a longitudinal and a population-based matched cohort. The investigators assessed conditions such as, but not limited to, mortality, suicide attempts, psychiatric hospitalization, and substance abuse in gender-reassigned persons and randomly selected unexposed controls matched by birth year and natal sex (1:10) as well as by birth year and the reassigned gender (1:10). Data were extracted from national databases including the Total Population Register (Statistics Sweden), the Medical Birth Register, the Cause of Death Register (Statistics Sweden), the Hospital Discharge Register (National Board of Health and Welfare), the Crime Register (National Council of Crime), and those from the Register of Education for highest educational level. The criteria required to obtain the initial certificate for reassignment surgery and change in legal status from the National Board of Health and Welfare were the 2002 WPATH criteria and included evaluation and treatment by one of six specialized teams, name change, a new national identity number indicative of gender, continued use of hormones, and sterilization/castration. Descriptive statistics with hazard ratios were provided.

Investigators identified 804 patients with gender identity disorder (or some other disorder) in Sweden during the period from 1973 to 2003 inclusive. Of these patients, 324 (40.3%) underwent gender-reassignment surgery (133 female-to-male [41.0%]; 191 male-to-female [59.0%]; ratio 1:1.4). The average follow-up time for all-cause mortality was 11.4 years (median 9.1). The average follow-up time for psychiatric hospitalization was 10.4 years (median 8.1).

The mean ages in female-to-male and male-to-female reassigned patients were: 33.3±8.7 (range 20–62) and 36.3± 10.1 (range 21–69) years, respectively. Immigrant status was two times higher in reassigned patients (n=70, 21.6%) than in either type of control (birth [natal] sex matched n=294 [9.1%] or reassigned gender matched n=264 [8.1%]). Educational attainment (10 or more years) was somewhat lower for reassigned patients (n=151 [57.8%]) than in either type of control (birth sex matched n=1,725 [61.5%] or reassigned gender matched n=1804 [64.3%]) (cohort data were incomplete). The biggest discordance in educational attainment was for female-to-male reassigned patients regardless of the control used. Prior psychiatric morbidity (which did not include hospitalization for gender dysphoria) was more than four times higher in reassigned patients (n=58, 17.9%) than in either type of control (birth sex matched n=123 [3.8%] or reassigned gender matched n=114 [3.5%]).

All-cause mortality was higher for patients who underwent gender reassignment surgery (n=27 [8.3%]) than in controls (hazard ratio 2.8 [CI 1.8-4.3]) even after adjustment for covariants (prior psychiatric morbidity and immigration status). Divergence in the survival curves began at 10 years. Survival rates at 20 year follow-up (as derived from figure 1) were: female control 97%, male controls 94%, female-to-male patients 88%, and male-to-female patients 82%. The major contributor to this mortality difference was completed suicide (n=10 [3.1%]; adjusted hazard ratio 19.1 [CI 5.8-62.9]). Mortality due to cardiovascular disease was modestly higher for reassigned patients (n=9 [2.8%]) than in controls (hazard ratio 2.5 [CI 1.2-5.3]).

Suicide attempts were more common in patients who underwent gender reassignment surgery (n= 29 [9.0%] than in controls (adjusted hazard ratio 4.9 [CI 2.9–8.5]). Male-to-female patients were at higher adjusted risk for attempted suicide than either control whereas female-to-male patients were at higher adjusted risk compared to only male controls and maintained the female pattern of higher attempted suicide risk. Hospitalizations for psychiatric conditions (not related to gender dysphoria) were more common in reassigned persons n= 64 [20.0%] than in controls (hazard ratio 2.8 [CI 2.0–3.9]) even after adjusting for prior psychiatric morbidity. Hospitalization for substance abuse was not greater than either type of control.

The nationwide mortality studies by Dhejne et al. (2011) includes much, if not all, of the Landén (1998) patient population and much of the Dhejne et al. (2014) population.

Dhejne C, Öberg K, Arver S, Landén M. An analysis of all applications for sex reassignment surgery in Sweden, 1960-2010: prevalence, incidence, and regrets. Arch Sex Behav. 2014 Nov;43(8):1535-45. Epub 2014 May 29 and Landén M, Wålinder J, Hambert G, Lundström B. Factors predictive of regret in sex reassignment. Acta Psychiatr Scand. 1998 Apr;97(4):284 (Dhejne et al., 2014; Landén et al., 1998) Sweden-All

Dhejne et al. conducted a non-blinded, observational study that was longitudinal for the capture of patients with "regret" in a national database. This same group (Landén et al., 1998) conducted a similar study along with retrospective acquisition of clinical data to explore the differences between the cohorts with and without regret. There were no external controls; only intra- group comparisons for this surgical series.

The investigators assessed the frequency of regret for gender reassignment surgery. Data were extracted from registries at the National Board of Health and Welfare to which patients seeking reassignment surgery or reversal of reassignment surgery make a formal application and which has maintained such records since a 1972 law regulating surgical and legal sex reassignment. The investigators reviewed application files from 1960 through 2010. The specific criteria to qualify for gender surgery were not delineated. Patients typically underwent diagnostic evaluation for at least one year. Diagnostic evaluation was typically followed by the initiation of gender confirmation treatment including hormonal therapy and real-life experience. After two years of evaluation and treatment, patients could make applications to the national board. Until recently sterilization or castration were the required minimal surgical procedures (Dhejne et al., 2011). Secular changes in this program included consolidation of care to limited sites, changes in accepted diagnostic criteria, and provision of non-genital surgery, e.g., mastectomy during the real- life experience phase, and family support.

There were 767 applicants for legal and surgical reassignment (289 [37.7%] female-to-male and 478 [62.3%] male-to-female; ratio 1:1.6). The number of applicants doubled each ten year interval starting in 1981.

Of the applicants, 88.8% or 681 (252 [37.0%] female-to-male and 429 [63.0%] male-to-female; ratio 1:1.7] had undergone surgery and changed legal status by June 30, 2011. This number included eight (four [50.0%] female-to-male and four [50.0%] male to female; ratio 1:1) people who underwent surgery prior to the 1972 law. This number appears to include 41 (two [4.9%] female-to-male and 39 [95.1%] male-to-female; ratio 1:19.5) people who underwent surgery abroad at their own expense (usually in Thailand or the U.S.). This cohort (6% of 681) includes one person who was denied reassignment surgery by Sweden.

Twenty-five (3.3%) of the applications were denied with the two most common reasons being an incomplete application or not meeting the diagnostic criteria. An additional 61(8.0%) withdrew their application, were wait-listed for surgery, postponed surgery (perhaps in hopes of the later revocation of the sterilization requirement), or were granted partial treatment.

The formal application for reversal of the legal gender status, the "regret rate", was 2.2%. No one who underwent sex- reassignment surgery outside of Sweden (36 of these 41 had surgery after 1991) has requested reversal. The authors noted, however, that this preliminary number may be low because the median time interval to reversal request was eight years-only three of which had elapsed by publication submission- and because it was the largest serial cohort. This number did not include other possible expressions of regret including suicide (Dhejne et al., 2011).

Dhejne et al. in 2014 reported that the female-to-male (n=5): male-to-female (n=10) ratio among those who made formal applications for reversal was 1:2. The investigators also reported that the female-to-male applicants for reversal were younger at the time of initial surgical application (median age 22 years) than the complete female-to-

male cohort at the time of surgical application (median age 27 years). By contrast the male-to-female applicants for reversal were older at the time of initial surgical application (median age 35 years) than the complete male-to-female cohort at the time of initial surgical application (median age 32 years). Other clinical data to explore the differences between the cohorts with and without regret were not presented in this update publication.

In their earlier publication, in addition to determining a regret rate (3.8%), Landén et al. extracted data from medical records and government verdicts. Pearson Chi-square testing with Yates' correction for small sample sizes was used to identify candidate variables predictive of regret. They observed that: (a) 25.0% of the cohort with regrets and 11.4% of the cohort without regrets were unemployed, (b) 16.7% of the cohort with regrets and 15.4% of the cohort without regrets were on "sick benefit", (c) 15.4% of the cohort with regrets and 13.9% of the cohort without regrets had problems with substance abuse, (d) 69.2% of the cohort with regrets and 34.6% of the cohort without regrets had undergone psychiatric treatment, (e) 15.4% of the cohort with regrets and 8.8% of the cohort without regrets had a mood disorder, and (f) 15.4% of the cohort with regrets and 1.5% of the cohort without regrets had a psychotic disorder.

The putative prognostic factors that were statistically different between the cohorts with and without regret included prior psychiatric treatment, a history of psychotic disorder, atypical features of gender identity, and poor family support. Factors that trended towards statistical difference included having an unstable personality, sexual orientation and transvestitism. Univariate regression analyses further clarified the most important variables. These variables were tested with logistic regression. Initial modeling included the variable "history of psychotic disorder". Although this variable was predictive, it was excluded from future analyses because it was already a contraindication to reassignment surgery. Additional multivariate regression analyses identified poor family support as the most predictive variable and atypical features of gender identity as the second most important variable. Presence of both variables had a more than additive effect.

The nationwide mortality studies by Dhejne et al. (2011) includes much, if not all, of the Landén (1998) patient population and most of the Dhejne (2014) population. There is a related paper by Landén et al. 1998b that included the criteria to qualify for surgical intervention at that time.

Heylens G, Verroken C, De Cock S, T'Sjoen G, De Cuypere G. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. J Sex Med. 2014 Jan;11(1):119-26. Epub 2013 Oct 28.

Heylens et al. conducted a prospective, non-blinded observational study using a longitudinal design in which patients served as their own controls. They used a non-specific psychiatric test with normative data along with two self-designed questionnaires. The investigators assessed psychosocial adjustment and psychopathology in patients with gender identity disorders. Patients were to be sequentially evaluated prior to institution of hormonal therapy, then 3 to 6 months after the start of cross-sex hormone treatment, and then again one to 12 months after reassignment surgery. The Dutch version of the SCL-90R with eight subscales (agoraphobia, anxiety, depression, hostility, interpersonal sensitivity, paranoid ideation/psychoticism, and sleeping problems) and a global score (psycho-neuroticism) was used serially. A seven parameter questionnaire was used serially to assess changes in social function. Another cross-sectional survey assessed emotional state. The cohorts at each time point consisted of patients who were in the treatment cohort at the time and who had submitted survey responses.

Ninety of the patients who applied for reassignment surgery between June 2005 and March 2009 were recruited. Fifty seven entered the study. Forty-six (51.1% of the recruited population) underwent reassignment surgery. Baseline questionnaire information was missing for 3 patients. Baseline SCL-90 scores were missing for 1 patient but included SCL-90 scores from some of the 11 recruits who had not yet undergone reassignment surgery. Time point 2 (after hormone therapy) SCL-90 information was missing for 10, but included SCL-90 scores from some of the 11

recruits who had not yet undergone reassignment surgery. At time point 3, 42 (91.3% of those who underwent reassignment surgery) patients completed some part of the SCL-90 survey and the psychosocial questionnaires. Some questionnaires were incomplete. The investigators reported response rates of 73.7% for the psychosocial questionnaires and 82.5% for the SCL-90.

Of those who responded at follow-up after surgery, 88.1% reported having good friends; 52.4% reported the absence of a relationship; 47.6% had no sexual contacts; 42.9% lived alone; 40.5% were unemployed, retired, students, or otherwise not working; 2.4% reported alcohol abuse; and 9.3% had attempted suicide. The frequency of these parameters reportedly did not change statistically during the study interval, but there was no adjustment for the inclusion of patients who did not undergo surgery.

In a cross-sectional, self-report mood survey, of the 42 study entrants who completed the entire treatment regimen including reassignment surgery and the final assessment (refers to the initial 57) reported improved body-related experience (97.6%), happiness (92.9%), mood (95.2%), and self-confidence (78.6%) and reduced anxiety (81.0%). Of participants, 16.7% reported thoughts of suicide. Patients also reported on the intervention phase that they believed was most helpful: hormone initiation (57.9%), reassignment surgery (31.6%), and diagnostic-psychotherapy phase (10.5%).

The global "psycho-neuroticism" SCL-90R score, along with scores of 7 of the 8 subscales, at baseline were statistically more pathologic than the general population. After hormone therapy, the score for global "psycho-neuroticism" normalized and remained normal after reassignment surgery. More specifically the range for the global score is 90 to 450 with higher scores being more pathologic. The score for the general population was 118.3±32.4. The respective scores for the various gender dysphoric cohorts were 157.7±49.8 at initial presentation, 119.7±32.1 after hormone therapy, and 127.9±37.2 after surgery. The scores for the general population and the scores after either hormone treatment or surgical treatment did not differ.

Kockott G, Fahrner EM. Transsexuals who have not undergone surgery: a follow-up study. Arch Sex Behav. 1987 Dec;16 (6):511-22.

Kockott and Fahrner conducted a single center (Munich, Germany) prospective, observational study using a longitudinal design. Treatment cohorts were used as controls, and patients served as their own controls. The investigators assessed psychosocial adjustment in patients with gender identity issues. Patients were to have met DSM III criteria. Trans-sexuality, transvestitism, and homosexuality were differentiated. The criteria required for patients to receive hormone therapy and/or reassignment surgery were not delineated. After receiving hormone therapy, patients were later classified by surgical reassignment status (pre-operative and post-operative) and desire for surgery (unchanged desire, hesitant, and no longer desired).

The first investigative tool was a semi-structured in-person interview consisting of 125 questions. The second investigative tool was a scale that organized the clinical material into nine domains which were then scored on a scale. The Psychological Integration of Trans-sexuals (PIT) instrument developed according to the scale used by Hunt and Hampson (1980) for assessment of 17 post-operative patients. There were 15 interviews and two separate interviewers. There were 80 patients identified, but 58 (72.5%) patients (26 pre-operative; 32 post-operative) were ultimately included in the analysis. The duration of follow-up was longer for post-operative patients (6.5 years) than for pre-operative patients (4.6 years) (including time for one patient subsequently excluded). The mean age of the post-operative patients was 35.5±13.1 years, and the age of the patients who maintained a continued desire for surgery was 31.7±10.2 years. The age of the patients who hesitated about surgery was somewhat older, 40.3±9.4 years. The age of the patients who were no longer interested in surgery was 31.8±6.5 years. All were employed or in school at baseline. Patients with hesitation were financially better-off, had longer-standing relationships even if unhappy, and had a statistical tendency to place less value on sex than those with an unchanged wish for surgery.

Post-operative patients more frequently reported contentment with the desired gender and the success of adaption to the gender role than the pre-operative patients with a persistent desire for surgery. Post-operative patients more frequently reported sexual satisfaction than pre-operative patients with a continuing desire for surgery. Post-operative patients also more frequently reported financial sufficiency and employment than pre-operative patients with a persistent desire for surgery. Suicide attempts were stated to be statistically less frequent in the post-surgical cohort.

Psychosocial adjustment scores were in the low end of the range with "distinct difficulties" (19-27) at the initial evaluation for the post-operative patients (19.7), the pre-operative patients with a persistent wish for surgery (20.2), and the hesitant patients (19.7). At initial evaluation, psychosocial adjustment scores for patients no longer wanting surgery were at the high end of the range with "few difficulties" (10-18). At the final evaluation, Psychosocial adjustment scores were at the high end of the range "few difficulties" (10-18) for the post-operative patients (13.2) and the patients no longer wanting surgery (16.5). Psychosocial adjustment scores at the final evaluation were in the borderline range between "few difficulties" (10-18) and "distinct difficulties" (19-27) for both the pre-operative patients with a persistent desire for surgery (18.7), and the hesitant patients (19.1).

The changes in the initial score and the final follow-up score within each group were tracked and reported to be statistically significant for the post-operative group, but not for the other groups. Statistical differences between groups were not presented. Moreover, the post-operative patients had an additional test immediately prior to surgery. The first baseline score (19.7) would have characterized the patients as having "distinct difficulties" in psychosocial adjustment while the second baseline score (16.7) would have categorized the patients as having "few difficulties" in psychosocial adjustment despite the absence of any intervention except the prospect of having imminent reassignment surgery. No statistics reporting on the change between scores of the initial test and the test immediately prior to surgery and the change between scores of the test immediately prior to surgery and the final follow-up were provided.

Meyer JK, Reter DJ. Sex reassignment. Follow-up. Arch Gen Psychiatry. 1979 Aug;36(9):1010-5. (United States study)

Meyer and Reter conducted a single-center (Baltimore, Maryland, U.S.) prospective, non-blinded, observational study using a longitudinal design and retrospective baseline data. Interview data were scored with a self-designed tool. There were treatment control cohorts, and patients served as their own controls. The investigators assessed patients with gender dysphoria. The 1971 criteria for surgery required documented cross-sex hormone use as well as living and working in the desired gender for at least one year in patients subsequently applying for surgery. Clinical data including initial interviews were used for baseline data. In follow-up, the investigators used extensive two to four hour interviews to collect information on (a) objective criteria of adaptation, (b) familial relationships and coping with life milestones, and (c) sexual activities and fantasies. The objective criteria, which were the subject of the publication, included employment status (Hollingshead job level), cohabitation patterns, and need for psychiatric intervention. The investigators designed a scoring mechanism for these criteria and used it to determine a global adjustment score. The score value or the change score that was considered to be biologically significant was not pre-specified in the methods.

The clinic opened with 100 patients, but when the follow-up was completed, 52 patients were interviewed and 50 gave consent for publication. Of these, 15 (four female-to-male, 11 male-to-female; ratio 1:2.8) were part of the initial operative cohort, 14 (one female-to-male; 13 male-to-female; ratio 1:13) later underwent reassignment surgery at the institution or elsewhere, and 21 (five female-to-male; 16 male-to-female; ratio 1:3.2) did not undergo surgery. The mean ages of these cohorts were 30.1, 30.9, and 26.7 years respectively. The mean follow-up time was 62 months (range 19-142) for those who underwent surgery and 25 months (range 15-48) for those who did not. Socioeconomic status was lowest in those who subsequently underwent reassignment surgery.

Of patients initially receiving surgery, 33% had some type of psychiatric contact prior to the initial clinic evaluation and 8% had psychiatric contact during the follow-up. Of the patients who had not under gone surgery or who had done so later, 72% had some type of psychiatric contact prior to the initial clinic evaluation and 28% had psychiatric contact during follow-up. There was a single female-to-male patient with multiple surgical complications who sought partial reassignment surgery reversal.

The adjustment scores improved over time with borderline statistical significance for the initial operative group and with statistical significance for the never operated group. The absolute score value at follow-up was the same for both groups (1.07+1.53 and 1.10+1.97 respectively). By contrast, the adjustment scores did not improve for those who were not in the cohort initially approved for surgery, but who subsequently underwent surgery later. This was particularly true if the surgery was performed elsewhere. The absolute score value at follow-up was 0.21+1.89.

Related papers include Meyer et al. (1971), Meyer et al. (1974a-d), and Derogatis et al. (1978) along with commentary response by Fleming et al. (1980).

Rakic Z, Starcevic V, Maric J, Kelin K. The outcome of sex reassignment surgery in Belgrade: 32 patients of both sexes. Arch Sex Behav. 1996 Oct;25(5):515-25.

Rakic et al. single-center (Belgrade, Yugoslavia) conducted a prospective, non-blinded, observational study using a cross-sectional design and an investigator- designed quality of life tool that asked longitudinal (pre- and post-treatment) questions. Patients served as their own controls. The authors state that the study was not designed to assess the predictors of poor outcomes.

The investigators assessed global satisfaction, body image, relationships, employment status, and sexual function in patients with gender dysphoria who underwent reassignment surgery between 1989 and 1993 and were at least six months post-operative. The criteria to qualify for gender surgery were delineated (1985 standards from the Harry Benjamin International Gender Dysphoria Association) and included cross-gender behavior for at least one year and sexual orientation to non-natal sex. The questionnaire consisted of 10 questions using yes/no answers or Likert-type scales. Findings were descriptive without statistical analysis. As such, changes or differences considered to be biologically significant were not pre-specified, and there were no adjustments for multiple comparisons.

Of the 38 patients who had undergone reassignment surgery, 34 were eligible for the study and 32 participated in the study (two were lost to follow-up and four were in the peri-operative period) - 10 (31.2%) female-to-male and 22 (68.8%) male-to-female (ratio 1:2.2). The duration of follow-up was 21.8 ±13.4 months (range 6 months to 4 years). The age was female-to-male 27.8±5.2 (range 23-37) and male-to-female 26.4±7.8 (range 19-47).

Using an investigator-designed quality of life tool, all patients reported satisfaction with having undergone the surgery. Of the total participants, four (12.5%) (all male-to-female) and eight (25%) (87.5% male-to-female) reported complete dissatisfaction or partial satisfaction with their appearance. Regarding relationships, 80% of female-to-male and 100% of male-to-female patients were dissatisfied with their relationships with others prior to surgery; whereas, no female-to-male patients and 18.1% of male-to-female patients were dissatisfied with relationships after surgery. Regarding sexual partners, 60% of female-to-male and 72.7% of male-to-female patients reported not having a sexual partner prior to surgery; whereas, 20% of female-to-male patients and 27.3% of male-to-female patients did not have a sexual partner after surgery. Of those with partners at each time interval, 100% of female-to-male and 50% of male-to-female patients reported not experiencing orgasm prior to surgery; whereas, 75% of female-to-male and 37.5% of male-to-female patients reported not experiencing orgasm after surgery.

Ruppin U, Pfäfflin F. Long-term follow-up of adults with gender identity disorder. Arch Sex Behav. 2015 Jul;44(5):1321-9. Epub 2015 Feb 18.

Ruppin and Pfafflin conducted a single-center (Ulm, Germany) partially prospective, non-blinded, observational study using a longitudinal design and non-specific psychometric tests and a self-designed interview tool and questionnaire. Patients served as their own controls.

The investigators assessed psychological symptoms, interpersonal difficulties, gender role stereotypes, personality characteristics, societal function, sexual function, and satisfaction with new gender role in patients with gender dysphoria. Patients were required to have met the ICD-10 criteria for trans-sexualism, been seen by the clinic by prior to 2001, and completed an official change in gender including name change prior to 2001. Assessment tools included German versions of standardized surveys with normative data: the SCL 90R, the Inventory of Interpersonal Problems (IIP), Bem Sex Role Inventory (BSRI), and the Freiburg Personality Inventory (FPI-R), along with semi-structured interviews with self-designed questionnaires. The prospective survey results were compared to retrospective survey results. Changes or inter-group differences considered to be biologically significant were not pre-specified. Diagnostic cut points were not provided. Statistical corrections for multiple comparisons were not included.

Overall, 140 patients received recruitment letters and then 71 (50.7%) agreed to participate. Of these participants, 36 (50.7%) were female-to-male; 35 (49.3%) were male-to-female (ratio 1:0.97). The ages of the patients were: 41.2±5.78 years (female-to-male) and 52.9±10.82 years (male-to-female). The intervals for follow-up were 14.1±1.97 years and 13.7±2.17 years, respectively.

All female-to-male patients had undergone mastectomy; 91.7% had undergone oopherectomy and/or hysterectomy; 61.1% had undergone radial forearm flap phalloplasty or metaoidioplasty. Of male-to-female patients, 94.3% had undergone vaginoplasty and perhaps an additional procedure (breast augmentation, larynx surgery, or vocal cord surgery). Two male-to-female patients had not undergone any reassignment surgery, but were still included in the analyses.

A total of 68 patients ranked their well-being as 4.35±0.86 out of five (three patients did not respond to this question). Of respondents, 40% reported not being in a steady relationship. Regular sexual relationships were reported by 57.1% of 35 female- to-male respondents and 39.4% of 33 male-to-female respondents (three patients did not respond to this question). A total of 11 patients reported receiving out-patient psychotherapy; 69 did not express a desire for gender role reversal (two did not respond to this question). The response rate was less than 100% for most of the self-designed survey questions.

Changes from the initial visit to the follow-up visit were assessed for the SCL-90R in 62 of 71 patients. The effect size was statistically significant and large only for the “Interpersonal Sensitivity” scale (one of 10 parameters). The absolute magnitude of mean change was small: from 0.70±0.67 to 0.26±0.34 (scale range 0-4). The duration of follow-up did not correlate with the magnitude of change on the various scales. Differences in baseline SCL-90R scores of 62 participants were compared with the score of 63 of the 69 eligible recruits who declined to enter the study and were notable for higher “Depression” scores for the latter.

Changes from the initial visit to the follow-up visit were assessed for the IIP in 55 of 71 patients. The effect size was statistically significant and large only for the “Overly Accommodating” scale (one of eight parameters). The absolute magnitude of mean change was small: from 11.64±5.99 to 7.04±4.73 (scale range 0-32). The duration of follow-up did not correlate with the magnitude of change on the various scales.

Changes from the initial visit to the follow-up visit were assessed for the FPI-R in 58 of 71 patients. The effect size was statistically significant and large only for the “Life Satisfaction” scale (one of 12 parameters). The absolute magnitude of mean change was substantive: from 4.43±2.99 to 8.31±2.63 (scale range 0-12). The duration of follow-up did not correlate with the magnitude of change on the various scales.

Changes from the initial visit to the follow-up visit were assessed for the BSRI in 16 of 36 female to male patients and 19 of 35 male to female patients. The "Social Desirability" score increased for the female-to-male respondents. At endpoint, both categories of respondents reported androgynous self-images.

This current report is an update of prior publications by Pfafflin including work with Junge which was published in a variety of formats and initially in German.

Smith YL, Van Goozen SH, Kuiper AJ, Cohen-Kettenis PT. Sex reassignment: outcomes and predictors of treatment for adolescent and adult transsexuals. Psychol Med. 2005 Jan;35(1):89-99.

Smith et al. conducted a single-center (Amsterdam, Netherlands) prospective, non-blinded, observational study using a longitudinal design and psychological function tools. Patients served as their own control prior to and after reassignment surgery. The investigators assessed gender dysphoria, body dissatisfaction, physical appearance, psychopathology, personality traits, and post-operative function in patients with gender dysphoria. Patients underwent some aspect of reassignment surgery. The test instruments included the Utrecht Gender Dysphoria Scale (12 items), the Body Image Scale adapted for a Dutch population (30 items), Appraisal of Appearance Inventory (3 observers, 14 items), the Dutch Short MMPI (83 items), the Dutch version of the Symptom Checklist (SCL)(90 items), and clinic-developed or modified questionnaires. Pre-treatment data was obtained shortly after the initial interview. Post- surgery data were acquired at least one year post reassignment surgery.

Three hundred twenty five consecutive adolescents and adults were screened for the study. One-hundred three (29 [28.2%] female-to-male patients and 74 [71.8%] male-to-female patients [ratio 1:2.6]) never started hormone therapy; 222 (76 [34.2%] female-to-male patients and 146 [65.8%] male-to-female patients [ratio 1:1.9]) initiated hormone therapy. Of the patients who started hormone therapy, 34 (5 [14.7%] female-to-male patients and 29 [85.3%] male-to-female patients [ratio 1:5.8]) discontinued hormone therapy.

Subsequently, the study analysis was limited to adults. One hundred sixty-two (58 [35.8%] female-to-male and 104 [64.2%] male-to-female [ratio 1:1.8]) were eligible and provided pre-surgical test data, and 126 (77.8% of eligible adults) (49 [38.9%] female-to-male and 77 [61.1%] male-to-female [ratio 1:1.6]) provided post-surgical data. For those patients who completed reassignment, the mean age at the time of surgical request was 30.9 years (range 17.7-68.1) and 35.2 years (range 21.3-71.9) years at the time of follow-up. The intervals between hormone treatment initiation and surgery and surgery and follow-up were 20.4 months (range 12 to 73) and 21.3 months (range 12 to 47) respectively.

Of the 126 adults who provided post-surgical data, 50 (40.0%) reported having a steady sexual partner, three (2.3%) were retired, and 58 (46.0%) were unemployed. Regarding regret, six patients expressed some regret regarding surgery, but did not want to resume their natal gender role, and one male-to-female had significant regret and would not make the same decision.

Post-surgery Utrecht dysphoria scores dropped substantially and approached reportedly normal values. The patients' appearance better matched their new gender. No one was dissatisfied with his/her overall appearance at follow-up. Satisfaction with primary sexual, secondary sexual, and non-sexual body traits improved over time. Male-to-female patients, however, were more dissatisfied with the appearance of primary sex traits than female-to-male patients. Regarding mastectomy, 27 of 38 (71.1%) female-to-male respondents (not including 11 non-respondents) reported incomplete satisfaction with their mastectomy procedure. For five of these patients, the incomplete satisfaction was because of scarring. Regarding vaginoplasty, 20 of 67 (29.8%) male-to-female respondents (not including 10 non-respondents) reported incomplete satisfaction with their vaginoplasty.

Most of the MMPI scales were already in the normal range at the time of initial testing and remained in the normal

range after surgery. SCL global scores for psycho- neuroticism were minimally elevated before surgery 143.0±40.7 (scoring range 90 to 450) and normalized after surgery 120.3±31.4. (An analysis using patient level data for only the completers was not conducted.)

Udeze B, Abdelmawla N, Khoosal D, Terry T. Psychological functions in male-to- female people before and after surgery. Sexual and Relationship Therapy. 2008 May; 23(2):141-5. (Not in PubMed) and Megeri D, Khoosal D. Anxiety and depression in males experiencing gender dysphoria. Sexual and Relationship Therapy. 2007 Feb; 22(1):77-81. (Not in PubMed)

Udeze et al. conducted a single-center (Leicester, United Kingdom) prospective, non-blinded, longitudinal study assessing a randomized subset of patients who had completed a non-specific psychological function tool prior to and after male-to-female reassignment surgery. Patients served as their own controls. The investigators used the WPATH criteria for patient selection. Psychiatric evaluations were routine. All patients selected for treatment were routinely asked to complete the self-administered SCL-90R voluntarily on admission to the program and post-operatively. A post-operative evaluations (psychiatric and SCL-90R assessment) were conducted within six months to minimize previously determined loss rates. The patient pool was domestic and international. There were 546 gender dysphoric patients from all over the United Kingdom and abroad, of whom 318 (58.2%) progressed to surgery. Of these, 127 were from the local Leicester area in the United Kingdom and 38 (29.9%) progressed to surgery. The mean age for the selected male-to-female patients at the time of study was 47.33±13.26 years (range 25 to 80) and reflected an average wait time for surgery of 14 months (range 2 months to 6 years). For this investigation, 40 male-to-female subjects were prospectively selected.

The raw SCL-90 global scores for psycho-neuroticism were unchanged over time: 48.33 prior to surgery and 49.15 after surgery. If the scale was consistent with T-scoring, the results were non-pathologic. No psychiatric disorders were otherwise identified prior to or after surgery.

Investigators from the same clinical group (Megeri, Khoosal, 2007) conducted additional testing to specifically address anxiety and depression with the Beck Depression Inventory, General Health Questionnaire (with 4 subscales), HADS, and Spielberger State and Trait Anxiety Questionnaire (STAI-X1 and STA-X2). The test population and study design appear to be the same. No absolute data were presented. Only changes in scores were presented. There were no statistically significant changes.

e. Randomized, surgical patients, longitudinal, with controls

Mate-Kole C, Freschi M, Robin A. A controlled study of psychological and social change after surgical gender reassignment in selected male transsexuals. Br J Psychiatry. 1990 Aug;157:261-4.

Mate-Kole at al. conducted a prospective, non-blinded, controlled, randomized, longitudinal study using investigator-designed patient self-report questionnaires and non-specific psychological tests with some normative data. The investigators assessed neuroticism and sex role in natal males with gender dysphoria who had qualified for male-to-female reassignment surgery at a single-center specialty clinic (London, United Kingdom). Forty sequential patients were alternately assigned to early reassignment surgery or to standard wait times for reassignment surgery. Patients were evaluated after acceptance and 2 years later. The criteria used to qualify for gender surgery were the 1985 standards from the Harry Benjamin International Gender Dysphoria Association. These included a ≥2 year desire to change gender, a ≥1 year demonstrable ability to live and be self-supporting in the chosen gender, and psychiatric assessment for diagnosis and reassessment at six months for diagnostic confirmation and exclusion of psychosis.

Reassignment surgery was defined as orchidectomy, penectomy, and construction of a neo-vagina. The instruments used were the CCEI for psychoneurotic symptoms and the Bem Sex Role Inventory along with an incompletely

described investigator- designed survey with questions about social life and sexual activity.

The mean age and range of the entire cohort was 32.5 years (21-53). Members of the early surgery cohort had a history of attempted suicide (one patient), psychiatric treatment for non-gender issues (six patients), and first degree relatives with psychiatric histories (four patients). Members of the standard surgery cohort were similar, with a history of attempted suicide (two patients), psychiatric treatment for non-gender issues (five patients), and first degree relatives with psychiatric histories (six patients). The early surgery group had surgery approximately 1.75 years prior to the follow-up evaluation. In both groups, cross-dressing began at about age 6.

At baseline, the Bem Sex Role Inventory femininity scores were slightly higher than masculinity scores for both cohorts and were similar to Bem North American female normative scores. The scores did not change in either group over time.

At baseline, the scores for the CCEI individual domains (free floating anxiety, phobic anxiety, somatic anxiety, depression, hysteria, and obsessionality) were similar for the cohorts. The total CCEI scores for the two cohorts were consistent with moderate symptoms (Birchnell et al. 1988). Over the two year interval, total CCEI scores increased for standard wait group and approached the relatively severe symptom category. During the same interval, scores dropped into the asymptomatic rage for the post-operative patients.

The investigator-designed survey assessed changes in social and sexual activity of the prior two years, but the authors only compared patients in a given cohort to themselves. Though the researchers did not conduct statistical studies to compare the differences between the two cohorts, they did report increased participation in some, but not all, types of social activities such as sports (solo or group), dancing, dining out, visiting pubs, and visiting others. Sexual interest also increased. By contrast, pre-operative patients did not increase their participation in these activities.

2. External Technology Assessments

a. CMS did not request an external technology assessment (TA) on this issue.

b. There were no AHRQ reviews on this topic.

c. There are no Blue Cross/Blue Shield Health Technology Assessments written on this topic within the last three years.

d. There were two publications in the COCHRANE database, and both were tangentially related. Both noted that there are gaps in the clinical evidence base for gender reassignment surgery.
Twenty Years of Public Health Research: Inclusion of Lesbian, Gay, Bisexual, and Transgender Populations Boehmer U. Am J Public Health. 2002; 92: 1125–30.

"Findings supported that LGBT issues have been neglected by public health research and that research unrelated to sexually transmitted diseases is lacking."

A systematic review of lesbian, gay, bisexual and transgender health in the West Midlands region of the UK compared to published UK research. West Midlands Health Technology Assessment Collaboration. Health Technology Assessment Database. Meads, et al., 2009. No.3.

"Further research is needed but must use more sophisticated designs with comparison groups. This systematic review demonstrated that there are so many gaps in knowledge around LGBT health that a wide variety of studies are needed."

e. There were no National Institute for Health and Care Excellence (NICE) reviews/guidance documents on this

topic.

f. There was a technology assessment commissioned by the New Zealand Ministry of Health and conducted by New Zealand Health Technology Assessment (NZHTA) (Christchurch School of Medicine and the University of Otago).

Tech Brief Series: Transgender Re-assignment Surgery Day P. NZHTA Report. February 2002;1(1). http://nzhta.chmeds.ac.nz/publications/trans_gender.pdf

The research questions included the following:
1. Are there particular subgroups of people with transsexualism who have met eligibility criteria for gender reassignment surgery (GRS) where evidence of effectiveness of that surgery exists?

2. If there is evidence of effectiveness, what subgroups would benefit from GRS?"

The authors concluded that there was not enough evidence to answer either of the research questions.

3. Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) Meeting

CMS did not convene a MEDCAC meeting.

4. Evidence-Based Guidelines

a. American College of Obstetricians and Gynecologists (ACOG)

Though ACOG did not have any evidence-based guidelines on this topic, they did have the following document:
Health Care for Transgender Individuals: Committee Opinion
Committee on Health Care for Underserved Women; The American College of Obstetricians and Gynecologists. Dec 2011, No. 512. Obstet Gyncol. 2011;118:1454-8.

"Questions [on patient visit records] should be framed in ways that do not make assumptions about gender identity, sexual orientation, or behavior. It is more appropriate for clinicians to ask their patients which terms they prefer. Language should be inclusive, allowing the patient to decide when and what to disclose. The adoption and posting of a nondiscrimination policy can also signal health care providers and patients alike that all persons will be treated with dignity and respect. Assurance of confidentiality can allow for a more open discussion, and confidentiality must be ensured if a patient is being referred to a different health care provider. Training staff to increase their knowledge and sensitivity toward transgender patients will also help facilitate a positive experience for the patient."

b. American Psychiatric Association

Report of the American Psychiatric Association Task Force on Treatment of Gender Identity Disorder. Byne, W, Bradley SJ, Coleman E, Eyler AE, Green R, Menvielle EJ, Meyer-Bahlburg HFL, Richard R. Pleak RR, Tompkins DA. Arch Sex Behav. 2012; 41:759–96.

The American Psychiatric Association (APA) was unable to identify any Randomized Controlled Trials (RTCs) regarding mental health issues for transgender individuals.

"There are some level B studies examining satisfaction/regret following sex reassignment (longitudinal follow-up after an intervention, without a control group); however, many of these studies obtained data retrospectively and without a control group (APA level G). Overall, the evidence suggests that sex reassignment is associated with an

improved sense of well-being in the majority of cases, and also indicates correlates of satisfaction and regret. No studies have directly compared various levels of mental health screening prior to hormonal and surgical treatments on outcome variables; however, existing studies suggest that comprehensive mental health screening may be successful in identifying those individuals most likely to experience regrets."

Relevant Descriptions of APA Evidence Coding System/Levels:

[B] Clinical trial. A prospective study in which an intervention is made and the results of that intervention are tracked longitudinally. Does not meet standards for a randomized clinical trial."

[G] Other. Opinion-like essays, case reports, and other reports not categorized above."

c. Endocrine Society

Endocrine Treatment of Transsexual Persons: an Endocrine Society Clinical Practice Guideline.

Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, Gooren LJ, Meyer WJ 3rd, Spack NP, Tangpricha V, Montori VM; Endocrine Society. J Clin Endocrinol Metab. 2009; 94:3132-54.

This guideline primarily addressed hormone management and surveillance for complications of that management. A small section addressed surgery and found the quality of evidence to be low.

"This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe the strength of recommendations and the quality of evidence, which was low or very low."

d. World Professional Association for Transgender Health (WPATH)

Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People (Version 7). Coleman E, Bockting W, Botzer M, Cohen-Kettenis P, DeCuypere G, Feldman J, Fraser L, Green J, Knudson G, Meyer WJ, Monstrey S, Adler RK, Brown GR, Devor AH, Ehrbar R, Ettner R, Eyler E, Garofalo R, Karasic DH, Lev AI, Mayer G, Meyer-Bahlburg H, Hall BP, Pfäfflin F, Rachlin K, Robinson B, Schechter LS, Tangpricha V, van Trotsenburg M, Vitale A, Winter S, Whittle S, Kevan R. Wylie KR, Zucker K.
www.wpath.org/_files/140/files/Standards%20of%20Care,%20V7%20Full%20Book.pdf
Int J Transgend. 2011;13:165–232.

The WPATH is "an international, multidisciplinary, professional association whose mission is to promote evidence-based care, education, research, advocacy, public policy, and respect in transsexual and transgender health."

WPATH reported, "The standards of care are intended to be flexible in order to meet the diverse health care needs of transsexual, transgender, and gender-nonconforming people. While flexible, they offer standards for promoting optimal health care and guiding the treatment of people experiencing gender dysphoria—broadly defined as discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics) (Fisk, 1974; Knudson, De Cuypere, & Bockting, 2010b)."

The WPATH standards of care (SOC) "acknowledge the role of making informed choices and the value of harm-

reduction approaches."

The SOC noted, "For individuals seeking care for gender dysphoria, a variety of therapeutic options can be considered. The number and type of interventions applied and the order in which these take place may differ from person to person (e.g., Bockting, Knudson, & Goldberg, 2006; Bolin, 1994; Rachlin, 1999; Rachlin, Green, & Lombardi, 2008; Rachlin, Hansbury, & Pardo, 2010). Treatment options include the following:

- Changes in gender expression and role (which may involve living part time or full time in another gender role, consistent with one's gender identity);
- Hormone therapy to feminize or masculinize the body;
- Surgery to change primary and/or secondary sex characteristics (e.g., breasts/chest, external and/or internal genitalia, facial features, body contouring);
- Psychotherapy (individual, couple, family, or group) for purposes such as exploring gender identity, role, and expression; addressing the negative impact of gender dysphoria and stigma on mental health; alleviating internalized transphobia; enhancing social and peer support; improving body image; or promoting resilience."

e. American Psychological Association

Suggested citation until formally published in the American Psychologist: American Psychological Association. (2015): *Guidelines for Psychological Practice with Transgender and Gender Nonconforming People Adopted by the Council of Representatives, August 5 & 7, 2015. www.apa.org/practice/guidelines/transgender.pdf*

"The purpose of the Guidelines for Psychological Practice with Transgender and Gender Nonconforming People (hereafter Guidelines) is to assist psychologists in the provision of culturally competent, developmentally appropriate, and trans-affirmative psychological practice with TGNC people."

"These Guidelines refer to psychological practice (e.g., clinical work, consultation, education, research, training) rather than treatment."

5. Other Reviews

a. Institute of Medicine (IOM)

The Health of Lesbian, Gay, Bisexual, and Transgender People: Building a Foundation for Better Understanding. Robert Graham (Chair); Committee on Lesbian, Gay, Bisexual, and Transgender Health Issues and Research Gaps and Opportunities. (Study Sponsor: The National Institutes of Health). Issued March 31, 2011. http://www.nationalacademies.org/hmd/Reports/2011/The-Health-of-Lesbian-Gay-Bisexual-and- Transgender-People.aspx

"To advance understanding of the health needs of all LGBT individuals, researchers need more data about the demographics of these populations, improved methods for collecting and analyzing data, and an increased participation of sexual and gender minorities in research. Building a more solid evidence base for LGBT health concerns will not only benefit LGBT individuals, but also add to the repository of health information we have that pertains to all people."

"Best practices for research on the health status of LGBT populations include scientific rigor and respectful involvement of individuals who represent the target population. Scientific rigor includes incorporating and monitoring culturally competent study designs, such as the use of appropriate measures to identify participants and

implementation processes adapted to the unique characteristics of the target population. Respectful involvement refers to the involvement of LGBT individuals and those who represent the larger LGBT community in the research process, from design through data collection to dissemination."

b. National Institutes of Health (NIH)

National Institutes of Health Lesbian, Gay, Bisexual, and Transgender (LGBT) Research Coordinating Committee. Consideration of the Institute of Medicine (IOM) report on the health of lesbian, gay, bisexual, and transgender (LGBT) individuals. Bethesda, MD: National Institutes of Health; 2013. http://report.nih.gov/UploadDocs/LGBT%20Health%20Report_FINAL_2013-01-03-508%20compliant.pdf

In response to the IOM report, the NIH LBGT research Coordinating Committee noted that most of the health research for this set of populations is "focused in the areas of Behavioral and Social Sciences, HIV (human immunodeficiency virus)/AIDS, Mental Health, and Substance Abuse. Relatively little research has been done in several key health areas for LGBT populations including the impact of smoking on health, depression, suicide, cancer, aging, obesity, and alcoholism."

6. Pending Clinical Trials

ClinicalTrials.gov
There is one currently listed and recently active trial directed at assessment of the clinical outcomes pertaining to individuals who have had gender reassignment surgery. The study appears to be a continuation of work conducted by investigators cited in the internal technology assessment.

NCT01072825 (Ghent, Belgium sponsor) European Network for the Investigation of Gender Incongruence (ENIGI) is assessing the physical and psychological effects of the hormonal treatment of transgender subjects in two years prior to reassignment surgery and subsequent to surgery. This observational cohort study started in 2010 and is still in progress.

7. Consultation with Outside Experts

Consistent with the authority at 1862(l)(4) of the Act, CMS consulted with outside experts on the topic of treatment for gender dysphoria and gender reassignment surgery.

Given that the majority of the clinical research was conducted outside of the United States, and some studies either took place in or a suggested continuity-of-care and coordination-of-care were beneficial to health outcomes, we conducted expert interviews with centers across the U.S. that provided some form of specialty-focused or coordinated care for transgender patients. These interviews informed our knowledge about the current healthcare options for transgender people, the qualifications of the professionals involved, and the uniqueness of treatment options. We are very grateful to the organizations that made time to discuss treatment for gender dysphoria with us.

From our discussions with the all of the experts we spoke with, we noted the following practices in some centers: (1) specialized training for all staff about transgender healthcare and transgender cultural issues; (2) use of an intake assessment by either a social worker or health care provider that addressed physical health, mental health, and other life factors such as housing, relationship, and employment status; (3) offering primary care services for transgender people in addition to services related to gender-affirming therapy/treatments; (4) navigators who connected patients with name-change information or other legal needs related to gender; (5) counseling for individuals, groups, and families; (6) an informed-consent model whereby individuals were often referred to as

"clients" instead of "patients," and (7) an awareness of depression among transgender people (often measured with tools such as the Adult Outcomes Questionnaire and the Patient Health Questionnaire).

8. Public Comments

We appreciate the thoughtful public comments we received on the proposed decision memorandum. In CMS' experience, public comments sometimes cite the published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum. All comments that were submitted without personal health information may be viewed in their entirety by using the following link: https://www.cms.gov/medicare-coverage-database/details/nca-view-public-comments.aspx?NCAId=282&ExpandComments=n#Results

a. Initial Comment Period: December 3, 2015 – January 2, 2016

During the initial comment period, we received 103 comments. Of those, 78% supported coverage of gender reassignment surgery, 15% opposed, and 7% were neutral. The majority of comments supporting coverage were from individuals and advocacy groups.

b. Second Comment Period: June 2, 2016 – July 2, 2016

During the second 30-day public comment period, we received a total of 45 public comments, 7 of which were not posted on the web due to personal health information content. Overall, 82% supported coverage of gender reassignment surgery, 11% opposed, and 7% were neutral or silent in their comment whether they supported or opposed coverage. Half of the comments were submitted by individuals who expressed support for coverage of gender reassignment surgery (51%). We also received comments from physicians, providers, and other health professionals who specialize in healthcare for transgender individuals (17%). We received one comment from a municipality, the San Francisco Department of Public Health. Associations (American Medical Association, American College of Physicians, American Academy of Nursing, American Psychological Association, and LBGT PA Caucus) and advocates (Center for American Progress with many other signatories, Jamison Green & Associates) also submitted comments.

Below is a summary of the comments CMS received. In some instances, commenters identified typographical errors, context missed, and opportunities for CMS to clarify wording and classify articles for ease of reading in the memorandum. As noted earlier, when appropriate and to the extent possible, we updated the decision memorandum to reflect those corrections, improved the context, and clarified the language. In light of public comments, we re-evaluated the evidence and our summaries. We updated our summaries of the studies and clarified the language when appropriate.

1. Contractor Discretion and National Coverage Determination

Comment: Some commenters, including advocates, associations, and providers, supported CMS' decision for MAC contractor discretion/case-by-case determination for gender reassignment surgery. One stakeholder stated, "We agree with the conclusion that a NCD is not warranted at this time."

Response: We appreciate the support and understanding among stakeholders for our proposed decision to have the MACs determine coverage on a case-by-case basis. We have clarified in this final decision memorandum that

coverage is available for gender reassignment surgery when determined reasonable and necessary and not otherwise excluded by any other relevant statutory requirements by the MAC on a case-by-case basis. "The case-by-case model affords more flexibility to consider a particular individual's medical condition than is possible when the agency establishes a generally applicable rule." (78 Fed. Reg. 48165 (August 7, 2013)).

Comment: Some commenters cautioned that CMS' choice to not issue a NCD at this time must not be interpreted as a national non-coverage determination or used in any way to inappropriately restrict access to coverage for transgender Medicare beneficiaries or other transgender individuals. Multiple commenters indicated their disappointment that CMS did not propose a National Coverage Determination (NCD) and, instead, chose to continue to have local MACs make the coverage decisions on a case-by-case basis. Commenters stated this could result in variability in coverage.

Response: We appreciate the comments. We are not issuing a NCD at this time because the available evidence for gender reassignment surgery provides limited data on specific health outcomes and the characteristics of specific patient populations that might benefit from surgery. In the absence of a NCD, the MAC's use the same statutory authority as NCDs, section 1862(a)(1)(A) of the Social Security Act (the Act). Under section 1862(a)(1)(A) an item or service must be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. While CMS did not have enough evidence to issue a NCD, we believe the MACs will be able to make appropriate coverage decisions on a case-by-case basis taking into account individual characteristics of the Medicare beneficiary.

Comment: Some commenters sought a NCD that would establish guidelines for coverage and include elements such as a prescribed set of surgeries and a shared decision making element.

Response: For the reasons stated above, we are not issuing a NCD at this time and, therefore, are not establishing specific gender reassignment surgery coverage guidelines for the Medicare program. We generally agree that shared decision-making is a fundamental approach to patient-centered health care decisions and strongly encourage providers to use these types of evidence based decision aids. We have not found a shared decision aid on GRS and encourage the development of this necessary element to conduct formal shared-decision making.

Comment: Some commenters expressed concern that there is a misunderstanding of transgender individuals as having a disorder or being abnormal. Some commenters indicated a history of bias and discrimination within society as a whole that has occurred when transgender individuals have sought health care services from the medical community. Some commenters are concerned that the decision not to make a NCD will subject individuals seeking these services to corporate bias by Medicare contractors.

Response: We acknowledge the public comments and that there has been a transformation in the treatment of individuals with gender dysphoria over time. In this NCA, we acknowledge that gender dysphoria is a recognized Diagnostic and Statistical Manual of Mental Disorders (DSM) condition. With respect to the concern about potential bias by Medicare contractors, we have no reason to expect that the judgments made on specific claims will be influenced by an overriding bias, hostility to patients with gender dysphoria, or discrimination. Moreover, the Medicare statue and our regulations provide a mechanism to appeal an adverse initial decision if a claim is denied and those rights may include the opportunity for judicial review. We believe the Medicare appeals process would provide an opportunity to correct any adverse decision that was perceived to have been influenced by bias.

Comment: Commenters mentioned the cost of gender reassignment surgery could influence MAC decision making.

Response: The decisions on whether to cover gender reassignment surgery in a particular case are made on the basis of the statutory language in section 1862 of the Social Security Act that establish exclusions from coverage and

would not depend on the cost of the procedure.

2. Coverage with Evidence Development and Research

Comment: In our proposed decision memorandum, we specifically invited comments on whether a study could be developed that would support coverage with evidence development (CED). One organization commented, "We strongly caution against instituting a CED protocol." Commenters were opposed to coverage limited in clinical trials, suggesting that such coverage would restrict access to care. Several commenters provided suggested topics for clinical research studies for the transgender population. For example, one commenter suggested a study of non-surgical treatment for transgender children prior to puberty.

Response: While we appreciate the comments supporting further research, in general, for gender reassignment surgery, we agree that CED is not the appropriate coverage pathway at this time. While CED is an important mechanism to support research and has the potential to be used to help address gaps in the current evidence, we are not aware of any available, appropriate studies, ongoing or in development, on gender reassignment surgery for individuals with gender dysphoria that could be used to support a CED decision.

3. Gender Reassignment Surgery as Treatment

Comment: One group of commenters requested that CMS consider that, "The established medical consensus is that GRS is a safe, effective, and medically necessary treatment for many individuals with gender dysphoria, and for some individuals with severe dysphoria, it is the only effective treatment."

Response: We acknowledge that GRS may be a reasonable and necessary service for certain beneficiaries with gender dysphoria. The current scientific information is not complete for CMS to make a NCD that identifies the precise patient population for whom the service would be reasonable and necessary.

4. Physician Recommendations

Comment: Several commenters stated that gender reassignment surgery should be covered as long as it was determined to be necessary, or medically necessary by a beneficiary's physician.

Response: Physician recommendation is one of many potential factors that the local MAC may consider when determining whether the documentation is sufficient to pay a claim.

5. WPATH Standards of Care

Comment: Several commenters suggested that CMS should recommend the WPATH Standards of Care (WPATH) as the controlling guideline for gender reassignment surgery. They asserted it could satisfy Medicare's reasonable and necessary criteria for determining coverage on a case-by-case basis.

Response: Based on our review of the evidence and conversations with the experts and patient advocates, we are aware some providers consult the WPATH Standards of Care, while others have created their own criteria and requirements for surgery, which they think best suit the needs of their patients. As such, and given that WPATH acknowledges the guidelines should be flexible, we are not in the position to endorse exclusive use of WPATH for coverage. The MACs, Medicare Advantage plans, and Medicare providers can use clinical guidelines they determine useful to inform their determination of whether an item or service is reasonable and necessary. When making this

determination, local MACs may take into account physician's recommendations, the individual's clinical characteristics, and available clinical evidence relevant to that individual.

6. Scope of the NCA Request

Comment: One commenter stated that CMS did not address the full scope of the NCA request.

Response: The formal request for a NCD is publicly available on our tracking sheet. (https://www.cms.gov/Medicare/Coverage/DeterminationProcess/downloads/id282.pdf) The letter did not explicitly seek a national coverage determination related to counseling or hormone therapies, but focused on surgical remedies. CMS is aware that beneficiaries with gender dysphoria use a variety of therapies.

Comment: Other commenters stated the scope of the proposed decision is unnecessarily broad because it discussed therapies other than surgery. They suggested this discussion could lead to the unintended consequence of restricting access to those services for transgender Medicare beneficiaries and other transgender individuals.

Response: As we noted in our proposed decision, our decision focused only on gender reassignment surgery. In the course of reviewing studies related to those surgeries, occasionally authors discussed other therapies that were mentioned in our summaries of the evidence. To the extent possible, we have modified our decision to eliminate the discussion of other therapies which were not fully evaluated in this NCA.

7. NCA Question

Comment: Some commenters expressed concern about the phrasing of the question in this NCA.

Response: The phrasing of the research question is consistent with most NCAs and we believe it is appropriate.

8. Evidence Summary and Analysis

Comment: Several commenters disagreed with our summary of the clinical evidence and analysis. A few commenters contended that the overall tone of the review was not neutral and seemed biased or flawed. One commenter noted that the Barrett publication was available on the Internet.

Response: We appreciate the comments that identified technical errors, and we made the necessary revisions to this document. However, we disagree with the contention that our evidence review was not neutral and seemed biased or flawed. We believe that the summary and analysis of the clinical evidence are objective. As with previous NCAs, our review of the evidence was rigorous and methodical. Additionally, we reviewed the Barrett publication, but it did not meet our inclusion criteria to be included in the Evidence section.

9. Evidence Review with Transgender Experts

Comment: Several commenters requested that CMS re-review the clinical evidence discussed in the proposed decision memorandum with outside experts in the field of transgender health and transition/gender reassignment-related surgeries. Several offered the expertise within their organization to assist in this effort.

Response: We appreciate these comments and the transgender health community's willingness to participate. For

this NCA we discussed gender reassignment surgery protocols with experts, primarily in coordinated care settings. Additionally, the public comment periods provide opportunities for expert stakeholder input. According to our process for all NCAs, we do not jointly review evidence with external stakeholders but have carefully reviewed the very detailed comments submitted by a number of outside experts in transgender health care.

10. Previous Non-Coverage NCD

Comment: One commenter noted that they thought research studies for gender reassignment surgery could not take place when the old NCD that prohibited coverage for gender reassignment surgery was in effect.

Response: CMS does not directly conduct clinical studies or pay for research grants. Some medical services are non-covered by Medicare; however, national non-coverage does not preclude research via a number of avenues and other funding entities such as the National Institutes of Health. In this instance, the previous NCD did not preclude interested parties from funding research for gender reassignment surgery that could have been generalizable to the Medicare population.

11. How the Medicare Population Differs from the General Population

Comment: One commenter questioned how the Medicare population differed from the general population, and why any differences would be important in our decision-making.

Response: The Medicare population is different from the general population in age (65 years and older) and/or disability as defined by the Social Security Administration. Due to the biology of aging, older adults may respond to health care treatments differently than younger adults. These differences can be due to, for example, multiple health conditions or co-morbidities, longer duration needed for healing, metabolic variances, and impact of reduced mobility. All of these factors can impact health outcomes. The disabled Medicare population, who are younger than age 65, is different from the general population and typical study populations due to the presence of the causes of disability such as psychiatric disorders, musculoskeletal health issues, and cardiovascular issues.

12. Medicare Evidence Development & Coverage Advisory Committee (MEDCAC)

Comment: One commenter suggested CMS should have convened a MEDCAC for this topic.

Response: We appreciate the comment. Given the limited evidence, we did not believe a MEDCAC was warranted according to our guidance document entitled "Factors CMS Considers in Referring Topics to the Medicare Evidence Development & Coverage Advisory Committee" (https://www.cms.gov/Regulations-and-Guidance/Guidance/FACA/MEDCAC.html).

13. §1557 of the Affordable Care Act (ACA)

Comment: Some commenters asserted that by not explicitly covering gender reassignment surgery at the national level, CMS was discriminating against transgender beneficiaries in conflict with Section 1557 of the Accountable Care Act (ACA).

Response: This decision does not affect the independent obligation of covered entities, including the Medicare program and MACs, to comply with Section 1557 in making individual coverage decisions. In accordance with Section 1557, MACs will apply neutral nondiscriminatory criteria when making case-by-case coverage determinations related

to gender reassignment surgery.

14. Medicaid

Comment: Some commenters observed that some states cover gender reassignment surgery through Medicaid or require commercial insurers operating in the state to cover the surgery.

Response: We appreciate the information about Medicaid and state requirements; however, State decisions are separate from Medicare coverage determinations. We make evidence-based determinations based on our statutory standards and processes.

15. Commercial Insurers

Comment: In several instances, commenters told us that the healthcare industry looks to CMS coverage determinations to guide commercial policy coverage.

Response: CMS makes evidence-based national coverage determinations based on our statutory standards and processes as defined in the Social Security Act, which may not be the same standards that are used in commercial insurance policies or by other health care programs. In addition as noted above, the Medicare population is different (e.g., Medicare covers 95% of adults 65 and older) than the typical population under commercial insurers. We do not issue coverage decisions to drive policy for other health organizations' coverage in one way or the other.

16. Healthcare for Transgender Individuals

Comment: Numerous professional associations wrote to CMS to explain their support for access to healthcare for transgender individuals.

Response: CMS recognizes that transgender beneficiaries have specific healthcare needs. Many health care treatments are available. We encourage all beneficiaries to utilize their Medicare benefits to help them achieve their best health.

17. Intended Use of the Decision Memorandum

Comment: Several commenters expressed concern that the analysis provided in the proposed and final decision memorandums may be used by individuals, entities, or payers for purposes unrelated to Medicare such as denial of coverage for transgender-related surgeries.

Response: The purpose of the decision memoranda is to memorialize CMS' analysis of the evidence, provide responses to the public comments received, and to make available the clinical evidence and other data used in making our decision consistent with our obligations under the § 1862 of the Act. The NCD process is open and transparent and our decisions are publicly available. Congress requires that we provide a clear statement of the basis for our determinations. The decision memoranda are an important part of the record of the NCD. Our focus is the Medicare population which, as noted above, is different than the general population in a number of ways. Other entities may conduct separate evidence reviews and analyses that are suited for their specific populations.

18. Cost Barriers to Care and Effects

Comment: A few commenters stated that without Medicare coverage, surgery is difficult to afford and there may be a risk of negative consequences for the individual. One commenter suggested that CMS should consider prior-authorization for these surgeries.

Response: CMS is aware that paying out-of-pocket for medical care is a strain on a beneficiary's finances. We are also aware of beneficiaries' hesitancy to undergo surgery prior to knowing whether or not Medicare will pay the claim. Gender reassignment surgeries are not the only procedures whereby payment is not determined until after the provider submits the claim to Medicare. Importantly, documentation for the claims need to be explicit about what procedures were performed and include the appropriate information in the documentation to justify using the code or codes for surgery. Of note, CMS has claims data that indicate Medicare has paid for gender reassignment surgeries in the recent past. Determining which services are designated for prior-authorization is outside of the scope of the NCA process.

19. Surgical Risks and Benefits

Comment: A number of commenters conveyed the benefits of gender reassignment surgery, while other commenters expressed concern that gender reassignment surgery was harmful.

Response: We appreciate these comments.

20. Expenditure of Federal Funds

Comment: Some commenters opposed spending Medicare program funds on gender reassignment surgery for a variety of reasons. For example, some commenters believe it is an "elective" procedure. Other commenters suggested that funds should first be spent on other priorities such as durable medical equipment (DME) or mobility items such as power chairs; increasing reimbursement to providers; or that spending should be limited to the proportion to the transgender adult population in the Medicare program.

Response: The purpose of this NCA is to determine whether or not CMS should issue a NCD to cover surgery for patients who have gender dysphoria. NCAs do not establish payment amounts or spending priorities and, therefore, these comments are outside the scope of this consideration.

VIII. CMS Analysis

National coverage determinations are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under § 1862(l)(6) of the Act. In general, in order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B and must not be otherwise excluded from coverage.

Moreover, in most circumstances, the item or service must be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member (§1862(a)(1)(A)). The Supreme Court has recognized that "[t]he Secretary's decision as to whether a particular medical service is 'reasonable and necessary' and the means by which she implements her decision, whether by promulgating a generally applicable rule or by allowing individual adjudication, are clearly discretionary decisions." Heckler v. Ringer, 466 U.S. 602, 617 (1984). See also, 78 Fed. Reg. 48,164, 48,165 (August 7, 2013)

When making national coverage determinations, we consider whether the evidence is relevant to the Medicare

beneficiary population. In considering the generalizability of the results of the body of evidence to the Medicare population, we carefully consider the demographic characteristics and comorbidities of study participants as well as the provider training and experience. This section provides an analysis of the evidence, which included the published medical literature and guidelines pertaining to gender dysphoria, that we considered during our review to answer the question:

Is there sufficient evidence to conclude that gender reassignment surgery improves health outcomes for Medicare beneficiaries with gender dysphoria?

CMS carefully considered all the studies listed in this decision memorandum to determine whether they answered the question posed in this NCA. While there appears to be many publications regarding gender reassignment surgery, it became clear that many of the publications did not meet our inclusion/exclusion criteria as explained earlier in the decision memorandum.

Thirty-three papers were eligible based on our inclusion/exclusion criteria for the subsequent review (Figure 1). All studies reviewed had potential methodological flaws which we describe below.

A. Quality of the Studies Reviewed

Overall, the quality and strength of evidence were low due to mostly observational study designs with no comparison groups, subjective endpoints, potential confounding (a situation where the association between the intervention and outcome is influenced by another factor such as a co-intervention), small sample sizes, lack of validated assessment tools, and considerable lost to follow-up (Appendices C and F). The impact of a specific therapeutic intervention can be difficult to determine when there are multiple serial treatments such as psychotherapy, hormone treatment and surgery. To reduce confounding, outcome assessment just prior to and after surgery such as in a longitudinal study would be helpful. The objective endpoints included psychiatric treatment, attempted suicide, requests for surgical reversal, morbidity (direct and indirect adverse events), and mortality (Appendix F). CMS agrees with the utility of these objective endpoints. Quality of life, while important, is more difficult to measure objectively (Appendix E).

Of the 33 studies reviewed, published results were conflicting – some were positive; others were negative. Collectively, the evidence is inconclusive for the Medicare population. The majority of studies were non-longitudinal, exploratory type studies (i.e., in a preliminary state of investigation or hypothesis generating), or did not include concurrent controls or testing prior to and after surgery. Several reported positive results but the potential issues noted above reduced strength and confidence. After careful assessment, we identified six studies that could provide useful information (Figure 1). Of these, the four best designed and conducted studies that assessed quality of life before and after surgery using validated (albeit non-specific) psychometric studies did not demonstrate clinically significant changes or differences in psychometric test results after GRS. (Heylens et al., 2014; Ruppin, Pfafflin, 2015; Smith et al., 2005; Udeze et al., 2008) (Appendix C Panel A and Appendix G.)

Two studies (three articles) assessed functional endpoints (request for surgical reassignment reversal and morbidity/mortality) (Dhejne et al., 2011; Dhejne et al., 2014 along with Landén et al., 1998) (Figure 1 and Appendix C, Panel A and Appendix G). Although the data are observational, they are robust because the Swedish national database is comprehensive (including all patients for which the government had paid for surgical services) and is notable for uniform criteria to qualify for treatment and financial coverage by the government. Dhejne et al. (2014) and Landén et al. (1998) reported cumulative rates of requests for surgical reassignment reversal or change in legal status of 3.3% while Dhejne et al. (2014) reported 2.2%. The authors indicated that the later updated calculation had the potential to be an underestimate because the most recent surgical cohorts were larger in size and had shorter periods of follow-up.

Dhejne et al., (2011) tracked all patients who had undergone reassignment surgery (mean age 35.1 years) over a 30 year interval and compared them to 6,480 matched controls. The study identified increased mortality and psychiatric hospitalization compared to the matched controls. The mortality was primarily due to completed suicides (19.1-fold greater than in control Swedes), but death due to neoplasm and cardiovascular disease was increased 2 to 2.5 times as well. We note, mortality from this patient population did not become apparent until after 10 years. The risk for psychiatric hospitalization was 2.8 times greater than in controls even after adjustment for prior psychiatric disease (18%). The risk for attempted suicide was greater in male-to-female patients regardless of the gender of the control. Further, we cannot exclude therapeutic interventions as a cause of the observed excess morbidity and mortality. The study, however, was not constructed to assess the impact of gender reassignment surgery *per se.*

We believe at minimum study designs should have a pre-test/post-test longitudinal design accompanied by characterization of all patients lost to follow-up over the entire treatment series as well as those patients who did not complete questionnaires, and the use of psychometric quality-of-life tools which are well validated with linkage to "hard" (objective) patient outcomes in this particular patient population (Trentacosti 2007, PRO 2009) (Appendices C and D).

Patient Care

Clinical evidentiary questions regarding the care of patients with gender dysphoria remain. Many of the publications focused on aspects of surgical technique as opposed to long-term patient outcomes. The specific type(s) of gender/sex reassignment surgery (e.g., genital, non-genital) that could improve health outcomes in adults remain(s) uncertain because most studies included patients who had undertaken one or more of a spectrum of surgical procedures or did not define the specific types of surgical procedures under study. Furthermore, surgical techniques have changed significantly over the last 60 years and may not reflect current practice (Bjerrome Ahlin et al., 2014; Doornaert, 2011; Green, 1998; Pauly, 1968; Selvaggi et al., 2007; Selvaggi, Bellringer, 2011; Tugnet et al., 2007; Doornaert, 2011).

The WPATH care recommendations present a general framework and guidance on the care of the transgender individual. The standards of care are often cited by entities that perform gender reassignment surgery. WPATH notes, "More studies are needed that focus on the outcomes of current assessment and treatment approaches for gender dysphoria." Appendix D in the WPATH Standards of Care briefly describes their evidence base and acknowledges the historical problems with evidentiary standards, the preponderance of retrospective data, and the confounding impact of multiple interventions, specifically distinguishing the impact of hormone therapy from surgical intervention.

Additionally, CMS met with several stakeholders and conducted several interviews with centers that focus on healthcare for transgender individuals in the U.S. Primary care rather than gender reassignment surgery was often the main focus. Few of the U.S.-based reassignment surgeons we could identify work as part of an integrated practice, and few provide the most complex procedures.

Psychometric Tools

CMS reviewed psychometric endpoints because gender dysphoria (inclusive of prior nomenclature) describes an incongruence between the gender assigned at birth and the gender(s) with which the person identifies.

The psychometric tools used to assess outcomes have limitations. Most instruments that were specific for gender dysphoria were designed by the investigators themselves or by other investigators within the field using limited populations and lacked well documented test characterization. (Appendices E and F) By contrast, test instruments with validation in large populations were non-specific and lacked validation in the gender dysphoric patient populations. (Appendices E and F). In addition, the presentation of psychometric results must be accompanied by

enough information about the test itself to permit adequate interpretation of test results. The relevant diagnostic cut-points for scores and changes in scores that are clinically significant should also be scientifically delineated for interpretation.

Generalizability

It is difficult to generalize these study results to the current Medicare population. Many of the studies are old given they were conducted more than 10 years ago. Most of these studies were conducted outside of the U.S. in very different medical systems for treatment and follow-up. Many of the programs were single-site centers without replication elsewhere. The study populations were young and without significant physical or psychiatric co-morbidity (Appendix D). As noted earlier, psychiatric co-morbidity may portend poor outcomes (Asscheman et al., 2011; Landén et al., 1998).

Knowledge Gaps

This patient population faces complex and unique challenges. The medical science in this area is evolving. This review has identified gaps in the evidentiary base as well as recommendations for good study designs. The Institute of Medicine, the National Institutes of Health, and others also identified many of the gaps in the data. (Boehmer, 2002; HHS-HP, 2011; IOM, 2011; Kreukels-ENIGI, 2012; Lancet, 2011; Murad et al., 2010; NIH-LGBT, 2013) The current or completed studies listed in ClinicalTrials.gov are not structured to assess these gaps. These gaps have been delineated as they represent areas in which patient care can be optimized and are opportunities for much needed research.

B. Health Disparities

Four studies included information on racial or ethnic background. The participants in the three U.S. based studies were predominantly Caucasian (Beatrice, 1985; Meyer, Reter, 1979; Newfield et al., 2006). All of the participants in the single Asian study were Chinese (Tsoi, 1993). Additional research is needed in this area.

C. Summary

Based on an extensive assessment of the clinical evidence as described above, there is not enough high quality evidence to determine whether gender reassignment surgery improves health outcomes for Medicare beneficiaries with gender dysphoria and whether patients most likely to benefit from these types of surgical intervention can be identified prospectively.

The knowledge on gender reassignment surgery for individuals with gender dysphoria is evolving. Much of the available research has been conducted in highly vetted patients at select care programs integrating psychotherapy, endocrinology, and various surgical disciplines. Additional research of contemporary practice is needed. To assess long-term quality of life and other psychometric outcomes, it will be necessary to develop and validate standardized psychometric tools in patients with gender dysphoria. Further, patient preference is an important aspect of any treatment. As study designs are completed, it is important to include patient-centered outcomes.

Because CMS is mindful of the unique and complex needs of this patient population and because CMS seeks sound data to guide proper care of the Medicare subset of this patient population, CMS strongly encourages robust clinical studies with adequate patient protections that will fill the evidence gaps delineated in this decision memorandum. As the Institute of Medicine (IOM, 2011) importantly noted: "Best practices for research on the health status of LGBT populations include scientific rigor and respectful involvement of individuals who represent the target population.

Scientific rigor includes incorporating and monitoring culturally competent study designs, such as the use of appropriate measures to identify participants and implementation processes adapted to the unique characteristics of the target population. Respectful involvement refers to the involvement of LGBT individuals and those who represent the larger LGBT community in the research process, from design through data collection to dissemination."

IX. Decision

Currently, the local Medicare Administrative Contractors (MACs) determine coverage of gender reassignment surgery on a case-by-case basis. We have a received a complete, formal request to make a national coverage determination on surgical remedies for gender identity disorder (GID), now known as gender dysphoria. The Centers for Medicare & Medicaid Services (CMS) is not issuing a National Coverage Determination (NCD) at this time on gender reassignment surgery for Medicare beneficiaries with gender dysphoria because the clinical evidence is inconclusive for the Medicare population.

In the absence of a NCD, coverage determinations for gender reassignment surgery, under section 1862(a)(1)(A) of the Social Security Act (the Act) and any other relevant statutory requirements, will continue to be made by the local MACs on a case-by-case basis. To clarify further, the result of this decision is not national non-coverage rather it is that no national policy will be put in place for the Medicare program. In the absence of a national policy, MACs will make the determination on whether or not to cover gender reassignment surgery based on whether gender reassignment surgery is reasonable and necessary for the individual beneficiary after considering the individual's specific circumstances. For Medicare beneficiaries enrolled in Medicare Advantage (MA) plans, the initial determination of whether or not surgery would be reasonable and necessary will be made by the MA plans.

Consistent with the request CMS received, the focus of this National Coverage Analysis (NCA) was gender reassignment surgery. Specific types of surgeries were not individually assessed. We did not analyze the clinical evidence for counseling or hormone therapy treatments for gender dysphoria. As requested by several public commenters, we have modified our final decision memorandum to remove language that was beyond the scope of the specific request. We are not making a national coverage determination relating to counseling, hormone therapy treatments, or any other potential treatment for gender dysphoria.

While we are not issuing a NCD, CMS encourages robust clinical studies that will fill the evidence gaps and help inform which patients are most likely to achieve improved health outcomes with gender reassignment surgery, which types of surgery are most appropriate, and what types of physician criteria and care setting(s) are needed to ensure that patients achieve improved health outcomes.

A. Appendix A

Diagnostic & Statistical Manual of Mental Disorders (DSM) Criteria for Disorders of Gender Identity since 1980

DSM Version	Condition Name	Criteria	Criteria	Comments
DSM III 1980 *Chapter: Psychosexual Disorders*	**Trans-sexualism** *302.5x [Gender Identity Disorder of*	Required A (cross-gender identification) and B (aversion to one's natal	Sense of discomfort and inappropriateness about one's anatomic sex. Wish to be rid of one's own genitals and to live as a member of the other sex. The	Further characterization by sexual orientation Distinguished from Atypical Gender

	Child-hood (302.6)]	gender) criteria Dx excluded by physical intersex condition Dx excluded by another mental disorder, e.g., schizophrenia	disturbance has been continuous (not limited to periods of stress) for at least 2 years.	Identity Disorder 302.85
DSM III-Revised 1987 *TS classified as an Axis II dx (personality disorders and mental retardation) in a different chapter. GID included under Disorders Usually First Evident in Infancy, Childhood, Adolescence*	**Trans-sexualism** *(TS) (302.50) [GID of C]*	Required A and B criteria	Persistent discomfort and sense of inappropriateness about one's assigned sex. Persistent preoccupation for at least 2 years with getting rid of one's 1^{o} and 2^{o} sex characteristics and acquiring the sex characteristics of the other sex. Has reached puberty	Further characterization by sexual orientation Distinguished from Gender Identity Disorder of Adolescence or Adulthood, Non-trans-sexual Type • e.g., cross-dressing not for the purposes of sexual excitement Gender Identity Disorder Not Otherwise Specified 302.6 • e.g., intersex conditions Gender Identity Disorder Not Otherwise Specified 302.85 • e.g., persistent preoccupation with castration or penectomy w/o desire to acquire the sex traits of the other sex
	GID of adulthood, non-trans-sexual type, added			
DSM IV 1994 *Chapter: Sexual & Gender Identity Disorders*	**Gender Identity Disorder** in Adolescents and Adults (302.85) (Separate criteria & code for children, but	Required A and B criteria Dx excluded by physical intersex condition	Cross-gender identification • e.g., Stated desire to be another sex • e.g., Desire to live or be treated as a member of the other sex • e.g., conviction that he/she has the typical feelings and reactions of the other sex	Further characterization by sexual orientation Distinguished from Gender Identity Disorder Not Otherwise Specified 302.6 • e.g., intersex

	same name)		• e.g., frequent passing as the other sex Persistent discomfort with his/her sex or sense of inappropriateness in the gender role of that sex. • e.g., belief the he/she was born the wrong sex • e.g., preoccupation with getting rid of 1^{O} and 2^{O} sex characteristics &/or acquiring sexual traits of the other sex • Clinically significant distress or impairment in social, occupational, or other important areas of functioning	conditions • e.g., stress related cross-dressing • e.g., persistent preoccupation with castration or penectomy w/o desire to acquire the sex traits of the other sex
DSM IV-Revised 2000 *Chapter: Sexual & Gender Identity Disorders*	**Gender Identity Disorder** (Term trans-sexual-ism eliminated)	Required A & B criteria Dx excluded by physical intersex condition	Cross-gender identification • e.g., stated desire to be the other sex • e.g., desire to live or be treated as the other sex • e.g., conviction that he/she has the typical feelings & reactions of the other sex • e.g., frequent passing as the other sex Persistent discomfort with his or her sex OR sense of inappropriateness in the gender role of that sex • e.g., belief the he/she was born the wrong sex • e.g., preoccupation with getting rid of 1^{O} and 2^{O} sex characteristics &/or acquiring sexual traits of the other sex Clinically significant distress or impairment in social, occupational, or other important areas of functioning	Outcome may depend on time of onset Further characterization by sexual orientation Distinguished from Gender Identity Disorder Not Otherwise Specified 302.6 • e.g., intersex conditions • e.g., stress related cross-dressing • e.g., persistent preoccupation with castration or penectomy w/o desire to acquire the sex traits of the other sex
DSM V 2013 *Separate Chapter from Sexual Dysfunctions & Paraphilic Disorders*	**Gender Dysphoria** *(302.85)*	Gender nonconformity itself not considered to be a mental disorder The dysphoria associated with the gender incongruence is Eliminates A & B criteria	• Marked discordance between natal 1^{O} and 2^{O} sex characteristics* and experienced/expressed gender • Conviction that he/she has the typical feelings & reactions of the other sex (or some alternative gender) • Marked desire to be the other sex (or some alternative gender) • Marked desire to desire be treated as the other sex (or some alternative gender)	Includes diagnosis for post transition state to permit continued treatment access Includes disorders of sexual development such as congenital hyperplasia and androgen insensitivity

		Considers gender incongruence to be a spectrum Considers intersex/ "disorders of sex development" to be a subsidiary and not exclusionary to dx of GD	• Marked desire to be rid of natal 1^{O} and 2^{O} sex characteristics** • Marked desire to acquire 1^{O} and 2^{O} sex characteristics of the other sex (or some alternative gender) Clinically significant distress or impairment in social, occupational, or other important areas of functioning * or in young adolescents, the anticipated 2^{O} sex characteristics ** or in young adolescents, prevent the development of the anticipated 2^{O} sex characteristics ≥ 6 month marked discordance between natal gender & experienced/expressed gender as demonstrated by ≥ 6 criteria: • Strong desire to be of the other gender or an insistence that one is of another gender. • Strong preference for cross-gender roles in make-believe play. • Strong preference for the toys, games, or activities of the other gender. • Strong preference for playmates of the other gender. • In boys, strong preference for cross-dressing; in girls, strong preference for wearing masculine clothing • In boys, rejection of masculine toys, games, activities, avoidance of rough and tumble play; in girls, rejection of feminine toys, games, and activities.	syndromes
	Unspecified Gender Dysphoria (302.6) (F64.9)		This category applies to presentations in which sx c/w gender dysphoria that cause clinically significant distress or impairment, but do not meet the full criteria for gender dysphoria & the reason for not meeting the criteria is not provided.	
	Specified Gender Dysphoria 302.6 (F64.8)		If the reason that the presentation does not meet the full criteria is provided then this dx should be used	

C/W=consistent with Dx=diagnosis GD=gender dysphoria Sx=symptoms TS=transsexual 1^{O}=primary 2^{O}=secondary

B. Appendix B

1. General Methodological Principles of Study Design

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).

- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well-designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

Randomized controlled trials
Non-randomized controlled trials
Prospective cohort studies
Retrospective case control studies
Cross-sectional studies
Surveillance studies (e.g., using registries or surveys)
Consecutive case series
Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Appendix C

Patient Population: Enrolled & Treated with Sex Reassignment Surgery Loss of Patients & Missing Data

Panel A (Controlled Studies)

Author	Study Type	Recruitment Pool	Enrolled	% GRS	Completion
Dhejne 2011	Longitudinal Controlled	804 w GD	324	324 (100%)	-
Dhejne 2014 Landén	Longitudinal for test variable Controlled	767 applied for SRS 25 applications denied. 61 not granted full legal status	681	681 (100%)	NA: Clinical data extracted retrospectively in earlier paper

		15 formal applications for surgical reversal			
Heylens	Longitudinal Controlled	90 applicants for SRS 33 excluded 11 later excluded had not yet received SRS by study close.	57 (→46)	46 (80.7%) Only those w SRS evaluated	Psycho-social survey missing data for 3 at baseline & 4 after SRS. SCL90 not completed by 1 at baseline, 10 after hormone tx, & 4 after SRS →missing data for another 1.1% to 11.1%.
Kockott	Longitudinal Controlled	80 applicants for SRS 21 excluded	59	32 (54.2%) went to surgery	1 preoperative patient was later excluded b/c lived completely in aspired gender w/o SRS. Questions on financial sufficiency not answered by 1 surgical pt. Questions on sexual satisfaction & gender contentment not answered by 1 & 2 patients awaiting surgery respectively.
Mate-Kole 1990	Longitudinal Controlled	40 sequential patients of accepted patients. The number in the available patient pool was not specified.	40	20 (50%) went to surgery	-
Meyer	Longitudinal Controlled	Recruitment pool: 100 50 were excluded.	50	15 (30%) had undergone surgery 14 (28%) underwent surgery later	The assessments of all were complete
Rakic	Longitudinal Controlled	92 were evaluated 54 were excluded from surgery 2 post SRS were lost to follow-up 2 post SRS were excluded for being in the peri-operative period	32	32 (100%)	Questionnaire completed by all.
Ruppin	Longitudinal Controlled	The number in the available patient pool was not specified. 140 received recruitment letters. 69 were excluded	71	69 (97.2%)	The SCL-90, BSRI, FPI-R, & IPP tests were not completed by 9, 34, 13, &16 respectively. Questions about romantic relationships, sexual relationships, friendships, & family relationships were not answered by 1, 3, 2, & 23 respectively.

					Questions regarding gender security & regret & were not answered by 1& 2 respectively.
Smith	Longitudinal Controlled	The number in the available adult patient pool was not specified. 325 adult & adolescent applicants for SRS were recruited. 103 were excluded from additional tx	162	162 (100%)	36 to 61 (22.2%-37.6% of those adults w pre-SRS data) did not complete various post-SRS tests.
Udeze Megeri	Longitudinal Controlled	International patient w GD 546 & post SRS 318. 40 M to F subjects were prospectively selected.	40	40 (100%)	-
Ainsworth	Internet/convention Survey Cross-sectional Controlled	Number of incomplete questionnaires not reported	247	72 (29.1%) 75 (30.6%) facial 147 (59.5%) had received neither facial nor reassignment surgery	-
Beatrice	Cross-sectional Controlled	14 excluded for demographic matching reasons	40	10 (25%)	The assessments were completed by all
Haraldsen	Cross-sectional Controlled	Recruitment pool: 99	86	59 (68.6%)	-
Kraemer	Cross-sectional Controlled	The number in the available patient pool was not specified.	45	22 (48.9%)	-
Kuhn	Cross-sectional Controlled	The number in the available patient pool was not specified.	75	55 (73.3%)	-
Mate-Kole 1988	Cross-sectional Controlled	150 in 3 cohorts. Matched on select traits. The number in the available patient pool was not specified.	150	50 (66.7%)	-
Wolfradt	Cross-sectional Controlled	The number in the available patient pool was not specified.	90	30 (33.3%)	-

Panel B (Surgical Series: No Concurrent Controls)

Author	Study Type	Recruitment Pool	Enrolled	% GRS	Completion
Blanchard	Cross-sectional	294 clinic patients w GD	79	79(100%)	-

et al.	Control: Normative test data	had completed study questionnaire 116 authorized for GRS. 103 completed GRS & 1 yr post-operative. 24 excluded			
Weyers et al.	Cross-sectional Control: Normative test data	>300 M to F patients had undergone GRS 70 eligible patients recruited 20 excluded	50	50 (100%)	SF-26 not completed by 1
Wierckx et al.	Cross-sectional except for recall questions Control: Normative test data	79 F to M patients had undergone GRS & were recruited. 3 additional non-clinic patients were recruited by other patients. 32 excluded initially; 1 later.	49	49 (100%)	SF-36 test not completed by 2. Questions regarding sexual re-lationship, sex function, & surgical satisfaction were answered by as few as 27, 28, 32 respectively.
Eldh et al.	Cross-sectional except for 1 variable Control: Self for 1 variable-employ-ment	136 were identified. 46 excluded	90	90 (100%)	Questions regarding gender iden-tity, sex life, acceptance, & overall satisfaction were not answered by 13, 14, 14 & 16 respectively. Employment data missing for 11.
Hess et al.	Cross-sectional No control	254 consecutive eligible patients post GRS identified & sent surveys. 135 excluded.	119	119 (100%)	Questions regarding the esthetics, functional, and social outcomes of GRS were not answered by 16 to 28 patients.
Lawrence	Cross-sectional No control	727 eligible patients were recruited. 495 were excluded	232	232 (100%)	-
Salvador et al.	Cross-sectional No control	243 had enrolled in the clinic 82 completed GRS 69 eligible patients were identified. 17 excluded.	52	52 (100%)	-
Tsoi	Cross-sectional No control	The number in the available patient pool was not specified.	81	81 (100%)	-

Panel C (Mixed Treatment Series: No Direct Control Groups)

Author	Study Type	Recruitment Pool	Enrolled	% GRS	Completion
Gómez-Gil et al. 2012	Cross-sectional No direct control: Analysis of variance	200 consecutive patients were recruited.	187	79 (42.2%)	See prior box.

		13 declined participation or were excluded for incomplete questionnaires.			
Hepp et al.	Cross-sectional No direct control: Analysis of variance	The number in the available patient pool was not specified.	31	7 (22.6%)	HADS test not completed by 1
Motmans et al.	Cross-sectional No direct control: Analysis of variance & regression	255 with GD were identified. 77 were excluded.	148 (→140)	Not clearly stated. At least 103 underwent some form of GRS.	8 later excluded for incomplete SF-36 tests. 37 w recent GRS or hormone initiation were excluded from analysis of SF-36 results→103.
Newfield et al.	Internet survey Cross-sectional No direct control: Analysis of variance	Number of incomplete questionnaires not reported 446 respondents; 384 U.S respondents 62 non-U.S. respondents excluded from SF-36 test results 8 U.S. respondents excluded	376 (U.S.)	139 to 150 (37.0-39.9%) in U.S.	-
Gomez-Gil et al. 2014	Cross-sectional No direct control: Analysis w regression	The number in the available patient pool was not specified. 277 were recruited. 25 excluded	252(→193)	80 (41.4%) non-genital surgery	59 were excluded for incomplete questionnaires. See prior box.
Asscherman	Longitudinal No analysis by tx status	The number in the available patient pool was not specified.	1331	1177 (88.4%)	-
Johansson et al.	Cross-sectional except for 1 variable No analysis by tx status except for 1 question	60 eligible patients 18 excluded.	42	32 (76.2% of enrolled & 53.3% of eligible) (genital surgery)	-
Leinung et al.	Cross-sectional No analysis by tx status	242 total clinic patients	242	91 (37.6%)	Employment status data missing for 81 of all patients

*Data obtained via a survey on a website and distributed at a conference
B/C=because
BSRI=Bem Sex Role Inventory
F=Female
FP-R=Freiberg Personality Inventory
GD=Gender dysphoria
GID=Gender identity disorder
HADS=Hospital Anxiety & Depression Scale

IPP=Inventory of Interpersonal Problems
M=Male
NA=Not applicable
SCL-90=Symptom Checklist-90
SF-36=Short Form 36
GRS=Sex reassignment surgery
Tx=Treatment
W/o=without

Appendix D

Demographic Features of Study Populations

Panel A (Controlled Studies)

Author	Age (years; mean, S.D., range)	Gender	Race
Ainsworth	Only reassignment surgery:50 (no S.D.) Only facial surgery: 51 (no S.D.) Both types of surgery: 49 (no S.D.) Neither surgery: 46 (no S.D.)	247 M to F	-
Beatrice	Pre-SRS M to F: 32.5 (27-42), Post-SRS: 35.1 (30-43)	20 M to F plus 20 M controls	100% Caucasian
Dehjne 2011	Post-SRS: all 35.1±9.7 (20-69), F to M 33.3+8.7 (20–62), M to F 36.3+ 10.1(21–69)	133 (41.0%) F to M, 191 (59.0%) M to F; ratio 1:1.4	-
Dhejne 2014 Landén	F to M SRS cohort: median age 27 M to F SRS cohort: median age 32 F to M applicants for reversal: median age 22 M to F applicants for reversal: median age 35	767 applicants for legal/surgical reassignment 289 (37.7%) F to M, 478 (62.3%) M to F; ratio 1:1.6 681 post SRS & legal change 252 (37.0%) F to M, 429 (63.0%) M to F; ratio 1:1.7 15 applicants for reversal 5 (33.3%) F to M, 10 (66.7%) M to F; ratio 1:2	-
Haraldsen	Pre-SRS & Post-SRS: F to M 34±9.5, F to M 33.3±10.0 Post-SRS cohort reportedly older. No direct data provided.	Pre & Post SRS 35 (40.7%) F to M, 51 (59.3%) M to F; ratio 1:1.5	-
Heylens	-	11 (19.3% of 57) F to M, 46 (80.7%); ratio 1:4.2 (80.7% underwent surgery)	-
Kockott	Pre-SRS (continued wish for surgery): 31.7±10.2 Post-SRS: 35.5±13.1	Pre-SRS (continued wish for surgery) 3 (25%) F to M, 9 (75%) M to F; ratio 1:3 Post SRS: 14 (43.8%) F to M, 18 (56.2%) M to F; ratio 1:1.3	-
Kraemer	Pre-SRS: 33.0±11.3, Post-SRS: 38.2±9.0	Pre-SRS 7 F to M (30.4%), 16 M to F (69.6%); ratio 1:2.3 Post-SRS 8 F to M (36.4%), 14 M to F	-

		(63.6%); ratio 1:1.8	
Kuhn	All post SRS: median (range): 51 (39-62) (long-term follow-up)	3 (5.4%) F to M, 52 (94.5%) M to F; ratio 1:17.3.	-
Mate-Kole 1988	Initial evaluation: 34, Pre-SRS: 35, Post-SRS: 37	150 M to F	-
Mate-Kole 1990	Early & Usual wait SRS: 32.5 years (21-53)	40 M to F	-
Meyer	Pre-SRS: 26.7 Delayed, but completed SRS: 30.9 Post-SRS: 30.1	Pre-SRS: 5 (23.8%) F to M, 16 (76.2%) M to F; ratio 1:3.2 Delayed, but completed SRS: 1 (7.1%) F to M, 13 (92.9%) M to F; ratio 1:13 Post-SRS: 4 (26.7%) F to M, 11 (73.3%) M to F; ratio 1:2.8	86% Caucasian
Rakic	All: 26.8±6.9 (median 25.5, range 19-47), F to M: 27.8±5.2 (median 27, range 23-37), M to F: 26.4±7.8 (median 24, range 19-47).	10 (31.2%) F to M, 22 (68.8%) M to F; ratio 1:2.2	-
Ruppin	All: 47.0±10.42 (but 2 w/o SRS) (13.8±2.8 yrs post legal name change) (long-term follow-up) F to M: 41.2±5.78, M to F 52.9±10.82	36 (50.7%) F to M, 35 (49.3%) M to F; ratio 1:0.97	-
Smith	Time of surgical request for post-SRS: 30.9 (range 17.7-68.1) Time of follow-up for post-SRS: 35.2 (range 21.3-71.9)	Pre-SRS: 162: 58 (35.8%) F to M, 104 [64.2%] M to F; ratio 1:1.8 Post-SRS: 126: 49 (38.9%) F to M, 77 (61.1%) M to F; ratio 1:1.6	-
Udeze Megeri	M to F: 47.33±13.26 (range 25-80).	40 M to F	-
Wolfradt	Patients & controls: 43 (range 29-67).	30 M to F plus 30 F controls plus 30 M controls.	-

*Data obtained via a survey on a website and distributed at a conference SD=Standard deviation

Panel B (Surgical Series: No Concurrent Controls)

Author	Age (years; mean, S.D., range)	Gender	Caucasian
Blanchard et al.	F to M: 32.6, M to F w M partner preference: 33.2, F to M w F partner preference: 47.7 years	Post-GRS: 47 (45.6%) F to M, 56 (54.4%) M to F; ratio 1:1.19. In study: 38 (48.1%) F to M, 32 (40.5%) M to F w M partner preference, 9 (11.4%) M to F w F partner preference; ratio 1:0.8: 0.2	-
Weyers et al.	Post-GRS M to F: 43.1 ±10.4 (long-term follow-up)	50 M to F	-
Wierckx et al.	Time of GRS: 30±8.2 years (range 16 to 49) Time of follow-up: 37.1 ±8.2.4 years (range 22 to 54)	49 M to F	-
Eldh et al.	-	50 (55.6%) F to M, 40 (44.4%) M to F; ratio 1:0.8 There is 1 inconsistency in the text	-

		suggesting that these should be reversed.	
Hess et al.	-	119 M to F	-
Lawrence	Time of GRS: 44±9 (range 18-70)	232 M to F	-
Salvador et al.	Time of follow-up for post-GRS: 36.28±8.94 (range 18-58) (Duration of follow-up: 3.8±1.7 [2-7])	52 M to F	-
Tsoi	Time of initial visit: All: 24.0±4.5, F to M: 25.4±4.4 (14-36), M to F: 22.9±4.6 (14-36). Time of GRS: All: 25.9±4.14, F to M: 27.4±4.0 (20-36), M to F: 24.7+4.3 (20-36).	36 (44.4%) F to M, 45 (55.6%) M to F; ratio 1:1.25	0% 100% Asian

Panel C (Mixed Treatment Series: No Direct Control Groups)

Author	Age (years; mean, S.D., range)	Gender	Caucasian
Gómez-Gil et al. 2012	W & W/O GRS: All: 29.87±9.15 (range 15-61), W/O hormone tx: 25.9±7.5, W current hormone tx: 33.6±9.1. (At hormone initiation: 24.6±8.1).	W/O hormone tx: 38 (56.7%) F to M, 29 (43.3%) M to F; ratio 1:0.8. W hormone tx: 36 (30.0%) F to M, 84 (70.0%) M to F; ratio 1:2.3. Post-GRS: 29 (36.7%) F to M, 50 (63.3%) M to F; ratio 1:1.7.	-
Hepp et al.	W & W/O GRS: 32.2±10.3	W & W/O GRS: 11 (35.5%) F to M; 20 (64.5%) M to F; ratio 1:1.8.	-
Motmans et al.	W & W/O GRS: All (n=140) : 39.9±10.2, F to M: 37.0±8.5, M to F: 42.3±10.4	W & W/O GRS: N=140 63(45.0%) F to M, 77 (55.0%) M to F; ratio 1:1.2 N=103 49 (47.6%) F to M; 54 (52.4%) M toF; ratio 1:1.1	-
Newfield et al.	W & W/O GRS: U.S.+ non-U.S. : 32.8±11.2, U.S. 32.6±10.8	W & W/O GRS: U.S.+ non-U.S.: F to M, 438, U.S.: F to M: 376	89% of 336 respondents Caucasian
Gomez-Gil, et al. 2014	W & W/O Non-genital GRS: 31.2±9.9 (range 16-67).	W & W/O Non-genital GRS: 74 (38.3%) F to M, 119 (61.7%) M to F; ratio1:1.6.	-
Asscherman	Time of hormone tx: F to M: 26.1±7.6 (16–56), M to F: 31.4±11.4 (16–76)	Met hormone tx requirements: 365 (27.4%) F to M, 966 (72.6%) M to F; ratio 1:2.6. Post-GRS: 343 (29.1%) F to M, 834 (70.9%) M to F; ratio 1:2.4.	-
Johanssen	Time of initial evaluation: F toM: 27.8 (18-46), M to F 37.3 (21-60). Time of GRS: F to M: 31.4 (22-49), M to F 38.2 (22-57). Time of follow-up for post-GRS: F to M: 38.9 (28-53), M to F 46.0 (25-69) (Long-term follow-up)	Approved for GRS: 21 (35%) F to M, 39 (65%) M to F; ratio 1:1.9) Post GRS: 14 (43.8%) F to M; 18 (56.2%) M to F; ratio 1:1.3)	-
Leinung et al.	Time of hormone initiation : F to M: 27.5, M to F 35.5	W & W/O GRS: 50 (20.7%) F to M, 192 M to F (79.3%); ratio 1:3.8. Post-GRS: 32 F to M (35.2%); 59 (64.8%) M to F; ratio 1:1.8.	-

Appendix E

Psychometric and Satisfaction Survey Instruments

Instrument Name and Developer	Development and Validation Information
APGAR Family Adaptability, Partner-ship Growth, Affection, and Resolve *Smilkstein*	Published in 1978 Initial data: 152 families in the U.S. A "friends" component was added in 1983. Utility has challenged by many including Gardner 2001
Beck Depression Inventory *Beck, Ward, Mendelson, Mock, & Erbaugh*	Published initially in 1961 with subsequent revisions It was initially evaluated in psychiatric patients in the U.S.A. Salkind (1969) evaluated its use in 80 general outpatients in the UK. Itis copyrighted and requires a fee for use
Bem Sex Role Inventory *Bem*	Published 1974 Initial data: 100 Stanford Undergraduates 1973 update: male 444; female 279 1978 update: 470; female 340
Body Image Questionnaire *Clement & Lowe*	Validity study published 1996 (German) Population: 405 psychosomatic patients, 141 medical students, 208 sports students
Body Image Scale *Lindgren & Pauly (Kuiper, Dutch adaptation 1991)*	1975 Initial data: 16 male and 16 female transsexual patients in Oregon
Crown Crisp Experiential Index (formerly Middlesex Hospital Questionnaire) *Crown & Crisp*	Developed circa 1966 Manual published 1970 Initial data: 52 nursing students while in class in the UK
(2nd) European Quality of Life Survey *Anderson, Mikuliç, Vermeylen, Lyly-Yrjanainen, & Zigante,*	Published in 2007 The pilot survey was tested in the UK and Holland with 200 interviews. The survey was revised especially for non-response questions. Another version was tested in 25 persons of each of the 31 countries to be surveyed. Sampling methods were devised. 35,634 Europeans were ultimately surveyed. Additional updates
Female Sexual Function Index *Rosen, Brown, Heiman, Leiblum, Meston, Shabsigh, Ferguson, D'Agostino Wiegel, Meston, & Rosen*	Published in 2000 Initial data: 131 normal controls & 128 age-matched subjects with female sexual arousal disorder from 5 U.S. research centers. Updated 2005: the addition of those with hypoactive sexual desire disorder, female sexual orgasm disorder, dyspareunia/vaginismus, & multiple sexual dysfunctions (n=568), plus more controls (n=261).

Fragebogen zur Beurteilung des eigenen Korpers *Strauss*	Published 1996 (German)
Freiberg Personality Inventory *Fahrenberg, Hampel, & Selg*	7th edition published 2001, 8th edition in 2009 (Not in PubMed) German equivalent of MMPI
"gender identity disorder in childhood" *Smith, van Goozen, Kuiper, & Cohen-Kettenis*	11 items derived from the Biographical Questionnaire for Trans-sexuals (Verschoor Poortinga 1988) (Modified by authors of the Smith study)
Gender Identity Trait Scale *Altstotter-Gleich*	Published 1989 (German)
General Health Questionnaire *Goldberg & Blackwell (initial study)* *Goldberg & Williams (manual)*	Initial publication 1970 Manual published ?1978, 1988 (Not in PubMed) Initial data: 553 consecutive adult patients in a single UK primary care practice were assessed. Sample of 200 underwent standardized psychiatric interview. Developed to screen for hidden psychological morbidity. Proprietary test. Now 4 versions.
Hospital Anxiety & Depression Scale *Zigmond & Snaith*	Published in 1983 Initial data: Patients between 16 & 65 in outpatient clinics in the UK >100 patients; 2 refusals. 1st 50 compared to 2nd 50.
Inventory of Interpersonal Problems *Horowitz*	Published 1988 Initial data: 103 patients about to undergo psychotherapy; some patients post psycho-therapy (Kaiser Permanente-San Francisco) Proprietary test
King's Health Questionnaire *Kelleher, Cardozo, Khullar, & Salvatore*	1997 Initial data: 293 consecutive women referred for urinary incontinence evaluation in London Comparison to SF-36
Minnesota Multi-phasic Personality Inventory *Hathaway & McKinley* *Butcher, Dahlstrom, Graham, & Tellegen*	Published in 1941 Updated in 1989 with new, larger, more diverse sample. MMPI-2: 1,138 men & 462 women from diverse communities & several geographic regions in the U.S.A. The test is copyrighted.
Modified Androphia-Gynephilia Index	Neither the underlying version or the Blanchard modified version could be located in PubMed (Designed by the author of the Blanchard et al. study)
"post-operative functioning 13 items" *Doorn, Kuiper, Verschoor, Cohen-Kettenis*	Published 1996 (Dutch) (Not in PubMed) (Designed by 1 of the authors of the Smith study)
"post-operative functioning 21 items" *Doorn, Kuiper, Verschoor,*	Published 1996 (Dutch) (Not in PubMed) (Designed by 1 of the authors of the Smith study)

Cohen-Kettenis	
Scale for Depersonalization Experiences *Wolfradt*	Unpublished manuscript 1998 (University of Halle) (Designed by 1 of the authors of the Wolfradt study)
"sex trait function" *Cohen-Kettenis & van Goozen*	Published 1997 Assessed in 22 adolescents (Designed by 1 of the authors of the Smith Study)
Self-Esteem Scale *Rosenberg*	Published 1965 (Not in PubMed) Initial data: 5,024 high-school juniors & seniors from 10 randomly selected New York schools
Short-Form 36 *RAND* *Ware & Sherbourne1992* *McHorney, Ware, & Raczek 1993*	Originally derived from the Rand Medical Outcomes Study (n=2471 in version 1; 6742 in version 2 1989). The earliest test version is free. Alternative scoring has been developed. There is a commercial version with a manual.
Social Anxiety & Distress Scale *Watson & Friend*	Initial publication in1969 Requires permission for use
Social Support Scale *Van Tilburg 1988*	Published 1988 (Dutch) (Not in PubMed)
Spielberger State & Trait Anxiety Questionnaire *Spielberger, Gorsuch, Lushene, Vagg, & Jacobs*	Current format published in 1983 Proprietary test
Symptom Checklist-90 *Derogatis, Lipman, Covi Derogatis & Cleary*	Published in 1973 & 1977 Reportedly with normative data for psychiatric patients (in- & out-patient) & normal subjects in the U.S. Has undergone a revision Requires qualification for use
Tennessee Self-Concept Scale *Fitts & Warren*	In use prior to 1988 publication. Initial data: 131 psychiatric day care patients. Updated manual published 1996. Update population >3000 with age stratification. No other innformation available. Requires qualification for use
Utrecht Gender Dysphoria Scale *Cohen-Kettenis & van Goozen*	Published in 1997 Initial population: 22 transgender adolescents who underwent reassignment surgery. (Designed by 1 of the authors of the Smith study)
WHO-Quality of Life (abbreviated version) *Harper for WHO group*	Field trial version released 1996 Tested in multiple countries. The Seattle site consisted of 192 of the 8294 subjects tested). Population not otherwise described. The minimal clinically important difference has not been determined. Permission required

Althof et al., 1983; Greenberg, Frank, 1965; Gurtman, 1996; Lang, Vernon, 1977; Paap et al., 2012; Salkind et al., 1969; Vacchiano, Strauss, 1968.

Appendix F

Endpoint Data Types and Sources

Panel A (Controlled Studies)

Author	National Data	Instrument w Substantive Normative Data	Instrument w/o Substantive &/or Accessible Normative Data	Investigator-designed	Other	Other
Dhejne 2011	Yes	-	-	-	-	Mortality (Suicide, Cardiovascular Disease [possible adverse events from Hormone Tx], Cancer), Psych hx & hospitalization, Suicide attempts
Dhejne Landén	Yes	-	-	-	Includes demographics*	Education, Employment, Formal application for reversal of status, Psych dx & tx, Substance abuse** More elements in earlier paper
Beatrice	-	MMPI form R, TSCS	-	-	Demographic	Education, Income, Relationships
Haraldsen	-	SCL-90/90R	-	-	Demographic	DSM Axis 1, II, V (GAF), Substance abuse
Heylens	-	SCL-90	-	Yes-2	Demographic	Employment, Relationships, Substance abuse, Suicide attempts
Ainsworth	-	Likely SF-36v2*	-	Yes-1	Demographic	-
Ruppin	-	SCL-90R	BSRI, FPI-R, IIP	Yes-2	Demographic	Adverse events from surgery, Employment, Psych tx, Relationships, Substance abuse
Smith	-	MMPI-short, SCL-90?R	BIS, UGDS, ? Cohen-Kettenis', Doorn's x2, (Gid-c, SSS)	Yes-1 or 2	Demographic	Adverse events from surgery, Employment, Relationships
Udeze Megeri	-	SCL-90R	BDI, GHQ, HADS,STAI-X1, STAI-X2	-	-	Psych eval & ICD-10 dx
Kuhn	-	-	KHQ	Yes-1	Demographic	Relationships

Mate-Kole 1990	-	-	BSRI, CCEI	Yes-1	Demographic	Employment (relative change), Psych hx, Suicide hx
Wolfradt	-	-	BIQ, GITS, SDE, SES	Yes-1	-	-
Kraemer	-	-	FBeK	-	Demographic	-
Mate-Kole 1988	-	-	BSRI, CCEI	-	Demographic	Employment, Psych hx, Suicide hx,
Kockott	-	-	-	Yes-1	Demographic	Employment, Income, Relationships, Suicide attempts
Meyer	-	-	-	Yes-1	Demographic	Education, Employment, Income, Psych tx, Phallus removal request
Rakic	-	-	-	Yes-1	Demographic	Employment, Relationships

Panel B (Surgical Series: No Concurrent Controls)

Author	**National Data**	**Instrument w Substantive Normative Data**	**Instrument w/o Substantive &/or Accessible Normative Data**	**Investigator-designed**	**Other**	**Other**
Weyers	-	SF-36	FSFI	Yes-2	Demographic	Hormone levels, Adverse events from surgery, Relationships
Blanchard	-	SCL-90R	(AG)	Yes-1	Demographic	Education, Employment, Income, Relationships, Suicide (Incidental finding)
Wierckx	-	SF-36	-	Yes-3	Demographic	Hormone levels, Adverse events from surgery, Relationships
Eldh	-	-	-	Yes-1	-	Adverse events from surgery, Employment, Relationships, Suicide attempts

Hess	-	-	-	Yes-1	-	-
Lawrence	-	-	-	Yes-4	Demographic	Adverse events from surgery
Salvador	-	-	-	Yes-1	Demographic	Relationships
Tsoi	-	-	-	Yes-1	Demographic	Education, Employment, Relationships (relative change)

Panel C (Mixed Treatment Series: No Direct Control Groups)

Author	**National Data**	**Instrument w Substantive Normative Data**	**Instrument w/o Sub-stantive &/or Accessible Normative Data**	**Investigator-designed**	**Other**	**Other**
Asscheman et al.	Yes	-	-	-	Demographic	Mortality (HIV, Possible adverse events from Hormone Tx, Substance abuse, Suicide)
Motmans et al.	-	SF36 EQOLS (2nd)	-	-	Demographic	Education, Employment, Income, Relationships
Newfield et al.	-	SF-36v2	-	-	Demographic	Income
Gómez-Gil et al. 2014	-	WHOQOL-BREF	APGAR	Yes-1	Demographic	Education, Employment, Relationships
Gómez-Gil et al. 2012	-	-	HADS, SADS	-	Demographic	Education, Employment, Living arrangements
Hepp et al.	-	-	HADS	-	Demographic	DSM Axis 1& II Psych dx
Johansson et al.	-	-	-	Yes-1	Demographic	Axis V change (Pt & Clinician) Employment (relative change) Relationship (relative change)
Leinung et al.	-	-	-	-	Demographic	Employment, Disability, DVT, HIV status, Psych dx

*Listed as San Francisco-36 in manuscript

** From medical charts & verdicts ?=Possibly self-designed

AG=Androphilia-Gynephilia Index (investigator designed 1985) (used more for classification)

APGAR=Family Adaptability, Partnership growth, Affection, and Resolve

BDI=Beck Depression Inventory

BIQ=Body Image Questionnaire
BIS=Body Image Scale
BSRI=Bem Sex Role Inventory
CCEI=Crown Crisp Experiential Index
Cohen-Kettenis'= Sex trait function (An author helped design)
Dorn's x2= Post-operative functioning 13 items (An author helped design)
Post-operative functioning 21 items (An author helped design)
EQOLS (2nd)=2nd European Quality of Life Survey
FBeK=Fragebogen zur Beurteilung des eigenen Korpers
FPI-R=A version of the Freiberg Personality Inventory
FSFI+Female Sexual Function Index
GHQ=General Health Questionnaire
Gid-c=Gender identity disorder in childhood (used more for predictors) (An author helped design)
GITS=Gender Identity Trait Scale
HADS=Hospital Anxiety Depression Scale
IIP=Inventory of Interpersonal Problems
KHQ=King's Health Questionnaire
MMPI=Minnesota Multi-phasic Personality Inventory
SADS=Social Anxiety & Distress Scale
SCL-90 (±R)=A version of the Symptom Checklist 90
SDE=Scale for Depersonalized Experiences (An author designed)
SES=Self-Esteem Scale
SF-36 (v2)=Short Form-36(version2)
SSS=Social Support Scale (used more for predictors)
STAI-X1, STAI-X2=Spielberger State and Trait Anxiety Questionnaire
TSCS=Tennessee Self-Concept Scale
UGDS=Utrecht Gender Dysphoria Scale (An author helped design)
WHOQOL-BREF=World Health Organization-Quality of Life (abbreviated version)

Appendix G.

Longitudinal Studies Which Used Patients as Their Own Controls and Which Used Psychometric Tests with Extensive Normative Data or Longitudinal Studies Which Used National Data Sets

Author		Test	Patient and Data Loss	Results
		Psychometric Test		
Heylens et al. Belgium 2014		SCL-90R	90 applicants for SRS were recruited. • 8 (8.9%) declined participation. • 12 (13.3%) excluded b/c GID-NOS dx. • 12 (13.3%) did not complete the treatment sequence b/c of psychiatric/physical co-morbidity, personal decision for no tx, or personal decision for only	At t=0, the mean global "psychoneuroticism" SCL-90R score, along with scores of 7 of 8 subscales, were statistically more pathologic than the general population. After hormone tx, the mean score for global "psychoneuroticism" normalized & remained normal after reassignment surgery.

			hormone tx. • 1 (1.1%) committed suicide during follow-up. 57 (63.3% of recruited) entered the study. • 1 (12.2% of initial recruits) had not yet received SRS by study close. →**46 (51.1% of recruited) underwent serial evaluation** • The test was not completed by 1 at t=0, 10 at t=1 (after hormone tx), & 4 at t=2 (after SRS) →**missing data for another 1.1% to 11.1%.**	
Ruppin,Pfafflin, Germany 2015		SCL-90R	The number in the available patient pool was not specified. 140 received recruitment letters. • 2 (1.4% of those with recruitment letters) had died. • 1 (0.7%) was institutionalized. • 5 (3.6%) were ill. • 8 (5.7%) did not have time. • 8 (5.7%) stated that GD was no longer an issue. • 8 (5.7%) provided no reason. • 28 (20.0%) declined further contact. • 9 (6.4%) were lost to follow-up. →**71 (50.7%) agreed to participate.** • **2 (1.4%) had not undergone SRS** • The test was not completed by 9. →**missing data for another 6.4%.**	At t=0, the "global severity index "SCL-90R score was 0.53±0.49. At post-SRS follow-up the score had decreased to 0.28±0.36. The scores were statistically different from one another, but are of limited biologic significance given the range of the score for this scale: 0-4. In the same way, all of the subscale scores were statistically different, but the effect size was reported as large only for "interpersonal sensitivity": 0.70±0.67 at t=0 and 0.26±0.34 post-SRS.
Smith et al. Holland		MMPI SCL-90	The number in the available adult patient	Most of the MMPI scales were already in the normal range at

2005			pool was not specified. 325 adult & adolescent applicants for SRS were recruited. • 103 (31.7%) were not eligible to start hormone tx & real-life experience. • 34 (10.7%) discontinued hormone tx 162 (an unknown percentage of the initial recruitment) provided pre-SRS test data. • **36 to 61 (22.2%-37.6% of those adults w pre-SRS data) did not complete post-SRS testing.**	the time of initial testing. At t=0, the global "psychoneuroticism" SCL-90 score, which included the drop-outs, was 143.0±40.7. At post SRS-follow-up, the score had decreased to 120.3±31.4. The scores were statistically different from one another, but are of limited biologic significance given the range of the score for this scale: 90 to 450, with higher scores consistent with more psychological instability.
Udeze, et al. 2008 Megeri, Khoosal 2007 UK		SCL-90R	The number in the available patient pool was not specified. 40 subjects were prospectively selected. • Post-operative testing was conducted within 6 months to minimize previously determined loss rates.	At t=0, the mean raw global score was 48.33. At post-SRS follow-up, the mean score was 49.15. There were no statistically significant changes in the global score or for any of the subscales.
	National Databases			
Dehjne Sweden 2011		Swedish National Records	804 with GID in Sweden 1973 to 2003 were identified. • 480 (59.7%) did not apply or were not approved for SRS 324 (40.3%) underwent SRS. • All were followed. 3240 controls of the natal sex and 3240 controls of the reassigned gender were randomly selected from national records	All cause mortality was higher (n=27[8%]) than in controls (H.R 2.8 [1.8-4.3]) even after adjustment for covariants. Divergence in survival curves was observed after 10 years. The major contributor was completed suicide (n=10 [3%]; adjusted H.R. 19.1 [5.8-62.9]). Suicide attempts were more common (n= 29 [9%]) than in controls (adjusted H.R. 4.9 [2.9–8.5]). Hospitalizations for psychiatric conditions (not related to gender dysphoria) were more common n= 64 [20%] than in controls (H.R. 2.8 [2.0–3.9]) even after adjusting for prior

				psychiatric morbidity.
Dhejne et al. 2014 Landén et al. 1998 Sweden		Swedish National Registry	767 applied for SRS/legal status (1960-2010) • 25 (3.3%) applications denied. • 61 (8.0%) not granted full legal status 681 (88.7%) underwent SRS. • All were followed.	15 formal applications for reversal to natal/original gender (2.2% of the SRS population) were identified thus far (preliminary number). (Does not reflect other manifestations of regret such as suicide.)

GID-NOS=Gender Identity Disorder-Not Otherwise Specified HR=Hazard Ratio SRS=Sex reassignment surgery Tx=Treatment

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DEFENDANT'S EXHIBIT 17

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Gender Dysphoria

In this chapter, there is one overarching diagnosis of gender dysphoria, with separate developmentally appropriate criteria sets for children and for adolescents and adults. The area of sex and gender is highly controversial and has led to a proliferation of terms whose meanings vary over time and within and between disciplines. An additional source of confusion is that in English "sex" connotes both male/female and sexuality. This chapter employs constructs and terms as they are widely used by clinicians from various disciplines with specialization in this area. In this chapter, *sex* and *sexual* refer to the biological indicators of male and female (understood in the context of reproductive capacity), such as in sex chromosomes, gonads, sex hormones, and nonambiguous internal and external genitalia. Disorders of sex development denote conditions of inborn somatic deviations of the reproductive tract from the norm and/or discrepancies among the biological indicators of male and female. *Cross-sex* hormone treatment denotes the use of feminizing hormones in an individual assigned male at birth based on traditional biological indicators or the use of masculinizing hormones in an individual assigned female at birth.

The need to introduce the term *gender* arose with the realization that for individuals with conflicting or ambiguous biological indicators of sex (i.e., "intersex"), the lived role in society and/or the identification as male or female could not be uniformly associated with or predicted from the biological indicators and, later, that some individuals develop an identity as female or male at variance with their uniform set of classical biological indicators. Thus, *gender* is used to denote the public (and usually legally recognized) lived role as boy or girl, man or woman, but, in contrast to certain social constructionist theories, biological factors are seen as contributing, in interaction with social and psychological factors, to gender development. *Gender assignment* refers to the initial assignment as male or female. This occurs usually at birth and, thereby, yields the "natal gender." *Gender-atypical* refers to somatic features or behaviors that are not typical (in a statistical sense) of individuals with the same assigned gender in a given society and historical era; for behavior, *gender-nonconforming* is an alternative descriptive term. *Gender reassignment* denotes an official (and usually legal) change of gender. *Gender identity* is a category of social identity and refers to an individual's identification as male, female, or, occasionally, some category other than male or female. *Gender dysphoria* as a general descriptive term refers to an individual's affective/cognitive discontent with the assigned gender but is more specifically defined when used as a diagnostic category. *Transgender* refers to the broad spectrum of individuals who transiently or persistently identify with a gender different from their natal gender. *Transsexual* denotes an individual who seeks, or has undergone, a social transition from male to female or female to male, which in many, but not all, cases also involves a somatic transition by cross-sex hormone treatment and genital surgery (*sex reassignment surgery*).

Gender dysphoria refers to the distress that may accompany the incongruence between one's experienced or expressed gender and one's assigned gender. Although not all individuals will experience distress as a result of such incongruence, many are distressed if the desired physical interventions by means of hormones and/or surgery are not available. The current term is more descriptive than the previous DSM-IV term *gender identity disorder* and focuses on dysphoria as the clinical problem, not identity per se.

Gender Dysphoria

Diagnostic Criteria

Gender Dysphoria in Children 302.6 (F64.2)

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least six of the following (one of which must be Criterion A1):

1. A strong desire to be of the other gender or an insistence that one is the other gender (or some alternative gender different from one's assigned gender).
2. In boys (assigned gender), a strong preference for cross-dressing or simulating female attire; or in girls (assigned gender), a strong preference for wearing only typical masculine clothing and a strong resistance to the wearing of typical feminine clothing.
3. A strong preference for cross-gender roles in make-believe play or fantasy play.
4. A strong preference for the toys, games, or activities stereotypically used or engaged in by the other gender.
5. A strong preference for playmates of the other gender.
6. In boys (assigned gender), a strong rejection of typically masculine toys, games, and activities and a strong avoidance of rough-and-tumble play; or in girls (assigned gender), a strong rejection of typically feminine toys, games, and activities.
7. A strong dislike of one's sexual anatomy.
8. A strong desire for the primary and/or secondary sex characteristics that match one's experienced gender.

B. The condition is associated with clinically significant distress or impairment in social, school, or other important areas of functioning.

Specify if:

With a disorder of sex development (e.g., a congenital adrenogenital disorder such as 255.2 [E25.0] congenital adrenal hyperplasia or 259.50 [E34.50] androgen insensitivity syndrome).

Coding note: Code the disorder of sex development as well as gender dysphoria.

Gender Dysphoria in Adolescents and Adults 302.85 (F64.1)

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least two of the following:

1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics).
2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics).
3. A strong desire for the primary and/or secondary sex characteristics of the other gender.
4. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender).
5. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).
6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

With a disorder of sex development (e.g., a congenital adrenogenital disorder such as 255.2 [E25.0] congenital adrenal hyperplasia or 259.50 [E34.50] androgen insensitivity syndrome).

Coding note: Code the disorder of sex development as well as gender dysphoria.

Specify if:

Posttransition: The individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one cross-sex medical procedure or treatment regimen—namely, regular cross-sex hormone treatment or gender reassignment surgery confirming the desired gender (e.g., penectomy, vaginoplasty in a natal male; mastectomy or phalloplasty in a natal female).

Specifiers

The posttransition specifier may be used in the context of continuing treatment procedures that serve to support the new gender assignment.

Diagnostic Features

Individuals with gender dysphoria have a marked incongruence between the gender they have been assigned to (usually at birth, referred to as *natal gender*) and their experienced/expressed gender. This discrepancy is the core component of the diagnosis. There must also be evidence of distress about this incongruence. Experienced gender may include alternative gender identities beyond binary stereotypes. Consequently, the distress is not limited to a desire to simply be of the other gender, but may include a desire to be of an alternative gender, provided that it differs from the individual's assigned gender.

Gender dysphoria manifests itself differently in different age groups. Prepubertal natal girls with gender dysphoria may express the wish to be a boy, assert they are a boy, or assert they will grow up to be a man. They prefer boys' clothing and hairstyles, are often perceived by strangers as boys, and may ask to be called by a boy's name. Usually, they display intense negative reactions to parental attempts to have them wear dresses or other feminine attire. Some may refuse to attend school or social events where such clothes are required. These girls may demonstrate marked cross-gender identification in role-playing, dreams, and fantasies. Contact sports, rough-and-tumble play, traditional boyhood games, and boys as playmates are most often preferred. They show little interest in stereotypically feminine toys (e.g., dolls) or activities (e.g., feminine dress-up or role-play). Occasionally, they refuse to urinate in a sitting position. Some natal girls may express a desire to have a penis or claim to have a penis or that they will grow one when older. They may also state that they do not want to develop breasts or menstruate.

Prepubertal natal boys with gender dysphoria may express the wish to be a girl or assert they are a girl or that they will grow up to be a woman. They have a preference for dressing in girls' or women's clothes or may improvise clothing from available materials (e.g., using towels, aprons, and scarves for long hair or skirts). These children may role-play female figures (e.g., playing "mother") and often are intensely interested in female fantasy figures. Traditional feminine activities, stereotypical games, and pastimes (e.g., "playing house"; drawing feminine pictures; watching television or videos of favorite female characters) are most often preferred. Stereotypical female-type dolls (e.g., Barbie) are often favorite toys, and girls are their preferred playmates. They avoid rough-and-tumble play and competitive sports and have little interest in stereotypically masculine toys (e.g., cars, trucks). Some may pretend not to have a penis and insist on sitting to urinate. More

rarely, they may state that they find their penis or testes disgusting, that they wish them removed, or that they have, or wish to have, a vagina.

In young adolescents with gender dysphoria, clinical features may resemble those of children or adults with the condition, depending on developmental level. As secondary sex characteristics of young adolescents are not yet fully developed, these individuals may not state dislike of them, but they are concerned about imminent physical changes.

In adults with gender dysphoria, the discrepancy between experienced gender and physical sex characteristics is often, but not always, accompanied by a desire to be rid of primary and/or secondary sex characteristics and/or a strong desire to acquire some primary and/or secondary sex characteristics of the other gender. To varying degrees, adults with gender dysphoria may adopt the behavior, clothing, and mannerisms of the experienced gender. They feel uncomfortable being regarded by others, or functioning in society, as members of their assigned gender. Some adults may have a strong desire to be of a different gender and treated as such, and they may have an inner certainty to feel and respond as the experienced gender without seeking medical treatment to alter body characteristics. They may find other ways to resolve the incongruence between experienced/expressed and assigned gender by partially living in the desired role or by adopting a gender role neither conventionally male nor conventionally female.

Associated Features Supporting Diagnosis

When visible signs of puberty develop, natal boys may shave their legs at the first signs of hair growth. They sometimes bind their genitals to make erections less visible. Girls may bind their breasts, walk with a stoop, or use loose sweaters to make breasts less visible. Increasingly, adolescents request, or may obtain without medical prescription and supervision, hormonal suppressors ("blockers") of gonadal steroids (e.g., gonadotropin-releasing hormone [GnRH] analog, spironolactone). Clinically referred adolescents often want hormone treatment and many also wish for gender reassignment surgery. Adolescents living in an accepting environment may openly express the desire to be and be treated as the experienced gender and dress partly or completely as the experienced gender, have a hairstyle typical of the experienced gender, preferentially seek friendships with peers of the other gender, and/or adopt a new first name consistent with the experienced gender. Older adolescents, when sexually active, usually do not show or allow partners to touch their sexual organs. For adults with an aversion toward their genitals, sexual activity is constrained by the preference that their genitals not be seen or touched by their partners. Some adults may seek hormone treatment (sometimes without medical prescription and supervision) and gender reassignment surgery. Others are satisfied with either hormone treatment or surgery alone.

Adolescents and adults with gender dysphoria before gender reassignment are at increased risk for suicidal ideation, suicide attempts, and suicides. After gender reassignment, adjustment may vary, and suicide risk may persist.

Prevalence

For natal adult males, prevalence ranges from 0.005% to 0.014%, and for natal females, from 0.002% to 0.003%. Since not all adults seeking hormone treatment and surgical reassignment attend specialty clinics, these rates are likely modest underestimates. Sex differences in rate of referrals to specialty clinics vary by age group. In children, sex ratios of natal boys to girls range from 2:1 to 4.5:1. In adolescents, the sex ratio is close to parity; in adults, the sex ratio favors natal males, with ratios ranging from 1:1 to 6.1:1. In two countries, the sex ratio appears to favor natal females (Japan: 2.2:1; Poland: 3.4:1).

Development and Course

Because expression of gender dysphoria varies with age, there are separate criteria sets for children versus adolescents and adults. Criteria for children are defined in a more con-

crete, behavioral manner than those for adolescents and adults. Many of the core criteria draw on well-documented behavioral gender differences between typically developing boys and girls. Young children are less likely than older children, adolescents, and adults to express extreme and persistent anatomic dysphoria. In adolescents and adults, incongruence between experienced gender and somatic sex is a central feature of the diagnosis. Factors related to distress and impairment also vary with age. A very young child may show signs of distress (e.g., intense crying) only when parents tell the child that he or she is "really" not a member of the other gender but only "desires" to be. Distress may not be manifest in social environments supportive of the child's desire to live in the role of the other gender and may emerge only if the desire is interfered with. In adolescents and adults, distress may manifest because of strong incongruence between experienced gender and somatic sex. Such distress may, however, be mitigated by supportive environments and knowledge that biomedical treatments exist to reduce incongruence. Impairment (e.g., school refusal, development of depression, anxiety, and substance abuse) may be a consequence of gender dysphoria.

Gender dysphoria without a disorder of sex development. For clinic-referred children, onset of cross-gender behaviors is usually between ages 2 and 4 years. This corresponds to the developmental time period in which most typically developing children begin expressing gendered behaviors and interests. For some preschool-age children, both pervasive cross-gender behaviors and the expressed desire to be the other gender may be present, or, more rarely, labeling oneself as a member of the other gender may occur. In some cases, the expressed desire to be the other gender appears later, usually at entry into elementary school. A small minority of children express discomfort with their sexual anatomy or will state the desire to have a sexual anatomy corresponding to the experienced gender ("anatomic dysphoria"). Expressions of anatomic dysphoria become more common as children with gender dysphoria approach and anticipate puberty.

Rates of persistence of gender dysphoria from childhood into adolescence or adulthood vary. In natal males, persistence has ranged from 2.2% to 30%. In natal females, persistence has ranged from 12% to 50%. Persistence of gender dysphoria is modestly correlated with dimensional measures of severity ascertained at the time of a childhood baseline assessment. In one sample of natal males, lower socioeconomic background was also modestly correlated with persistence. It is unclear if particular therapeutic approaches to gender dysphoria in children are related to rates of long-term persistence. Extant follow-up samples consisted of children receiving no formal therapeutic intervention or receiving therapeutic interventions of various types, ranging from active efforts to reduce gender dysphoria to a more neutral, "watchful waiting" approach. It is unclear if children "encouraged" or supported to live socially in the desired gender will show higher rates of persistence, since such children have not yet been followed longitudinally in a systematic manner. For both natal male and female children showing persistence, almost all are sexually attracted to individuals of their natal sex. For natal male children whose gender dysphoria does not persist, the majority are *androphilic* (sexually attracted to males) and often self-identify as gay or homosexual (ranging from 63% to 100%). In natal female children whose gender dysphoria does not persist, the percentage who are *gynephilic* (sexually attracted to females) and self-identify as lesbian is lower (ranging from 32% to 50%).

In both adolescent and adult natal males, there are two broad trajectories for development of gender dysphoria: early onset and late onset. *Early-onset gender dysphoria* starts in childhood and continues into adolescence and adulthood; or, there is an intermittent period in which the gender dysphoria desists and these individuals self-identify as gay or homosexual, followed by recurrence of gender dysphoria. *Late-onset gender dysphoria* occurs around puberty or much later in life. Some of these individuals report having had a desire to be of the other gender in childhood that was not expressed verbally to others. Others do not recall any signs of childhood gender dysphoria. For adolescent males with late-onset gender dysphoria, parents often report surprise because they did not see signs of gender

dysphoria during childhood. Expressions of anatomic dysphoria are more common and salient in adolescents and adults once secondary sex characteristics have developed.

Adolescent and adult natal males with early-onset gender dysphoria are almost always sexually attracted to men (androphilic). Adolescents and adults with late-onset gender dysphoria frequently engage in transvestic behavior with sexual excitement. The majority of these individuals are gynephilic or sexually attracted to other posttransition natal males with late-onset gender dysphoria. A substantial percentage of adult males with late-onset gender dysphoria cohabit with or are married to natal females. After gender transition, many self-identify as lesbian. Among adult natal males with gender dysphoria, the early-onset group seeks out clinical care for hormone treatment and reassignment surgery at an earlier age than does the late-onset group. The late-onset group may have more fluctuations in the degree of gender dysphoria and be more ambivalent about and less likely satisfied after gender reassignment surgery.

In both adolescent and adult natal females, the most common course is the early-onset form of gender dysphoria. The late-onset form is much less common in natal females compared with natal males. As in natal males with gender dysphoria, there may have been a period in which the gender dysphoria desisted and these individuals self-identified as lesbian; however, with recurrence of gender dysphoria, clinical consultation is sought, often with the desire for hormone treatment and reassignment surgery. Parents of natal adolescent females with the late-onset form also report surprise, as no signs of childhood gender dysphoria were evident. Expressions of anatomic dysphoria are much more common and salient in adolescents and adults than in children.

Adolescent and adult natal females with early-onset gender dysphoria are almost always gynephilic. Adolescents and adults with the late-onset form of gender dysphoria are usually androphilic and after gender transition self-identify as gay men. Natal females with the late-onset form do not have co-occurring transvestic behavior with sexual excitement.

Gender dysphoria in association with a disorder of sex development. Most individuals with a disorder of sex development who develop gender dysphoria have already come to medical attention at an early age. For many, starting at birth, issues of gender assignment were raised by physicians and parents. Moreover, as infertility is quite common for this group, physicians are more willing to perform cross-sex hormone treatments and genital surgery before adulthood.

Disorders of sex development in general are frequently associated with gender-atypical behavior starting in early childhood. However, in the majority of cases, this does not lead to gender dysphoria. As individuals with a disorder of sex development become aware of their medical history and condition, many experience uncertainty about their gender, as opposed to developing a firm conviction that they are another gender. However, most do not progress to gender transition. Gender dysphoria and gender transition may vary considerably as a function of a disorder of sex development, its severity, and assigned gender.

Risk and Prognostic Factors

Temperamental. For individuals with gender dysphoria without a disorder of sex development, atypical gender behavior among individuals with early-onset gender dysphoria develops in early preschool age, and it is possible that a high degree of atypicality makes the development of gender dysphoria and its persistence into adolescence and adulthood more likely.

Environmental. Among individuals with gender dysphoria without a disorder of sex development, males with gender dysphoria (in both childhood and adolescence) more commonly have older brothers than do males without the condition. Additional predisposing

factors under consideration, especially in individuals with late-onset gender dysphoria (adolescence, adulthood), include habitual fetishistic transvestism developing into autogynephilia (i.e., sexual arousal associated with the thought or image of oneself as a woman) and other forms of more general social, psychological, or developmental problems.

Genetic and physiological. For individuals with gender dysphoria without a disorder of sex development, some genetic contribution is suggested by evidence for (weak) familiality of transsexualism among nontwin siblings, increased concordance for transsexualism in monozygotic compared with dizygotic same-sex twins, and some degree of heritability of gender dysphoria. As to endocrine findings, no endogenous systemic abnormalities in sex-hormone levels have been found in 46,XY individuals, whereas there appear to be increased androgen levels (in the range found in hirsute women but far below normal male levels) in 46,XX individuals. Overall, current evidence is insufficient to label gender dysphoria without a disorder of sex development as a form of intersexuality limited to the central nervous system.

In gender dysphoria associated with a disorder of sex development, the likelihood of later gender dysphoria is increased if prenatal production and utilization (via receptor sensitivity) of androgens are grossly atypical relative to what is usually seen in individuals with the same assigned gender. Examples include 46,XY individuals with a history of normal male prenatal hormone milieu but inborn nonhormonal genital defects (as in cloacal bladder exstrophy or penile agenesis) and who have been assigned to the female gender. The likelihood of gender dysphoria is further enhanced by additional, prolonged, highly gender-atypical postnatal androgen exposure with somatic virilization as may occur in female-raised and noncastrated 46,XY individuals with 5-alpha reductase-2 deficiency or 17-beta-hydroxysteroid dehydrogenase-3 deficiency or in female-raised 46,XX individuals with classical congenital adrenal hyperplasia with prolonged periods of non-adherence to glucocorticoid replacement therapy. However, the prenatal androgen milieu is more closely related to gendered behavior than to gender identity. Many individuals with disorders of sex development and markedly gender-atypical behavior do not develop gender dysphoria. Thus, gender-atypical behavior by itself should not be interpreted as an indicator of current or future gender dysphoria. There appears to be a higher rate of gender dysphoria and patient-initiated gender change from assigned female to male than from assigned male to female in 46,XY individuals with a disorder of sex development.

Culture-Related Diagnostic Issues

Individuals with gender dysphoria have been reported across many countries and cultures. The equivalent of gender dysphoria has also been reported in individuals living in cultures with institutionalized gender categories other than male or female. It is unclear whether with these individuals the diagnostic criteria for gender dysphoria would be met.

Diagnostic Markers

Individuals with a somatic disorder of sex development show some correlation of final gender identity outcome with the degree of prenatal androgen production and utilization. However, the correlation is not robust enough for the biological factor, where ascertainable, to replace a detailed and comprehensive diagnostic interview evaluation for gender dysphoria.

Functional Consequences of Gender Dysphoria

Preoccupation with cross-gender wishes may develop at all ages after the first 2–3 years of childhood and often interfere with daily activities. In older children, failure to develop age-typical same-sex peer relationships and skills may lead to isolation from peer groups and to distress. Some children may refuse to attend school because of teasing and harass-

ment or pressure to dress in attire associated with their assigned sex. Also in adolescents and adults, preoccupation with cross-gender wishes often interferes with daily activities. Relationship difficulties, including sexual relationship problems, are common, and functioning at school or at work may be impaired. Gender dysphoria, along with atypical gender expression, is associated with high levels of stigmatization, discrimination, and victimization, leading to negative self-concept, increased rates of mental disorder comorbidity, school dropout, and economic marginalization, including unemployment, with attendant social and mental health risks, especially in individuals from resource-poor family backgrounds. In addition, these individuals' access to health services and mental health services may be impeded by structural barriers, such as institutional discomfort or inexperience in working with this patient population.

Differential Diagnosis

Nonconformity to gender roles. Gender dysphoria should be distinguished from simple nonconformity to stereotypical gender role behavior by the strong desire to be of another gender than the assigned one and by the extent and pervasiveness of gender-variant activities and interests. The diagnosis is not meant to merely describe nonconformity to stereotypical gender role behavior (e.g., "tomboyism" in girls, "girly-boy" behavior in boys, occasional cross-dressing in adult men). Given the increased openness of atypical gender expressions by individuals across the entire range of the transgender spectrum, it is important that the clinical diagnosis be limited to those individuals whose distress and impairment meet the specified criteria.

Transvestic disorder. Transvestic disorder occurs in heterosexual (or bisexual) adolescent and adult males (rarely in females) for whom cross-dressing behavior generates sexual excitement and causes distress and/or impairment without drawing their primary gender into qūestion. It is occasionally accompanied by gender dysphoria. An individual with transvestic disorder who also has clinically significant gender dysphoria can be given both diagnoses. In many cases of late-onset gender dysphoria in gynephilic natal males, transvestic behavior with sexual excitement is a precursor.

Body dysmorphic disorder. An individual with body dysmorphic disorder focuses on the alteration or removal of a specific body part because it is perceived as abnormally formed, not because it represents a repudiated assigned gender. When an individual's presentation meets criteria for both gender dysphoria and body dysmorphic disorder, both diagnoses can be given. Individuals wishing to have a healthy limb amputated (termed by some *body integrity identity disorder*) because it makes them feel more "complete" usually do not wish to change gender, but rather desire to live as an amputee or a disabled person.

Schizophrenia and other psychotic disorders. In schizophrenia, there may rarely be delusions of belonging to some other gender. In the absence of psychotic symptoms, insistence by an individual with gender dysphoria that he or she is of some other gender is not considered a delusion. Schizophrenia (or other psychotic disorders) and gender dysphoria may co-occur.

Other clinical presentations. Some individuals with an emasculinization desire who develop an alternative, nonmale/nonfemale gender identity do have a presentation that meets criteria for gender dysphoria. However, some males seek castration and/or penectomy for aesthetic reasons or to remove psychological effects of androgens without changing male identity; in these cases, the criteria for gender dysphoria are not met.

Comorbidity

Clinically referred children with gender dysphoria show elevated levels of emotional and behavioral problems—most commonly, anxiety, disruptive and impulse-control, and de-

pressive disorders. In prepubertal children, increasing age is associated with having more behavioral or emotional problems; this is related to the increasing non-acceptance of gender-variant behavior by others. In older children, gender-variant behavior often leads to peer ostracism, which may lead to more behavioral problems. The prevalence of mental health problems differs among cultures; these differences may also be related to differences in attitudes toward gender variance in children. However, also in some non-Western cultures, anxiety has been found to be relatively common in individuals with gender dysphoria, even in cultures with accepting attitudes toward gender-variant behavior. Autism spectrum disorder is more prevalent in clinically referred children with gender dysphoria than in the general population. Clinically referred adolescents with gender dysphoria appear to have comorbid mental disorders, with anxiety and depressive disorders being the most common. As in children, autism spectrum disorder is more prevalent in clinically referred adolescents with gender dysphoria than in the general population. Clinically referred adults with gender dysphoria may have coexisting mental health problems, most commonly anxiety and depressive disorders.

Other Specified Gender Dysphoria

302.6 (F64.8)

This category applies to presentations in which symptoms characteristic of gender dysphoria that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for gender dysphoria. The other specified gender dysphoria category is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for gender dysphoria. This is done by recording "other specified gender dysphoria" followed by the specific reason (e.g., "brief gender dysphoria").

An example of a presentation that can be specified using the "other specified" designation is the following:

The current disturbance meets symptom criteria for gender dysphoria, but the duration is less than 6 months.

Unspecified Gender Dysphoria

302.6 (F64.9)

This category applies to presentations in which symptoms characteristic of gender dysphoria that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for gender dysphoria. The unspecified gender dysphoria category is used in situations in which the clinician chooses *not* to specify the reason that the criteria are not met for gender dysphoria, and includes presentations in which there is insufficient information to make a more specific diagnosis.

DEFENDANT'S EXHIBIT 18

WPATH WORLD PROFESSIONAL ASSOCIATION for TRANSGENDER HEALTH

www.wpath.org

Standards of Care

for the Health of Transsexual, Transgender, and Gender-Nonconforming People

The World Professional Association for Transgender Health

Version 7

WPATH WORLD PROFESSIONAL ASSOCIATION for TRANSGENDER HEALTH

Standards of Care

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Table of Contents

Purpose and Use of the *Standards of Care*

The World Professional Association for Transgender Health (WPATH)[I] is an international, multidisciplinary, professional association whose mission is to promote evidence-based care, education, research, advocacy, public policy, and respect in transsexual and transgender health. The vision of WPATH is a world wherein transsexual, transgender, and gender-nonconforming people benefit from access to evidence-based health care, social services, justice, and equality.

One of the main functions of WPATH is to promote the highest standards of health care for individuals through the articulation of *Standards of Care (SOC) for the Health of Transsexual, Transgender, and Gender Nonconforming People*. The *SOC* are based on the best available science and expert professional consensus.[II] Most of the research and experience in this field comes from a North American and Western European perspective; thus, adaptations of the *SOC* to other parts of the world are necessary. Suggestions for ways of thinking about cultural relativity and cultural competence are included in this version of the *SOC*.

The overall goal of the *SOC* is to provide clinical guidance for health professionals to assist transsexual, transgender, and gender-nonconforming people with safe and effective pathways to achieving lasting personal comfort with their gendered selves, in order to maximize their overall health, psychological well-being, and self-fulfillment. This assistance may include primary care, gynecologic and urologic care, reproductive options, voice and communication therapy, mental health services (e.g., assessment, counseling, psychotherapy), and hormonal and surgical treatments. While this is primarily a document for health professionals, the *SOC* may also be used by individuals, their families, and social institutions to understand how they can assist with promoting optimal health for members of this diverse population.

WPATH recognizes that health is dependent upon not only good clinical care but also social and political climates that provide and ensure social tolerance, equality, and the full rights of citizenship. Health is promoted through public policies and legal reforms that promote tolerance and equity

I Formerly the Harry Benjamin International Gender Dysphoria Association

II The *Standards of Care (SOC), Version 7*, represents a significant departure from previous versions. Changes in this version are based upon significant cultural shifts, advances in clinical knowledge, and appreciation of the many health care issues that can arise for transsexual, transgender, and gender-nonconforming people beyond hormone therapy and surgery (Coleman, 2009a, b, c, d).

for gender and sexual diversity and that eliminate prejudice, discrimination, and stigma. WPATH is committed to advocacy for these changes in public policies and legal reforms.

The *Standards of Care* Are Flexible Clinical Guidelines

The *SOC* are intended to be flexible in order to meet the diverse health care needs of transsexual, transgender, and gender-nonconforming people. While flexible, they offer standards for promoting optimal health care and guiding the treatment of people experiencing gender dysphoria—broadly defined as discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics) (Fisk, 1974; Knudson, De Cuypere, & Bockting, 2010b).

As in all previous versions of the *SOC*, the criteria put forth in this document for hormone therapy and surgical treatments for gender dysphoria are clinical guidelines; individual health professionals and programs may modify them. Clinical departures from the *SOC* may come about because of a patient's unique anatomic, social, or psychological situation; an experienced health professional's evolving method of handling a common situation; a research protocol; lack of resources in various parts of the world; or the need for specific harm-reduction strategies. These departures should be recognized as such, explained to the patient, and documented through informed consent for quality patient care and legal protection. This documentation is also valuable for the accumulation of new data, which can be retrospectively examined to allow for health care—and the *SOC*—to evolve.

The *SOC* articulate standards of care but also acknowledge the role of making informed choices and the value of harm-reduction approaches. In addition, this version of the *SOC* recognizes and validates various expressions of gender that may not necessitate psychological, hormonal, or surgical treatments. Some patients who present for care will have made significant self-directed progress towards gender role changes, transition, or other resolutions regarding their gender identity or gender dysphoria. Other patients will require more intensive services. Health professionals can use the *SOC* to help patients consider the full range of health services open to them, in accordance with their clinical needs and goals for gender expression.

Global Applicability of the *Standards of Care*

While the *SOC* are intended for worldwide use, WPATH acknowledges that much of the recorded clinical experience and knowledge in this area of health care is derived from North American and Western European sources. From place to place, both across and within nations, there are differences in all of the following: social attitudes towards transsexual, transgender, and gender-nonconforming people; constructions of gender roles and identities; language used to describe different gender identities; epidemiology of gender dysphoria; access to and cost of treatment; therapies offered; number and type of professionals who provide care; and legal and policy issues related to this area of health care (Winter, 2009).

It is impossible for the *SOC* to reflect all of these differences. In applying these standards to other cultural contexts, health professionals must be sensitive to these differences and adapt the *SOC* according to local realities. For example, in a number of cultures, gender-nonconforming people are found in such numbers and living in such ways as to make them highly socially visible (Peletz, 2006). In settings such as these, it is common for people to initiate a change in their gender expression and physical characteristics while in their teens or even earlier. Many grow up and live in a social, cultural, and even linguistic context quite unlike that of Western cultures. Yet almost all experience prejudice (Peletz, 2006; Winter, 2009). In many cultures, social stigma towards gender nonconformity is widespread and gender roles are highly prescriptive (Winter et al., 2009). Gender-nonconforming people in these settings are forced to be hidden and, therefore, may lack opportunities for adequate health care (Winter, 2009).

The *SOC* are not intended to limit efforts to provide the best available care to all individuals. Health professionals throughout the world—even in areas with limited resources and training opportunities—can apply the many core principles that undergird the *SOC*. These principles include the following: Exhibit respect for patients with nonconforming gender identities (do not pathologize differences in gender identity or expression); provide care (or refer to knowledgeable colleagues) that affirms patients' gender identities and reduces the distress of gender dysphoria, when present; become knowledgeable about the health care needs of transsexual, transgender, and gender-nonconforming people, including the benefits and risks of treatment options for gender dysphoria; match the treatment approach to the specific needs of patients, particularly their goals for gender expression and need for relief from gender dysphoria; facilitate access to appropriate care; seek patients' informed consent before providing treatment; offer continuity of care; and be prepared to support and advocate for patients within their families and communities (schools, workplaces, and other settings).

Terminology is culture- and time-dependent and is rapidly evolving. It is important to use respectful language in different places and times, and among different people. As the *SOC* are translated into other languages, great care must be taken to ensure that the meanings of terms are accurately translated. Terminology in English may not be easily translated into other languages, and vice versa. Some languages do not have equivalent words to describe the various terms within this document; hence, translators should be cognizant of the underlying goals of treatment and articulate culturally applicable guidance for reaching those goals.

The Difference Between Gender Nonconformity and Gender Dysphoria

Being Transsexual, Transgender, or Gender-Nonconforming Is a Matter of Diversity, Not Pathology

WPATH released a statement in May 2010 urging the de-psychopathologization of gender nonconformity worldwide (WPATH Board of Directors, 2010). This statement noted that "the expression of gender characteristics, including identities, that are not stereotypically associated with one's assigned sex at birth is a common and culturally diverse human phenomenon [that] should not be judged as inherently pathological or negative."

Unfortunately, there is stigma attached to gender nonconformity in many societies around the world. Such stigma can lead to prejudice and discrimination, resulting in "minority stress" (I. H. Meyer, 2003). Minority stress is unique (additive to general stressors experienced by all people), socially based, and chronic, and may make transsexual, transgender, and gender-nonconforming individuals more vulnerable to developing mental health concerns such as anxiety and depression (Institute of Medicine, 2011). In addition to prejudice and discrimination in society at large, stigma can contribute to abuse and neglect in one's relationships with peers and family members, which in turn can lead to psychological distress. However, these symptoms are socially induced and are not inherent to being transsexual, transgender, or gender-nonconforming.

Gender Nonconformity Is Not the Same as Gender Dysphoria

Gender nonconformity refers to the extent to which a person's gender identity, role, or expression differs from the cultural norms prescribed for people of a particular sex (Institute of Medicine, 2011). *Gender dysphoria* refers to discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics) (Fisk, 1974; Knudson, De Cuypere, & Bockting, 2010b). Only *some* gender-nonconforming people experience gender dysphoria at *some* point in their lives.

Treatment is available to assist people with such distress to explore their gender identity and find a gender role that is comfortable for them (Bockting & Goldberg, 2006). Treatment is individualized: What helps one person alleviate gender dysphoria might be very different from what helps another person. This process may or may not involve a change in gender expression or body modifications. Medical treatment options include, for example, feminization or masculinization of the body through hormone therapy and/or surgery, which are effective in alleviating gender dysphoria and are medically necessary for many people. Gender identities and expressions are diverse, and hormones and surgery are just two of many options available to assist people with achieving comfort with self and identity.

Gender dysphoria can in large part be alleviated through treatment (Murad et al., 2010). Hence, while transsexual, transgender, and gender-nonconforming people may experience gender dysphoria at some points in their lives, many individuals who receive treatment will find a gender role and expression that is comfortable for them, even if these differ from those associated with their sex assigned at birth, or from prevailing gender norms and expectations.

Diagnoses Related to Gender Dysphoria

Some people experience gender dysphoria at such a level that the distress meets criteria for a formal diagnosis that might be classified as a mental disorder. Such a diagnosis is not a license for stigmatization or for the deprivation of civil and human rights. Existing classification systems such as the *Diagnostic Statistical Manual of Mental Disorders (DSM)* (American Psychiatric Association, 2000) and the *International Classification of Diseases* (*ICD*) (World Health Organization, 2007) define hundreds of mental disorders that vary in onset, duration, pathogenesis, functional disability, and treatability. All of these systems attempt to classify clusters of symptoms and conditions, not the individuals themselves. A disorder is a description of something with which a person might struggle, not a description of the person or the person's identity.

Thus, transsexual, transgender, and gender-nonconforming individuals are not inherently disordered. Rather, the distress of gender dysphoria, when present, is the concern that might be diagnosable and for which various treatment options are available. The existence of a diagnosis for such dysphoria often facilitates access to health care and can guide further research into effective treatments.

Research is leading to new diagnostic nomenclatures, and terms are changing in both the *DSM* (Cohen-Kettenis & Pfäfflin, 2010; Knudson, De Cuypere, & Bockting, 2010b; Meyer-Bahlburg, 2010; Zucker, 2010) and the *ICD*. For this reason, familiar terms are employed in the *SOC* and definitions are provided for terms that may be emerging. Health professionals should refer to the most current diagnostic criteria and appropriate codes to apply in their practice areas.

IV
Epidemiologic Considerations

Formal epidemiologic studies on the incidence[III] and prevalence[IV] of transsexualism specifically or transgender and gender-nonconforming identities in general have not been conducted, and efforts to achieve realistic estimates are fraught with enormous difficulties (Institute of Medicine, 2011; Zucker & Lawrence, 2009). Even if epidemiologic studies established that a similar proportion of transsexual, transgender, or gender-nonconforming people existed all over the world, it is likely that cultural differences from one country to another would alter both the behavioral expressions of different gender identities and the extent to which gender dysphoria—distinct from one's gender identity—is actually occurring in a population. While in most countries, crossing normative gender boundaries generates moral censure rather than compassion, there are examples in certain cultures of gender-nonconforming behaviors (e.g., in spiritual leaders) that are less stigmatized and even revered (Besnier, 1994; Bolin, 1988; Chiñas, 1995; Coleman, Colgan, & Gooren, 1992; Costa & Matzner, 2007; Jackson & Sullivan, 1999; Nanda, 1998; Taywaditep, Coleman, & Dumronggittigule, 1997).

For various reasons, researchers who have studied incidence and prevalence have tended to focus on the most easily counted subgroup of gender-nonconforming individuals: transsexual individuals who experience gender dysphoria and who present for gender-transition-related care at specialist gender clinics (Zucker & Lawrence, 2009). Most studies have been conducted in European countries such as Sweden (Wålinder, 1968, 1971), the United Kingdom (Hoenig & Kenna, 1974),

III **incidence**—the number of new cases arising in a given period (e.g., a year)
IV **prevalence**—the number of individuals having a condition, divided by the number of people in the general population

the Netherlands (Bakker, Van Kesteren, Gooren, & Bezemer, 1993; Eklund, Gooren, & Bezemer, 1988; van Kesteren, Gooren, & Megens, 1996), Germany (Weitze & Osburg, 1996), and Belgium (De Cuypere et al., 2007). One was conducted in Singapore (Tsoi, 1988).

De Cuypere and colleagues (2007) reviewed such studies, as well as conducted their own. Together, those studies span 39 years. Leaving aside two outlier findings from Pauly in 1965 and Tsoi in 1988, ten studies involving eight countries remain. The prevalence figures reported in these ten studies range from 1:11,900 to 1:45,000 for male-to-female individuals (MtF) and 1:30,400 to 1:200,000 for female-to-male (FtM) individuals. Some scholars have suggested that the prevalence is much higher, depending on the methodology used in the research (e.g., Olyslager & Conway, 2007).

Direct comparisons across studies are impossible, as each differed in their data collection methods and in their criteria for documenting a person as transsexual (e.g., whether or not a person had undergone genital reconstruction, versus had initiated hormone therapy, versus had come to the clinic seeking medically supervised transition services). The trend appears to be towards higher prevalence rates in the more recent studies, possibly indicating increasing numbers of people seeking clinical care. Support for this interpretation comes from research by Reed and colleagues (2009), who reported a doubling of the numbers of people accessing care at gender clinics in the United Kingdom every five or six years. Similarly, Zucker and colleagues (2008) reported a four- to five-fold increase in child and adolescent referrals to their Toronto, Canada clinic over a 30-year period.

The numbers yielded by studies such as these can be considered minimum estimates at best. The published figures are mostly derived from clinics where patients met criteria for severe gender dysphoria and had access to health care at those clinics. These estimates do not take into account that treatments offered in a particular clinic setting might not be perceived as affordable, useful, or acceptable by all self-identified gender dysphoric individuals in a given area. By counting only those people who present at clinics for a specific type of treatment, an unspecified number of gender dysphoric individuals are overlooked.

Other clinical observations (not yet firmly supported by systematic study) support the likelihood of a higher prevalence of gender dysphoria: (i) Previously unrecognized gender dysphoria is occasionally diagnosed when patients are seen with anxiety, depression, conduct disorder, substance abuse, dissociative identity disorders, borderline personality disorder, sexual disorders, and disorders of sex development (Cole, O'Boyle, Emory, & Meyer III, 1997). (ii) Some crossdressers, drag queens/kings or female/male impersonators, and gay and lesbian individuals may be experiencing gender dysphoria (Bullough & Bullough, 1993). (iii) The intensity of some people's gender dysphoria fluctuates below and above a clinical threshold (Docter, 1988). (iv) Gender nonconformity among FtM individuals tends to be relatively invisible in many cultures, particularly to Western health

professionals and researchers who have conducted most of the studies on which the current estimates of prevalence and incidence are based (Winter, 2009).

Overall, the existing data should be considered a starting point, and health care would benefit from more rigorous epidemiologic study in different locations worldwide.

V

Overview of Therapeutic Approaches for Gender Dysphoria

Advancements in the Knowledge and Treatment of Gender Dysphoria

In the second half of the 20th century, awareness of the phenomenon of gender dysphoria increased when health professionals began to provide assistance to alleviate gender dysphoria by supporting changes in primary and secondary sex characteristics through hormone therapy and surgery, along with a change in gender role. Although Harry Benjamin already acknowledged a spectrum of gender nonconformity (Benjamin, 1966), the initial clinical approach largely focused on identifying who was an appropriate candidate for sex reassignment to facilitate a physical change from male to female or female to male as completely as possible (e.g., Green & Fleming, 1990; Hastings, 1974). This approach was extensively evaluated and proved to be highly effective. Satisfaction rates across studies ranged from 87% of MtF patients to 97% of FtM patients (Green & Fleming, 1990), and regrets were extremely rare (1–1.5% of MtF patients and <1% of FtM patients; Pfäfflin, 1993). Indeed, hormone therapy and surgery have been found to be medically necessary to alleviate gender dysphoria in many people (American Medical Association, 2008; Anton, 2009; World Professional Association for Transgender Health, 2008).

As the field matured, health professionals recognized that while many individuals need both hormone therapy and surgery to alleviate their gender dysphoria, others need only one of these treatment options and some need neither (Bockting & Goldberg, 2006; Bockting, 2008; Lev, 2004). Often with the help of psychotherapy, some individuals integrate their trans- or cross-gender feelings into the gender role they were assigned at birth and do not feel the need to feminize or masculinize their body. For others, changes in gender role and expression are sufficient to alleviate

gender dysphoria. Some patients may need hormones, a possible change in gender role, but not surgery; others may need a change in gender role along with surgery, but not hormones. In other words, treatment for gender dysphoria has become more individualized.

As a generation of transsexual, transgender, and gender-nonconforming individuals has come of age—many of whom have benefitted from different therapeutic approaches—they have become more visible as a community and demonstrated considerable diversity in their gender identities, roles, and expressions. Some individuals describe themselves not as gender-nonconforming but as unambiguously cross-sexed (i.e., as a member of the other sex; Bockting, 2008). Other individuals affirm their unique gender identity and no longer consider themselves to be either male or female (Bornstein, 1994; Kimberly, 1997; Stone, 1991; Warren, 1993). Instead, they may describe their gender identity in specific terms such as transgender, bigender, or genderqueer, affirming their unique experiences that may transcend a male/female binary understanding of gender (Bockting, 2008; Ekins & King, 2006; Nestle, Wilchins, & Howell, 2002). They may not experience their process of identity affirmation as a "transition," because they never fully embraced the gender role they were assigned at birth or because they actualize their gender identity, role, and expression in a way that does not involve a change from one gender role to another. For example, some youth identifying as genderqueer have always experienced their gender identity and role as such (genderqueer). Greater public visibility and awareness of gender diversity (Feinberg, 1996) has further expanded options for people with gender dysphoria to actualize an identity and find a gender role and expression that are comfortable for them.

Health professionals can assist gender dysphoric individuals with affirming their gender identity, exploring different options for expression of that identity, and making decisions about medical treatment options for alleviating gender dysphoria.

Options for Psychological and Medical Treatment of Gender Dysphoria

For individuals seeking care for gender dysphoria, a variety of therapeutic options can be considered. The number and type of interventions applied and the order in which these take place may differ from person to person (e.g., Bockting, Knudson, & Goldberg, 2006; Bolin, 1994; Rachlin, 1999; Rachlin, Green, & Lombardi, 2008; Rachlin, Hansbury, & Pardo, 2010). Treatment options include the following:

- Changes in gender expression and role (which may involve living part time or full time in another gender role, consistent with one's gender identity);
- Hormone therapy to feminize or masculinize the body;

- Surgery to change primary and/or secondary sex characteristics (e.g., breasts/chest, external and/or internal genitalia, facial features, body contouring);
- Psychotherapy (individual, couple, family, or group) for purposes such as exploring gender identity, role, and expression; addressing the negative impact of gender dysphoria and stigma on mental health; alleviating internalized transphobia; enhancing social and peer support; improving body image; or promoting resilience.

Options for Social Support and Changes in Gender Expression

In addition (or as an alternative) to the psychological- and medical-treatment options described above, other options can be considered to help alleviate gender dysphoria, for example:

- In-person and online peer support resources, groups, or community organizations that provide avenues for social support and advocacy;
- In-person and online support resources for families and friends;
- Voice and communication therapy to help individuals develop verbal and non-verbal communication skills that facilitate comfort with their gender identity;
- Hair removal through electrolysis, laser treatment, or waxing;
- Breast binding or padding, genital tucking or penile prostheses, padding of hips or buttocks;
- Changes in name and gender marker on identity documents.

VI

Assessment and Treatment of Children and Adolescents With Gender Dysphoria

There are a number of differences in the phenomenology, developmental course, and treatment approaches for gender dysphoria in children, adolescents, and adults. In children and adolescents, a rapid and dramatic developmental process (physical, psychological, and sexual) is involved and

there is greater fluidity and variability in outcomes, particularly in prepubertal children. Accordingly, this section of the *SOC* offers specific clinical guidelines for the assessment and treatment of gender dysphoric children and adolescents.

Differences Between Children and Adolescents with Gender Dysphoria

An important difference between gender dysphoric children and adolescents is in the proportion for whom dysphoria persists into adulthood. Gender dysphoria during childhood does not inevitably continue into adulthood.[V] Rather, in follow-up studies of prepubertal children (mainly boys) who were referred to clinics for assessment of gender dysphoria, the dysphoria persisted into adulthood for only 6–23% of children (Cohen-Kettenis, 2001; Zucker & Bradley, 1995). Boys in these studies were more likely to identify as gay in adulthood than as transgender (Green, 1987; Money & Russo, 1979; Zucker & Bradley, 1995; Zuger, 1984). Newer studies, also including girls, showed a 12–27% persistence rate of gender dysphoria into adulthood (Drummond, Bradley, Peterson-Badali, & Zucker, 2008; Wallien & Cohen-Kettenis, 2008).

In contrast, the persistence of gender dysphoria into adulthood appears to be much higher for adolescents. No formal prospective studies exist. However, in a follow-up study of 70 adolescents who were diagnosed with gender dysphoria and given puberty-suppressing hormones, all continued with actual sex reassignment, beginning with feminizing/masculinizing hormone therapy (de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2010).

Another difference between gender dysphoric children and adolescents is in the sex ratios for each age group. In clinically referred, gender dysphoric children under age 12, the male/female ratio ranges from 6:1 to 3:1 (Zucker, 2004). In clinically referred, gender dysphoric adolescents older than age 12, the male/female ratio is close to 1:1 (Cohen-Kettenis & Pfäfflin, 2003).

As discussed in section IV and by Zucker and Lawrence (2009), formal epidemiologic studies on gender dysphoria—in children, adolescents, and adults—are lacking. Additional research is needed to refine estimates of its prevalence and persistence in different populations worldwide.

V Gender-nonconforming behaviors in children may continue into adulthood, but such behaviors are not necessarily indicative of gender dysphoria and a need for treatment. As described in section III, gender dysphoria is not synonymous with diversity in gender expression.

Phenomenology in Children

Children as young as age two may show features that could indicate gender dysphoria. They may express a wish to be of the other sex and be unhappy about their physical sex characteristics and functions. In addition, they may prefer clothes, toys, and games that are commonly associated with the other sex and prefer playing with other-sex peers. There appears to be heterogeneity in these features: Some children demonstrate extremely gender-nonconforming behavior and wishes, accompanied by persistent and severe discomfort with their primary sex characteristics. In other children, these characteristics are less intense or only partially present (Cohen-Kettenis et al., 2006; Knudson, De Cuypere, & Bockting, 2010a).

It is relatively common for gender dysphoric children to have coexisting internalizing disorders such as anxiety and depression (Cohen-Kettenis, Owen, Kaijser, Bradley, & Zucker, 2003; Wallien, Swaab, & Cohen-Kettenis, 2007; Zucker, Owen, Bradley, & Ameeriar, 2002). The prevalence of autism spectrum disorders seems to be higher in clinically referred, gender dysphoric children than in the general population (de Vries, Noens, Cohen-Kettenis, van Berckelaer-Onnes, & Doreleijers, 2010).

Phenomenology in Adolescents

In most children, gender dysphoria will disappear before, or early in, puberty. However, in some children these feelings will intensify and body aversion will develop or increase as they become adolescents and their secondary sex characteristics develop (Cohen-Kettenis, 2001; Cohen-Kettenis & Pfäfflin, 2003; Drummond et al., 2008; Wallien & Cohen-Kettenis, 2008; Zucker & Bradley, 1995). Data from one study suggest that more extreme gender nonconformity in childhood is associated with persistence of gender dysphoria into late adolescence and early adulthood (Wallien & Cohen-Kettenis, 2008). Yet many adolescents and adults presenting with gender dysphoria do not report a history of childhood gender-nonconforming behaviors (Docter, 1988; Landén, Wålinder, & Lundström, 1998). Therefore, it may come as a surprise to others (parents, other family members, friends, and community members) when a youth's gender dysphoria first becomes evident in adolescence.

Adolescents who experience their primary and/or secondary sex characteristics and their sex assigned at birth as inconsistent with their gender identity may be intensely distressed about it. Many, but not all, gender dysphoric adolescents have a strong wish for hormones and surgery. Increasing numbers of adolescents have already started living in their desired gender role upon entering high school (Cohen-Kettenis & Pfäfflin, 2003).

Among adolescents who are referred to gender identity clinics, the number considered eligible for early medical treatment—starting with GnRH analogues to suppress puberty in the first Tanner stages—differs among countries and centers. Not all clinics offer puberty suppression. If such treatment is offered, the pubertal stage at which adolescents are allowed to start varies from Tanner stage 2 to stage 4 (Delemarre-van de Waal & Cohen-Kettenis, 2006; Zucker et al., 2012). The percentages of treated adolescents are likely influenced by the organization of health care, insurance aspects, cultural differences, opinions of health professionals, and diagnostic procedures offered in different settings.

Inexperienced clinicians may mistake indications of gender dysphoria for delusions. Phenomenologically, there is a qualitative difference between the presentation of gender dysphoria and the presentation of delusions or other psychotic symptoms. The vast majority of children and adolescents with gender dysphoria are not suffering from underlying severe psychiatric illness such as psychotic disorders (Steensma, Biemond, de Boer, & Cohen-Kettenis, published online ahead of print January 7, 2011).

It is more common for adolescents with gender dysphoria to have coexisting internalizing disorders such as anxiety and depression, and/or externalizing disorders such as oppositional defiant disorder (de Vries et al., 2010). As in children, there seems to be a higher prevalence of autistic spectrum disorders in clinically referred, gender dysphoric adolescents than in the general adolescent population (de Vries et al., 2010).

Competency of Mental Health Professionals Working with Children or Adolescents with Gender Dysphoria

The following are recommended minimum credentials for mental health professionals who assess, refer, and offer therapy to children and adolescents presenting with gender dysphoria:

1. Meet the competency requirements for mental health professionals working with adults, as outlined in section VII;

2. Trained in childhood and adolescent developmental psychopathology;

3. Competent in diagnosing and treating the ordinary problems of children and adolescents.

Roles of Mental Health Professionals Working with Children and Adolescents with Gender Dysphoria

The roles of mental health professionals working with gender dysphoric children and adolescents may include the following:

1. Directly assess gender dysphoria in children and adolescents (see general guidelines for assessment, below).

2. Provide family counseling and supportive psychotherapy to assist children and adolescents with exploring their gender identity, alleviating distress related to their gender dysphoria, and ameliorating any other psychosocial difficulties.

3. Assess and treat any coexisting mental health concerns of children or adolescents (or refer to another mental health professional for treatment). Such concerns should be addressed as part of the overall treatment plan.

4. Refer adolescents for additional physical interventions (such as puberty-suppressing hormones) to alleviate gender dysphoria. The referral should include documentation of an assessment of gender dysphoria and mental health, the adolescent's eligibility for physical interventions (outlined below), the mental health professional's relevant expertise, and any other information pertinent to the youth's health and referral for specific treatments.

5. Educate and advocate on behalf of gender dysphoric children, adolescents, and their families in their community (e.g., day care centers, schools, camps, other organizations). This is particularly important in light of evidence that children and adolescents who do not conform to socially prescribed gender norms may experience harassment in school (Grossman, D'Augelli, & Salter, 2006; Grossman, D'Augelli, Howell, & Hubbard, 2006; Sausa, 2005), putting them at risk for social isolation, depression, and other negative sequelae (Nuttbrock et al., 2010).

6. Provide children, youth, and their families with information and referral for peer support, such as support groups for parents of gender-nonconforming and transgender children (Gold & MacNish, 2011; Pleak, 1999; Rosenberg, 2002).

Assessment and psychosocial interventions for children and adolescents are often provided within a multidisciplinary gender identity specialty service. If such a multidisciplinary service is not available, a mental health professional should provide consultation and liaison arrangements with a pediatric endocrinologist for the purpose of assessment, education, and involvement in any decisions about physical interventions.

Psychological Assessment of Children and Adolescents

When assessing children and adolescents who present with gender dysphoria, mental health professionals should broadly conform to the following guidelines:

1. Mental health professionals should not dismiss or express a negative attitude towards nonconforming gender identities or indications of gender dysphoria. Rather, they should acknowledge the presenting concerns of children, adolescents, and their families; offer a thorough assessment for gender dysphoria and any coexisting mental health concerns; and educate clients and their families about therapeutic options, if needed. Acceptance, and alleviation of secrecy, can bring considerable relief to gender dysphoric children/adolescents and their families.

2. Assessment of gender dysphoria and mental health should explore the nature and characteristics of a child's or adolescent's gender identity. A psychodiagnostic and psychiatric assessment—covering the areas of emotional functioning, peer and other social relationships, and intellectual functioning/school achievement—should be performed. Assessment should include an evaluation of the strengths and weaknesses of family functioning. Emotional and behavioral problems are relatively common, and unresolved issues in a child's or youth's environment may be present (de Vries, Doreleijers, Steensma, & Cohen-Kettenis, 2011; Di Ceglie & Thümmel, 2006; Wallien et al., 2007).

3. For adolescents, the assessment phase should also be used to inform youth and their families about the possibilities and limitations of different treatments. This is necessary for informed consent, but also important for assessment. The way that adolescents respond to information about the reality of sex reassignment can be diagnostically informative. Correct information may alter a youth's desire for certain treatment, if the desire was based on unrealistic expectations of its possibilities.

Psychological and Social Interventions for Children and Adolescents

When supporting and treating children and adolescents with gender dysphoria, health professionals should broadly conform to the following guidelines:

1. Mental health professionals should help families to have an accepting and nurturing response to the concerns of their gender dysphoric child or adolescent. Families play an important role in the psychological health and well-being of youth (Brill & Pepper, 2008; Lev, 2004). This also applies to peers and mentors from the community, who can be another source of social support.

2. Psychotherapy should focus on reducing a child's or adolescent's distress related to the gender dysphoria and on ameliorating any other psychosocial difficulties. For youth pursuing sex reassignment, psychotherapy may focus on supporting them before, during, and after reassignment. Formal evaluations of different psychotherapeutic approaches for this situation have not been published, but several counseling methods have been described (Cohen-Kettenis, 2006; de Vries, Cohen-Kettenis, & Delemarre-van de Waal, 2006; Di Ceglie & Thümmel, 2006; Hill, Menvielle, Sica, & Johnson, 2010; Malpas, in press; Menvielle & Tuerk, 2002; Rosenberg, 2002; Vanderburgh, 2009; Zucker, 2006).

   Treatment aimed at trying to change a person's gender identity and expression to become more congruent with sex assigned at birth has been attempted in the past without success (Gelder & Marks, 1969; Greenson, 1964), particularly in the long term (Cohen-Kettenis & Kuiper, 1984; Pauly, 1965). Such treatment is no longer considered ethical.

3. Families should be supported in managing uncertainty and anxiety about their child's or adolescent's psychosexual outcomes and in helping youth to develop a positive self-concept.

4. Mental health professionals should not impose a binary view of gender. They should give ample room for clients to explore different options for gender expression. Hormonal or surgical interventions are appropriate for some adolescents, but not for others.

5. Clients and their families should be supported in making difficult decisions regarding the extent to which clients are allowed to express a gender role that is consistent with their gender identity, as well as the timing of changes in gender role and possible social transition. For example, a client might attend school while undergoing social transition only partly (e.g., by wearing clothing and having a hairstyle that reflects gender identity) or completely (e.g., by also using a name and pronouns congruent with gender identity). Difficult issues include whether and when to inform other people of the client's situation, and how others in their lives might respond.

6. Health professionals should support clients and their families as educators and advocates in their interactions with community members and authorities such as teachers, school boards, and courts.

7. Mental health professionals should strive to maintain a therapeutic relationship with gender-nonconforming children/adolescents and their families throughout any subsequent social changes or physical interventions. This ensures that decisions about gender expression and the treatment of gender dysphoria are thoughtfully and recurrently considered. The same reasoning applies if a child or adolescent has already socially changed gender role prior to being seen by a mental health professional.

Social Transition in Early Childhood

Some children state that they want to make a social transition to a different gender role long before puberty. For some children, this may reflect an expression of their gender identity. For others, this could be motivated by other forces. Families vary in the extent to which they allow their young children to make a social transition to another gender role. Social transitions in early childhood do occur within some families with early success. This is a controversial issue, and divergent views are held by health professionals. The current evidence base is insufficient to predict the long-term outcomes of completing a gender role transition during early childhood. Outcomes research with children who completed early social transitions would greatly inform future clinical recommendations.

Mental health professionals can help families to make decisions regarding the timing and process of any gender role changes for their young children. They should provide information and help parents to weigh the potential benefits and challenges of particular choices. Relevant in this respect are the previously described relatively low persistence rates of childhood gender dysphoria (Drummond et al., 2008; Wallien & Cohen-Kettenis, 2008). A change back to the original gender role can be highly distressing and even result in postponement of this second social transition on the child's part (Steensma & Cohen-Kettenis, 2011). For reasons such as these, parents may want to present this role change as an exploration of living in another gender role rather than an irreversible situation. Mental health professionals can assist parents in identifying potential in-between solutions or compromises (e.g., only when on vacation). It is also important that parents explicitly let the child know that there is a way back.

Regardless of a family's decisions regarding transition (timing, extent), professionals should counsel and support them as they work through the options and implications. If parents do not allow their young child to make a gender-role transition, they may need counseling to assist them with meeting their child's needs in a sensitive and nurturing way, ensuring that the child has ample possibilities to explore gender feelings and behavior in a safe environment. If parents do allow their young child to make a gender role transition, they may need counseling to facilitate a positive experience for their child. For example, they may need support in using correct pronouns, maintaining a safe and supportive environment for their transitioning child (e.g., in school, peer group settings), and communicating with other people in their child's life. In either case, as a child nears puberty, further assessment may be needed as options for physical interventions become relevant.

Physical Interventions for Adolescents

Before any physical interventions are considered for adolescents, extensive exploration of psychological, family, and social issues should be undertaken, as outlined above. The duration of this exploration may vary considerably depending on the complexity of the situation.

Physical interventions should be addressed in the context of adolescent development. Some identity beliefs in adolescents may become firmly held and strongly expressed, giving a false impression of irreversibility. An adolescent's shift towards gender conformity can occur primarily to please the parents and may not persist or reflect a permanent change in gender dysphoria (Hembree et al., 2009; Steensma et al., published online ahead of print January 7, 2011).

Physical interventions for adolescents fall into three categories or stages (Hembree et al., 2009):

1. *Fully reversible interventions*. These involve the use of GnRH analogues to suppress estrogen or testosterone production and consequently delay the physical changes of puberty. Alternative treatment options include progestins (most commonly medroxyprogesterone) or other medications (such as spironolactone) that decrease the effects of androgens secreted by the testicles of adolescents who are not receiving GnRH analogues. Continuous oral contraceptives (or depot medroxyprogesterone) may be used to suppress menses.

2. *Partially reversible interventions*. These include hormone therapy to masculinize or feminize the body. Some hormone-induced changes may need reconstructive surgery to reverse the effect (e.g., gynaecomastia caused by estrogens), while other changes are not reversible (e.g., deepening of the voice caused by testosterone).

3. *Irreversible interventions*. These are surgical procedures.

A staged process is recommended to keep options open through the first two stages. Moving from one stage to another should not occur until there has been adequate time for adolescents and their parents to assimilate fully the effects of earlier interventions.

Fully Reversible Interventions

Adolescents may be eligible for puberty-suppressing hormones as soon as pubertal changes have begun. In order for adolescents and their parents to make an informed decision about pubertal delay, it is recommended that adolescents experience the onset of puberty to at least Tanner Stage 2. Some children may arrive at this stage at very young ages (e.g., 9 years of age). Studies

evaluating this approach have only included children who were at least 12 years of age (Cohen-Kettenis, Schagen, Steensma, de Vries, & Delemarre-van de Waal, 2011; de Vries, Steensma et al., 2010; Delemarre-van de Waal, van Weissenbruch, & Cohen Kettenis, 2004; Delemarre-van de Waal & Cohen-Kettenis, 2006).

Two goals justify intervention with puberty-suppressing hormones: (i) their use gives adolescents more time to explore their gender nonconformity and other developmental issues; and (ii) their use may facilitate transition by preventing the development of sex characteristics that are difficult or impossible to reverse if adolescents continue on to pursue sex reassignment.

Puberty suppression may continue for a few years, at which time a decision is made to either discontinue all hormone therapy or transition to a feminizing/masculinizing hormone regimen. Pubertal suppression does not inevitably lead to social transition or to sex reassignment.

Criteria for Puberty-Suppressing Hormones

In order for adolescents to receive puberty-suppressing hormones, the following minimum criteria must be met:

1. The adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed);

2. Gender dysphoria emerged or worsened with the onset of puberty;

3. Any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment;

4. The adolescent has given informed consent and, particularly when the adolescent has not reached the age of medical consent, the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process.

Regimens, Monitoring, and Risks for Puberty Suppression

For puberty suppression, adolescents with male genitalia should be treated with GnRH analogues, which stop luteinizing hormone secretion and therefore testosterone secretion. Alternatively, they may be treated with progestins (such as medroxyprogesterone) or with other medications that block testosterone secretion and/or neutralize testosterone action. Adolescents with female genitalia should be treated with GnRH analogues, which stop the production of estrogens and

progesterone. Alternatively, they may be treated with progestins (such as medroxyprogesterone). Continuous oral contraceptives (or depot medroxyprogesterone) may be used to suppress menses. In both groups of adolescents, use of GnRH analogues is the preferred treatment (Hembree et al., 2009), but their high cost is prohibitive for some patients.

During pubertal suppression, an adolescent's physical development should be carefully monitored—preferably by a pediatric endocrinologist—so that any necessary interventions can occur (e.g., to establish an adequate gender appropriate height, to improve iatrogenic low bone mineral density) (Hembree et al., 2009).

Early use of puberty-suppressing hormones may avert negative social and emotional consequences of gender dysphoria more effectively than their later use would. Intervention in early adolescence should be managed with pediatric endocrinological advice, when available. Adolescents with male genitalia who start GnRH analogues early in puberty should be informed that this could result in insufficient penile tissue for penile inversion vaginoplasty techniques (alternative techniques, such as the use of a skin graft or colon tissue, are available).

Neither puberty suppression nor allowing puberty to occur is a neutral act. On the one hand, functioning in later life can be compromised by the development of irreversible secondary sex characteristics during puberty and by years spent experiencing intense gender dysphoria. On the other hand, there are concerns about negative physical side effects of GnRH analogue use (e.g., on bone development and height). Although the very first results of this approach (as assessed for adolescents followed over 10 years) are promising (Cohen-Kettenis et al., 2011; Delemarre-van de Waal & Cohen-Kettenis, 2006), the long-term effects can only be determined when the earliest-treated patients reach the appropriate age.

Partially Reversible Interventions

Adolescents may be eligible to begin feminizing/masculinizing hormone therapy, preferably with parental consent. In many countries, 16-year-olds are legal adults for medical decision-making and do not require parental consent. Ideally, treatment decisions should be made among the adolescent, the family, and the treatment team.

Regimens for hormone therapy in gender dysphoric adolescents differ substantially from those used in adults (Hembree et al., 2009). The hormone regimens for youth are adapted to account for the somatic, emotional, and mental development that occurs throughout adolescence (Hembree et al., 2009).

Irreversible Interventions

Genital surgery should not be carried out until (i) patients reach the legal age of majority to give consent for medical procedures in a given country, and (ii) patients have lived continuously for at least 12 months in the gender role that is congruent with their gender identity. The age threshold should be seen as a minimum criterion and not an indication in and of itself for active intervention.

Chest surgery in FtM patients could be carried out earlier, preferably after ample time of living in the desired gender role and after one year of testosterone treatment. The intent of this suggested sequence is to give adolescents sufficient opportunity to experience and socially adjust in a more masculine gender role, before undergoing irreversible surgery. However, different approaches may be more suitable, depending on an adolescent's specific clinical situation and goals for gender identity expression.

Risks of Withholding Medical Treatment for Adolescents

Refusing timely medical interventions for adolescents might prolong gender dysphoria and contribute to an appearance that could provoke abuse and stigmatization. As the level of gender-related abuse is strongly associated with the degree of psychiatric distress during adolescence (Nuttbrock et al., 2010), withholding puberty suppression and subsequent feminizing or masculinizing hormone therapy is not a neutral option for adolescents.

VII
Mental Health

Transsexual, transgender, and gender-nonconforming people might seek the assistance of a mental health professional for any number of reasons. Regardless of a person's reason for seeking care, mental health professionals should have familiarity with gender nonconformity, act with appropriate cultural competence, and exhibit sensitivity in providing care.

This section of the *SOC* focuses on the role of mental health professionals in the care of adults seeking help for gender dysphoria and related concerns. Professionals working with gender dysphoric children, adolescents, and their families should consult section VI.

Competency of Mental Health Professionals Working with Adults Who Present with Gender Dysphoria

The training of mental health professionals competent to work with gender dysphoric adults rests upon basic general clinical competence in the assessment, diagnosis, and treatment of mental health concerns. Clinical training may occur within any discipline that prepares mental health professionals for clinical practice, such as psychology, psychiatry, social work, mental health counseling, marriage and family therapy, nursing, or family medicine with specific training in behavioral health and counseling. The following are recommended minimum credentials for mental health professionals who work with adults presenting with gender dysphoria:

1. A master's degree or its equivalent in a clinical behavioral science field. This degree, or a more advanced one, should be granted by an institution accredited by the appropriate national or regional accrediting board. The mental health professional should have documented credentials from a relevant licensing board or equivalent for that country.

2. Competence in using the *Diagnostic Statistical Manual of Mental Disorders* and/or the *International Classification of Diseases* for diagnostic purposes.

3. Ability to recognize and diagnose coexisting mental health concerns and to distinguish these from gender dysphoria.

4. Documented supervised training and competence in psychotherapy or counseling.

5. Knowledgeable about gender-nonconforming identities and expressions, and the assessment and treatment of gender dysphoria.

6. Continuing education in the assessment and treatment of gender dysphoria. This may include attending relevant professional meetings, workshops, or seminars; obtaining supervision from a mental health professional with relevant experience; or participating in research related to gender nonconformity and gender dysphoria.

In addition to the minimum credentials above, it is recommended that mental health professionals develop and maintain cultural competence to facilitate their work with transsexual, transgender, and gender-nonconforming clients. This may involve, for example, becoming knowledgeable about current community, advocacy, and public policy issues relevant to these clients and their families. Additionally, knowledge about sexuality, sexual health concerns, and the assessment and treatment of sexual disorders is preferred.

Mental health professionals who are new to the field (irrespective of their level of training and other experience) should work under the supervision of a mental health professional with established competence in the assessment and treatment of gender dysphoria.

Tasks of Mental Health Professionals Working with Adults Who Present with Gender Dysphoria

Mental health professionals may serve transsexual, transgender, and gender-nonconforming individuals and their families in many ways, depending on a client's needs. For example, mental health professionals may serve as a psychotherapist, counselor, or family therapist, or as a diagnostician/assessor, advocate, or educator.

Mental health professionals should determine a client's reasons for seeking professional assistance. For example, a client may be presenting for any combination of the following health care services: psychotherapeutic assistance to explore gender identity and expression or to facilitate a coming-out process; assessment and referral for feminizing/masculinizing medical interventions; psychological support for family members (partners, children, extended family); psychotherapy unrelated to gender concerns; or other professional services.

Below are general guidelines for common tasks that mental health professionals may fulfill in working with adults who present with gender dysphoria.

Tasks Related to Assessment and Referral

1. Assess Gender Dysphoria

Mental health professionals assess clients' gender dysphoria in the context of an evaluation of their psychosocial adjustment (Bockting et al., 2006; Lev, 2004, 2009). The evaluation includes, at a minimum, assessment of gender identity and gender dysphoria, history and development of gender dysphoric feelings, the impact of stigma attached to gender nonconformity on mental health, and the availability of support from family, friends, and peers (for example, in-person or online contact with other transsexual, transgender, or gender-nonconforming individuals or groups). The evaluation may result in no diagnosis, in a formal diagnosis related to gender dysphoria, and/or in other diagnoses that describe aspects of the client's health and psychosocial adjustment. The role

of mental health professionals includes making reasonably sure that the gender dysphoria is not secondary to, or better accounted for, by other diagnoses.

Mental health professionals with the competencies described above (hereafter called "a qualified mental health professional") are best prepared to conduct this assessment of gender dysphoria. However, this task may instead be conducted by another type of health professional who has appropriate training in behavioral health and is competent in the assessment of gender dysphoria, particularly when functioning as part of a multidisciplinary specialty team that provides access to feminizing/masculinizing hormone therapy. This professional may be the prescribing hormone therapy provider or a member of that provider's health care team.

2. Provide Information Regarding Options for Gender Identity and Expression and Possible Medical Interventions

An important task of mental health professionals is to educate clients regarding the diversity of gender identities and expressions and the various options available to alleviate gender dysphoria. Mental health professionals then may facilitate a process (or refer elsewhere) in which clients explore these various options, with the goals of finding a comfortable gender role and expression and becoming prepared to make a fully informed decision about available medical interventions, if needed. This process may include referral for individual, family, and group therapy and/or to community resources and avenues for peer support. The professional and the client discuss the implications, both short- and long-term, of any changes in gender role and use of medical interventions. These implications can be psychological, social, physical, sexual, occupational, financial, and legal (Bockting et al., 2006; Lev, 2004).

This task is also best conducted by a qualified mental health professional, but may be conducted by another health professional with appropriate training in behavioral health and with sufficient knowledge about gender-nonconforming identities and expressions and about possible medical interventions for gender dysphoria, particularly when functioning as part of a multidisciplinary specialty team that provides access to feminizing/masculinizing hormone therapy.

3. Assess, Diagnose, and Discuss Treatment Options for Coexisting Mental Health Concerns

Clients presenting with gender dysphoria may struggle with a range of mental health concerns (Gómez-Gil, Trilla, Salamero, Godás, & Valdés, 2009; Murad et al., 2010) whether related or unrelated to what is often a long history of gender dysphoria and/or chronic minority stress. Possible concerns include anxiety, depression, self-harm, a history of abuse and neglect, compulsivity, substance abuse, sexual concerns, personality disorders, eating disorders, psychotic disorders, and autistic spectrum disorders (Bockting et al., 2006; Nuttbrock et al., 2010; Robinow, 2009). Mental health professionals should screen for these and other mental health concerns and incorporate

the identified concerns into the overall treatment plan. These concerns can be significant sources of distress and, if left untreated, can complicate the process of gender identity exploration and resolution of gender dysphoria (Bockting et al., 2006; Fraser, 2009a; Lev, 2009). Addressing these concerns can greatly facilitate the resolution of gender dysphoria, possible changes in gender role, the making of informed decisions about medical interventions, and improvements in quality of life.

Some clients may benefit from psychotropic medications to alleviate symptoms or treat coexisting mental health concerns. Mental health professionals are expected to recognize this and either provide pharmacotherapy or refer to a colleague who is qualified to do so. The presence of coexisting mental health concerns does not necessarily preclude possible changes in gender role or access to feminizing/masculinizing hormones or surgery; rather, these concerns need to be optimally managed prior to, or concurrent with, treatment of gender dysphoria. In addition, clients should be assessed for their ability to provide educated and informed consent for medical treatments.

Qualified mental health professionals are specifically trained to assess, diagnose, and treat (or refer to treatment for) these coexisting mental health concerns. Other health professionals with appropriate training in behavioral health, particularly when functioning as part of a multidisciplinary specialty team providing access to feminizing/masculinizing hormone therapy, may also screen for mental health concerns and, if indicated, provide referral for comprehensive assessment and treatment by a qualified mental health professional.

4. If Applicable, Assess Eligibility, Prepare, and Refer for Hormone Therapy

The *SOC* provide criteria to guide decisions regarding feminizing/masculinizing hormone therapy (outlined in section VIII and Appendix C). Mental health professionals can help clients who are considering hormone therapy to be both psychologically prepared (e.g., client has made a fully informed decision with clear and realistic expectations; is ready to receive the service in line with the overall treatment plan; has included family and community as appropriate) and practically prepared (e.g., has been evaluated by a physician to rule out or address medical contraindications to hormone use; has considered the psychosocial implications). If clients are of childbearing age, reproductive options (section IX) should be explored before initiating hormone therapy.

It is important for mental health professionals to recognize that decisions about hormones are first and foremost a client's decisions—as are all decisions regarding healthcare. However, mental health professionals have a responsibility to encourage, guide, and assist clients with making fully informed decisions and becoming adequately prepared. To best support their clients' decisions, mental health professionals need to have functioning working relationships with their clients and sufficient information about them. Clients should receive prompt and attentive evaluation, with the goal of alleviating their gender dysphoria and providing them with appropriate medical services.

Referral for feminizing/masculinizing hormone therapy

People may approach a specialized provider in any discipline to pursue feminizing/masculinizing hormone therapy. However, transgender health care is an interdisciplinary field, and coordination of care and referral among a client's overall care team is recommended.

Hormone therapy can be initiated with a referral from a qualified mental health professional. Alternatively, a health professional who is appropriately trained in behavioral health and competent in the assessment of gender dysphoria may assess eligibility, prepare, and refer the patient for hormone therapy, particularly in the absence of significant coexisting mental health concerns and when working in the context of a multidisciplinary specialty team. The referring health professional should provide documentation—in the chart and/or referral letter—of the patient's personal and treatment history, progress, and eligibility. Health professionals who recommend hormone therapy share the ethical and legal responsibility for that decision with the physician who provides the service.

The recommended content of the referral letter for feminizing/masculinizing hormone therapy is as follows:

1. The client's general identifying characteristics;

2. Results of the client's psychosocial assessment, including any diagnoses;

3. The duration of the referring health professional's relationship with the client, including the type of evaluation and therapy or counseling to date;

4. An explanation that the criteria for hormone therapy have been met, and a brief description of the clinical rationale for supporting the client's request for hormone therapy;

5. A statement that informed consent has been obtained from the patient;

6. A statement that the referring health professional is available for coordination of care and welcomes a phone call to establish this.

For providers working within a multidisciplinary specialty team, a letter may not be necessary; rather, the assessment and recommendation can be documented in the patient's chart.

5. If Applicable, Assess Eligibility, Prepare, and Refer for Surgery

The *SOC* also provide criteria to guide decisions regarding breast/chest surgery and genital surgery (outlined in section XI and Appendix C). Mental health professionals can help clients who are

considering surgery to be both psychologically prepared (e.g., has made a fully informed decision with clear and realistic expectations; is ready to receive the service in line with the overall treatment plan; has included family and community as appropriate) and practically prepared (e.g., has made an informed choice about a surgeon to perform the procedure; has arranged aftercare). If clients are of childbearing age, reproductive options (section IX) should be explored before undergoing genital surgery.

The *SOC* do not state criteria for other surgical procedures, such as feminizing or masculinizing facial surgery; however, mental health professionals can play an important role in helping their clients to make fully informed decisions about the timing and implications of such procedures in the context of the overall coming-out or transition process.

It is important for mental health professionals to recognize that decisions about surgery are first and foremost a client's decisions—as are all decisions regarding healthcare. However, mental health professionals have a responsibility to encourage, guide, and assist clients with making fully informed decisions and becoming adequately prepared. To best support their clients' decisions, mental health professionals need to have functioning working relationships with their clients and sufficient information about them. Clients should receive prompt and attentive evaluation, with the goal of alleviating their gender dysphoria and providing them with appropriate medical services.

Referral for surgery

Surgical treatments for gender dysphoria can be initiated by a referral (one or two, depending on the type of surgery) from a qualified mental health professional. The mental health professional provides documentation—in the chart and/or referral letter—of the patient's personal and treatment history, progress, and eligibility. Mental health professionals who recommend surgery share the ethical and legal responsibility for that decision with the surgeon.

- One referral from a qualified mental health professional is needed for breast/chest surgery (e.g., mastectomy, chest reconstruction, or augmentation mammoplasty).

- Two referrals—from qualified mental health professionals who have independently assessed the patient—are needed for genital surgery (i.e., hysterectomy/salpingo-oophorectomy, orchiectomy, genital reconstructive surgeries). If the first referral is from the patient's psychotherapist, the second referral should be from a person who has only had an evaluative role with the patient. Two separate letters, or one letter signed by both (e.g., if practicing within the same clinic) may be sent. Each referral letter, however, is expected to cover the same topics in the areas outlined below.

The recommended content of the referral letters for surgery is as follows:

1. The client's general identifying characteristics;
2. Results of the client's psychosocial assessment, including any diagnoses;
3. The duration of the mental health professional's relationship with the client, including the type of evaluation and therapy or counseling to date;
4. An explanation that the criteria for surgery have been met, and a brief description of the clinical rationale for supporting the patient's request for surgery;
5. A statement about the fact that informed consent has been obtained from the patient;
6. A statement that the mental health professional is available for coordination of care and welcomes a phone call to establish this.

For providers working within a multidisciplinary specialty team, a letter may not be necessary, rather, the assessment and recommendation can be documented in the patient's chart.

Relationship of Mental Health Professionals with Hormone-Prescribing Physicians, Surgeons, and Other Health Professionals

It is ideal for mental health professionals to perform their work and periodically discuss progress and obtain peer consultation from other professionals (both in mental health care and other health disciplines) who are competent in the assessment and treatment of gender dysphoria. The relationship among professionals involved in a client's health care should remain collaborative, with coordination and clinical dialogue taking place as needed. Open and consistent communication may be necessary for consultation, referral, and management of postoperative concerns.

Tasks Related to Psychotherapy

1. Psychotherapy Is Not an Absolute Requirement for Hormone Therapy and Surgery

A mental health screening and/or assessment as outlined above is needed for referral to hormonal and surgical treatments for gender dysphoria. In contrast, psychotherapy—although highly recommended—is not a requirement.

The *SOC* do not recommend a minimum number of psychotherapy sessions prior to hormone therapy or surgery. The reasons for this are multifaceted (Lev, 2009). First, a minimum number of sessions tends to be construed as a hurdle, which discourages the genuine opportunity for personal growth. Second, mental health professionals can offer important support to clients throughout all phases of exploration of gender identity, gender expression, and possible transition—not just prior to any possible medical interventions. Third, clients and their psychotherapists differ in their abilities to attain similar goals in a specified time period.

2. Goals of Psychotherapy for Adults with Gender Concerns

The general goal of psychotherapy is to find ways to maximize a person's overall psychological well-being, quality of life, and self-fulfillment. Psychotherapy is not intended to alter a person's gender identity; rather, psychotherapy can help an individual to explore gender concerns and find ways to alleviate gender dysphoria, if present (Bockting et al., 2006; Bockting & Coleman, 2007; Fraser, 2009a; Lev, 2004). Typically, the overarching treatment goal is to help transsexual, transgender, and gender-nonconforming individuals achieve long-term comfort in their gender identity expression, with realistic chances for success in their relationships, education, and work. For additional details, see Fraser (Fraser, 2009c).

Therapy may consist of individual, couple, family, or group psychotherapy, the latter being particularly important to foster peer support.

3. Psychotherapy for Transsexual, Transgender, and Gender-Nonconforming Clients, Including Counseling and Support for Changes in Gender Role

Finding a comfortable gender role is, first and foremost, a psychosocial process. Psychotherapy can be invaluable in assisting transsexual, transgender, and gender-nonconforming individuals with all of the following: (i) clarifying and exploring gender identity and role, (ii) addressing the impact of stigma and minority stress on one's mental health and human development, and (iii) facilitating a coming-out process (Bockting & Coleman, 2007; Devor, 2004; Lev, 2004), which for some individuals may include changes in gender role expression and the use of feminizing/masculinizing medical interventions.

Mental health professionals can provide support and promote interpersonal skills and resilience in individuals and their families as they navigate a world that often is ill-prepared to accommodate and respect transgender, transsexual, and gender-nonconforming people. Psychotherapy can also aid in alleviating any coexisting mental health concerns (e.g., anxiety, depression) identified during screening and assessment.

For transsexual, transgender, and gender-nonconforming individuals who plan to change gender roles permanently and make a social gender role transition, mental health professionals can facilitate the development of an individualized plan with specific goals and timelines. While the experience of changing one's gender role differs from person to person, the social aspects of the experience are usually challenging—often more so than the physical aspects. Because changing gender role can have profound personal and social consequences, the decision to do so should include an awareness of what the familial, interpersonal, educational, vocational, economic, and legal challenges are likely to be, so that people can function successfully in their gender role.

Many transsexual, transgender, and gender-nonconforming people will present for care without ever having been related to, or accepted in, the gender role that is most congruent with their gender identity. Mental health professionals can help these clients to explore and anticipate the implications of changes in gender role, and to pace the process of implementing these changes. Psychotherapy can provide a space for clients to begin to express themselves in ways that are congruent with their gender identity and, for some clients, overcome fears about changes in gender expression. Calculated risks can be taken outside of therapy to gain experience and build confidence in the new role. Assistance with coming out to family and community (friends, school, workplace) can be provided.

Other transsexual, transgender, and gender-nonconforming individuals will present for care already having acquired experience (minimal, moderate, or extensive) living in a gender role that differs from that associated with their birth-assigned sex. Mental health professionals can help these clients to identify and work through potential challenges and foster optimal adjustment as they continue to express changes in their gender role.

4. Family Therapy or Support for Family Members

Decisions about changes in gender role and medical interventions for gender dysphoria have implications for, not only clients, but also their families (Emerson & Rosenfeld, 1996; Fraser, 2009a; Lev, 2004). Mental health professionals can assist clients with making thoughtful decisions about communicating with family members and others about their gender identity and treatment decisions. Family therapy may include work with spouses or partners, as well as with children and other members of a client's extended family.

Clients may also request assistance with their relationships and sexual health. For example, they may want to explore their sexuality and intimacy-related concerns.

Family therapy might be offered as part of the client's individual therapy and, if clinically appropriate, by the same provider. Alternatively, referrals can be made to other therapists with relevant expertise

for working with family members or to sources of peer support (e.g., in-person or offline support networks of partners or families).

5. Follow-Up Care Throughout Life

Mental health professionals may work with clients and their families at many stages of their lives. Psychotherapy may be helpful at different times and for various issues throughout the life cycle.

6. E-Therapy, Online Counseling, or Distance Counseling

Online or e-therapy has been shown to be particularly useful for people who have difficulty accessing competent in-person psychotherapeutic treatment and who may experience isolation and stigma (Derrig-Palumbo & Zeine, 2005; Fenichel et al., 2004; Fraser, 2009b). By extrapolation, e-therapy may be a useful modality for psychotherapy with transsexual, transgender, and gender-nonconforming people. E-therapy offers opportunities for potentially enhanced, expanded, creative, and tailored delivery of services; however, as a developing modality it may also carry unexpected risk. Telemedicine guidelines are clear in some disciplines in some parts of the United States (Fraser, 2009b; Maheu, Pulier, Wilhelm, McMenamin, & Brown-Connolly, 2005) but not all; the international situation is even less well-defined (Maheu et al., 2005). Until sufficient evidence-based data on this use of e-therapy is available, caution in its use is advised.

Mental health professionals engaging in e-therapy are advised to stay current with their particular licensing board, professional association, and country's regulations, as well as the most recent literature pertaining to this rapidly evolving medium. A more thorough description of the potential uses, processes, and ethical concerns related to e-therapy has been published (Fraser, 2009b).

Other Tasks of Mental Health Professionals

1. Educate and Advocate on Behalf of Clients Within Their Community (Schools, Workplaces, Other Organizations) and Assist Clients with Making Changes in Identity Documents

Transsexual, transgender, and gender-nonconforming people may face challenges in their professional, educational, and other types of settings as they actualize their gender identity and expression (Lev, 2004, 2009). Mental health professionals can play an important role by educating people in these settings regarding gender nonconformity and by advocating on behalf of their clients (Currah, Juang, & Minter, 2006; Currah & Minter, 2000). This role may involve consultation

with school counselors, teachers, and administrators, human resources staff, personnel managers and employers, and representatives from other organizations and institutions. In addition, health providers may be called upon to support changes in a client's name and/or gender marker on identity documents such as passports, driver's licenses, birth certificates, and diplomas.

2. Provide Information and Referral for Peer Support

For some transsexual, transgender, and gender-nonconforming people, an experience in peer support groups may be more instructive regarding options for gender expression than anything individual psychotherapy could offer (Rachlin, 2002). Both experiences are potentially valuable, and all people exploring gender issues should be encouraged to participate in community activities, if possible. Resources for peer support and information should be made available.

Culture and Its Ramifications for Assessment and Psychotherapy

Health professionals work in enormously different environments across the world. Forms of distress that cause people to seek professional assistance in any culture are understood and classified by people in terms that are products of their own cultures (Frank & Frank, 1993). Cultural settings also largely determine how such conditions are understood by mental health professionals. Cultural differences related to gender identity and expression can affect patients, mental health professionals, and accepted psychotherapy practice. WPATH recognizes that the *SOC* have grown out of a Western tradition and may need to be adapted depending on the cultural context.

Ethical Guidelines Related to Mental Health Care

Mental health professionals need to be certified or licensed to practice in a given country according to that country's professional regulations (Fraser, 2009b; Pope & Vasquez, 2011). Professionals must adhere to the ethical codes of their professional licensing or certifying organizations in all of their work with transsexual, transgender, and gender-nonconforming clients.

Treatment aimed at trying to change a person's gender identity and lived gender expression to become more congruent with sex assigned at birth has been attempted in the past (Gelder & Marks, 1969; Greenson, 1964), yet without success, particularly in the long-term (Cohen-Kettenis & Kuiper, 1984; Pauly, 1965). Such treatment is no longer considered ethical.

If mental health professionals are uncomfortable with, or inexperienced in, working with transsexual, transgender, and gender-nonconforming individuals and their families, they should refer clients to a competent provider or, at minimum, consult with an expert peer. If no local practitioners are available, consultation may be done via telehealth methods, assuming local requirements for distance consultation are met.

Issues of Access to Care

Qualified mental health professionals are not universally available; thus, access to quality care might be limited. WPATH aims to improve access and provides regular continuing education opportunities to train professionals from various disciplines to provide quality, transgender-specific health care. Providing mental health care from a distance through the use of technology may be one way to improve access (Fraser, 2009b).

In many places around the world, access to health care for transsexual, transgender, and gender-nonconforming people is also limited by a lack of health insurance or other means to pay for needed care. WPATH urges health insurance companies and other third-party payers to cover the medically necessary treatments to alleviate gender dysphoria (American Medical Association, 2008; Anton, 2009; The World Professional Association for Transgender Health, 2008).

When faced with a client who is unable to access services, referral to available peer support resources (offline and online) is recommended. Finally, harm-reduction approaches might be indicated to assist clients with making healthy decisions to improve their lives.

VIII
Hormone Therapy

Medical Necessity of Hormone Therapy

Feminizing/masculinizing hormone therapy—the administration of exogenous endocrine agents to induce feminizing or masculinizing changes—is a medically necessary intervention for many transsexual, transgender, and gender-nonconforming individuals with gender dysphoria

(Newfield, Hart, Dibble, & Kohler, 2006; Pfäfflin & Junge, 1998). Some people seek maximum feminization/masculinization, while others experience relief with an androgynous presentation resulting from hormonal minimization of existing secondary sex characteristics (Factor & Rothblum, 2008). Evidence for the psychosocial outcomes of hormone therapy is summarized in Appendix D.

Hormone therapy must be individualized based on a patient's goals, the risk/benefit ratio of medications, the presence of other medical conditions, and consideration of social and economic issues. Hormone therapy can provide significant comfort to patients who do not wish to make a social gender role transition or undergo surgery, or who are unable to do so (Meyer III, 2009). Hormone therapy is a recommended criterion for some, but not all, surgical treatments for gender dysphoria (see section XI and Appendix C).

Criteria for Hormone Therapy

Initiation of hormone therapy may be undertaken after a psychosocial assessment has been conducted and informed consent has been obtained by a qualified health professional, as outlined in section VII of the *SOC*. A referral is required from the mental health professional who performed the assessment, unless the assessment was done by a hormone provider who is also qualified in this area.

The criteria for hormone therapy are as follows:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* outlined in section VI);
4. If significant medical or mental health concerns are present, they must be reasonably well-controlled.

As noted in section VII of the *SOC*, the presence of coexisting mental health concerns does not necessarily preclude access to feminizing/masculinizing hormones; rather, these concerns need to be managed prior to, or concurrent with, treatment of gender dysphoria.

In selected circumstances, it can be acceptable practice to provide hormones to patients who have not fulfilled these criteria. Examples include facilitating the provision of monitored therapy using hormones of known quality as an alternative to illicit or unsupervised hormone use or to patients

who have already established themselves in their affirmed gender and who have a history of prior hormone use. It is unethical to deny availability or eligibility for hormone therapy solely on the basis of blood seropositivity for blood-borne infections such as HIV or hepatitis B or C.

In rare cases, hormone therapy may be contraindicated due to serious individual health conditions. Health professionals should assist these patients with accessing nonhormonal interventions for gender dysphoria. A qualified mental health professional familiar with the patient is an excellent resource in these circumstances.

Informed Consent

Feminizing/masculinizing hormone therapy may lead to irreversible physical changes. Thus, hormone therapy should be provided only to those who are legally able to provide informed consent. This includes people who have been declared by a court to be emancipated minors, incarcerated people, and cognitively impaired people who are considered competent to participate in their medical decisions (Bockting et al., 2006). Providers should document in the medical record that comprehensive information has been provided and understood about all relevant aspects of the hormone therapy, including both possible benefits and risks and the impact on reproductive capacity.

Relationship Between the *Standards of Care* and Informed Consent Model Protocols

A number of community health centers in the United States have developed protocols for providing hormone therapy based on an approach that has become known as the Informed Consent Model (Callen Lorde Community Health Center, 2000, 2011; Fenway Community Health Transgender Health Program, 2007; Tom Waddell Health Center, 2006). These protocols are consistent with the guidelines presented in the WPATH *Standards of Care, Version 7*. The *SOC* are flexible clinical guidelines; they allow for tailoring of interventions to the needs of the individual receiving services and for tailoring of protocols to the approach and setting in which these services are provided (Ehrbar & Gorton, 2010).

Obtaining informed consent for hormone therapy is an important task of providers to ensure that patients understand the psychological and physical benefits and risks of hormone therapy, as well as its psychosocial implications. Providers prescribing the hormones or health professionals recommending the hormones should have the knowledge and experience to assess gender

dysphoria. They should inform individuals of the particular benefits, limitations, and risks of hormones, given the patient's age, previous experience with hormones, and concurrent physical or mental health concerns.

Screening for and addressing acute or current mental health concerns is an important part of the informed consent process. This may be done by a mental health professional or by an appropriately trained prescribing provider (see section VII of the *SOC*). The same provider or another appropriately trained member of the health care team (e.g., a nurse) can address the psychosocial implications of taking hormones when necessary (e.g., the impact of masculinization/feminization on how one is perceived and its potential impact on relationships with family, friends, and coworkers). If indicated, these providers will make referrals for psychotherapy and for the assessment and treatment of coexisting mental health concerns such as anxiety or depression.

The difference between the Informed Consent Model and *SOC, Version 7,* is that the *SOC* puts greater emphasis on the important role that mental health professionals can play in alleviating gender dysphoria and facilitating changes in gender role and psychosocial adjustment. This may include a comprehensive mental health assessment and psychotherapy, when indicated. In the Informed Consent Model, the focus is on obtaining informed consent as the threshold for the initiation of hormone therapy in a multidisciplinary, harm-reduction environment. Less emphasis is placed on the provision of mental health care until the patient requests it, unless significant mental health concerns are identified that would need to be addressed before hormone prescription.

Physical Effects of Hormone Therapy

Feminizing/masculinizing hormone therapy will induce physical changes that are more congruent with a patient's gender identity.

- In FtM patients, the following physical changes are expected to occur: deepened voice, clitoral enlargement (variable), growth in facial and body hair, cessation of menses, atrophy of breast tissue, and decreased percentage of body fat compared to muscle mass.

- In MtF patients, the following physical changes are expected to occur: breast growth (variable), decreased erectile function, decreased testicular size, and increased percentage of body fat compared to muscle mass.

Most physical changes, whether feminizing or masculinizing, occur over the course of two years. The amount of physical change and the exact timeline of effects can be highly variable. Tables 1a and 1b outline the approximate time course of these physical changes.

TABLE 1A: EFFECTS AND EXPECTED TIME COURSE OF MASCULINIZING HORMONES [A]

Effect	Expected onset[B]	Expected maximum effect[B]
Skin oiliness/acne	1–6 months	1–2 years
Facial/body hair growth	3–6 months	3–5 years
Scalp hair loss	>12 months[C]	Variable
Increased muscle mass/strength	6–12 months	2–5 years[D]
Body fat redistribution	3–6 months	2–5 years
Cessation of menses	2–6 months	n/a
Clitoral enlargement	3–6 months	1–2 years
Vaginal atrophy	3–6 months	1–2 years
Deepened voice	3–12 months	1–2 years

[A] Adapted with permission from Hembree et al.(2009). Copyright 2009, The Endocrine Society.
[B] Estimates represent published and unpublished clinical observations.
[C] Highly dependent on age and inheritance; may be minimal.
[D] Significantly dependent on amount of exercise.

TABLE 1B: EFFECTS AND EXPECTED TIME COURSE OF FEMINIZING HORMONES [A]

Effect	Expected onset[B]	Expected maximum effect[B]
Body fat redistribution	3–6 months	2–5 years
Decreased muscle mass/ strength	3–6 months	1–2 years[C]
Softening of skin/decreased oiliness	3–6 months	Unknown
Decreased libido	1–3 months	1–2 years
Decreased spontaneous erections	1–3 months	3–6 months
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 months	2–3 years
Decreased testicular volume	3–6 months	2–3 years
Decreased sperm production	Variable	Variable
Thinning and slowed growth of body and facial hair	6–12 months	> 3 years[D]
Male pattern baldness	No regrowth, loss stops 1–3 months	1–2 years

[A] Adapted with permission from Hembree et al. (2009). Copyright 2009, The Endocrine Society.
[B] Estimates represent published and unpublished clinical observations.
[C] Significantly dependent on amount of exercise.
[D] Complete removal of male facial and body hair requires electrolysis, laser treatment, or both.

The degree and rate of physical effects depends in part on the dose, route of administration, and medications used, which are selected in accordance with a patient's specific medical goals (e.g., changes in gender role expression, plans for sex reassignment) and medical risk profile. There is no current evidence that response to hormone therapy—with the possible exception of voice deepening in FtM persons—can be reliably predicted based on age, body habitus, ethnicity, or family appearance. All other factors being equal, there is no evidence to suggest that any medically approved type or method of administering hormones is more effective than any other in producing the desired physical changes.

Risks of Hormone Therapy

All medical interventions carry risks. The likelihood of a serious adverse event is dependent on numerous factors: the medication itself, dose, route of administration, and a patient's clinical characteristics (age, comorbidities, family history, health habits). It is thus impossible to predict whether a given adverse effect will happen in an individual patient.

The risks associated with feminizing/masculinizing hormone therapy for the transsexual, transgender, and gender-nonconforming population as a whole are summarized in Table 2. Based on the level of evidence, risks are categorized as follows: (i) likely increased risk with hormone therapy, (ii) possibly increased risk with hormone therapy, or (iii) inconclusive or no increased risk. Items in the last category include those that may present risk, but for which the evidence is so minimal that no clear conclusion can be reached.

Additional detail about these risks can be found in Appendix B, which is based on two comprehensive, evidence-based literature reviews of masculinizing/feminizing hormone therapy (Feldman & Safer, 2009; Hembree et al., 2009), along with a large cohort study (Asscheman et al., 2011). These reviews can serve as detailed references for providers, along with other widely recognized, published clinical materials (Dahl, Feldman, Goldberg, & Jaberi, 2006; Ettner, Monstrey, & Eyler, 2007).

TABLE 2: RISKS ASSOCIATED WITH HORMONE THERAPY. BOLDED ITEMS ARE CLINICALLY SIGNIFICANT

Risk Level	Feminizing hormones	Masculinizing hormones
Likely increased risk	Venous thromboembolic disease[A] Gallstones Elevated liver enzymes Weight gain **Hypertriglyceridemia**	**Polycythemia** Weight gain Acne Androgenic alopecia (balding) Sleep apnea
Likely increased risk with presence of additional risk factors[B]	Cardiovascular disease	
Possible increased risk	**Hypertension** Hyperprolactinemia or prolactinoma	Elevated liver enzymes **Hyperlipidemia**
Possible increased risk with presence of additional risk factors[B]	**Type 2 diabetes**[A]	**Destabilization of certain psychiatric disorders**[C] **Cardiovascular disease** **Hypertension** **Type 2 diabetes**
No increased risk or inconclusive	**Breast cancer**	Loss of bone density **Breast cancer** **Cervical cancer** **Ovarian cancer** **Uterine cancer**

* **Note:** Risk is greater with oral estrogen administration than with transdermal estrogen administration.

[A] Risk is greater with oral estrogen administration than with transdermal estrogen administration.

[B] Additional risk factors include age.

[C] Includes bipolar, schizoaffective, and other disorders that may include manic or psychotic symptoms. This adverse event appears to be associated with higher doses or supraphysiologic blood levels of testosterone.

Competency of Hormone-Prescribing Physicians, Relationship with Other Health Professionals

Feminizing/masculinizing hormone therapy is best undertaken in the context of a complete approach to health care that includes comprehensive primary care and a coordinated approach to psychosocial issues (Feldman & Safer, 2009). While psychotherapy or ongoing counseling is not required for the initiation of hormone therapy, if a therapist is involved, then regular communication among health professionals is advised (with the patient's consent) to ensure that the transition process is going well, both physically and psychosocially.

With appropriate training, feminizing/masculinizing hormone therapy can be managed by a variety of providers, including nurse practitioners, physician assistants, and primary care physicians (Dahl et al., 2006). Medical visits relating to hormone maintenance provide an opportunity to deliver broader care to a population that is often medically underserved (Clements, Wilkinson, Kitano, & Marx, 1999; Feldman, 2007; Xavier, 2000). Many of the screening tasks and management of comorbidities associated with long-term hormone use, such as cardiovascular risk factors and cancer screening, fall more uniformly within the scope of primary care rather than specialist care (American Academy of Family Physicians, 2005; Eyler, 2007; World Health Organization, 2008), particularly in locations where dedicated gender teams or specialized physicians are not available.

Given the multidisciplinary needs of transsexual, transgender, and gender-nonconforming people seeking hormone therapy, as well as the difficulties associated with fragmentation of care in general (World Health Organization, 2008), WPATH strongly encourages the increased training and involvement of primary care providers in the area of feminizing/masculinizing hormone therapy. If hormones are prescribed by a specialist, there should be close communication with the patient's primary care provider. Conversely, an experienced hormone provider or endocrinologist should be involved if the primary care physician has no experience with this type of hormone therapy, or if the patient has a pre-existing metabolic or endocrine disorder that could be affected by endocrine therapy.

While formal training programs in transgender medicine do not yet exist, hormone providers have a responsibility to obtain appropriate knowledge and experience in this field. Clinicians can increase their experience and comfort in providing feminizing/masculinizing hormone therapy by co-managing care or consulting with a more experienced provider, or by providing more limited types of hormone therapy before progressing to initiation of hormone therapy. Because this field of medicine is evolving, clinicians should become familiar and keep current with the medical literature, and discuss emerging issues with colleagues. Such discussions might occur through networks established by WPATH and other national/local organizations.

Responsibilities of Hormone-Prescribing Physicians

In general, clinicians who prescribe hormone therapy should engage in the following tasks:

1. Perform an initial evaluation that includes discussion of a patient's physical transition goals, health history, physical examination, risk assessment, and relevant laboratory tests.

2. Discuss with patients the expected effects of feminizing/masculinizing medications and the possible adverse health effects. These effects can include a reduction in fertility (Feldman & Safer, 2009; Hembree et al., 2009). Therefore, reproductive options should be discussed with patients before starting hormone therapy (see section IX).

3. Confirm that patients have the capacity to understand the risks and benefits of treatment and are capable of making an informed decision about medical care.

4. Provide ongoing medical monitoring, including regular physical and laboratory examination to monitor hormone effectiveness and side effects.

5. Communicate as needed with a patient's primary care provider, mental health professional, and surgeon.

6. If needed, provide patients with a brief written statement indicating that they are under medical supervision and care that includes feminizing/masculinizing hormone therapy. Particularly during the early phases of hormone treatment, a patient may wish to carry this statement at all times to help prevent difficulties with the police and other authorities.

Depending on the clinical situation for providing hormones (see below), some of these responsibilities are less relevant. Thus, the degree of counseling, physical examinations, and laboratory evaluations should be individualized to a patient's needs.

Clinical Situations for Hormone Therapy

There are circumstances in which clinicians may be called upon to provide hormones without necessarily initiating or maintaining long-term feminizing/masculinizing hormone therapy. By acknowledging these different clinical situations (see below, from least to highest level of complexity), it may be possible to involve clinicians in feminizing/masculinizing hormone therapy who might not otherwise feel able to offer this treatment.

1. Bridging

Whether prescribed by another clinician or obtained through other means (e.g., purchased over the Internet), patients may present for care already on hormone therapy. Clinicians can provide a limited (1–6 month) prescription for hormones while helping patients find a provider who can prescribe long-term hormone therapy. Providers should assess a patient's current regimen for safety and drug interactions and substitute safer medications or doses when indicated (Dahl et al., 2006; Feldman & Safer, 2009). If hormones were previously prescribed, medical records should be requested (with the patient's permission) to obtain the results of baseline examinations and laboratory tests and any adverse events. Hormone providers should also communicate with any mental health professional who is currently involved in a patient's care. If a patient has never had a psychosocial assessment as recommended by the *SOC* (see section VII), clinicians should refer the patient to a qualified mental health professional if appropriate and feasible (Feldman & Safer, 2009). Providers who prescribe bridging hormones need to work with patients to establish limits as to the duration of bridging therapy.

2. Hormone Therapy Following Gonad Removal

Hormone replacement with estrogen or testosterone is usually continued lifelong after an oophorectomy or orchiectomy, unless medical contraindications arise. Because hormone doses are often decreased after these surgeries (Basson, 2001; Levy, Crown, & Reid, 2003; Moore, Wisniewski, & Dobs, 2003) and only adjusted for age and comorbid health concerns, hormone management in this situation is quite similar to hormone replacement in any hypogonadal patient.

3. Hormone Maintenance Prior to Gonad Removal

Once patients have achieved maximal feminizing/masculinizing benefits from hormones (typically two or more years), they remain on a maintenance dose. The maintenance dose is then adjusted for changes in health conditions, aging, or other considerations such as lifestyle changes (Dahl et al., 2006). When a patient on maintenance hormones presents for care, the provider should assess the patient's current regimen for safety and drug interactions and substitute safer medications or doses when indicated. The patient should continue to be monitored by physical examinations and laboratory testing on a regular basis, as outlined in the literature (Feldman & Safer, 2009; Hembree et al., 2009). The dose and form of hormones should be revisited regularly with any changes in the patient's health status and available evidence on the potential long-term risks of hormones (See *Hormone Regimens,* below).

4. Initiating Hormonal Feminization/Masculinization

This clinical situation requires the greatest commitment in terms of provider time and expertise. Hormone therapy must be individualized based on a patient's goals, the risk/benefit ratio of medications, the presence of other medical conditions, and consideration of social and economic issues. Although a wide variety of hormone regimens have been published (Dahl et al., 2006; Hembree et al., 2009; Moore et al., 2003), there are no published reports of randomized clinical trials comparing safety and efficacy. Despite this variation, a reasonable framework for initial risk assessment and ongoing monitoring of hormone therapy can be constructed, based on the efficacy and safety evidence presented above.

Risk Assessment and Modification for Initiating Hormone Therapy

The initial evaluation for hormone therapy assesses a patient's clinical goals and risk factors for hormone-related adverse events. During the risk assessment, the patient and clinician should develop a plan for reducing risks wherever possible, either prior to initiating therapy or as part of ongoing harm reduction.

All assessments should include a thorough physical exam, including weight, height, and blood pressure. The need for breast, genital, and rectal exams, which are sensitive issues for most transsexual, transgender, and gender-nonconforming patients, should be based on individual risks and preventive health care needs (Feldman & Goldberg, 2006; Feldman, 2007).

Preventive Care

Hormone providers should address preventive health care with patients, particularly if a patient does not have a primary care provider. Depending on a patient's age and risk profile, there may be appropriate screening tests or exams for conditions affected by hormone therapy. Ideally, these screening tests should be carried out prior to the start of hormone therapy.

Risk Assessment and Modification for Feminizing Hormone Therapy (MtF)

There are no absolute contraindications to feminizing therapy per se, but absolute contraindications exist for the different feminizing agents, particularly estrogen. These include previous venous thrombotic events related to an underlying hypercoagulable condition, history of estrogen-sensitive neoplasm, and end-stage chronic liver disease (Gharib et al., 2005).

Other medical conditions, as noted in Table 2 and Appendix B, can be exacerbated by estrogen or androgen blockade, and therefore should be evaluated and reasonably well controlled prior to starting hormone therapy (Feldman & Safer, 2009; Hembree et al., 2009). Clinicians should particularly attend to tobacco use, as it is associated with increased risk of venous thrombosis, which is further increased with estrogen use. Consultation with a cardiologist may be advisable for patients with known cardio- or cerebrovascular disease.

Baseline laboratory values are important to both assess initial risk and evaluate possible future adverse events. Initial labs should be based on the risks of feminizing hormone therapy outlined in Table 2, as well as individual patient risk factors, including family history. Suggested initial lab panels have been published (Feldman & Safer, 2009; Hembree et al., 2009). These can be modified for patients or health care systems with limited resources, and in otherwise healthy patients.

Risk Assessment and Modification for Masculinizing Hormone Therapy (FtM)

Absolute contraindications to testosterone therapy include pregnancy, unstable coronary artery disease, and untreated polycythemia with a hematocrit of 55% or higher (Carnegie, 2004). Because the aromatization of testosterone to estrogen may increase risk in patients with a history of breast or other estrogen dependent cancers (Moore et al., 2003), consultation with an oncologist may be indicated prior to hormone use. Comorbid conditions likely to be exacerbated by testosterone use should be evaluated and treated, ideally prior to starting hormone therapy (Feldman & Safer, 2009; Hembree et al., 2009). Consultation with a cardiologist may be advisable for patients with known cardio- or cerebrovascular disease. (Dhejne et al., 2011).

An increased prevalence of polycystic ovarian syndrome (PCOS) has been noted among FtM patients even in the absence of testosterone use (Baba et al., 2007; Balen, Schachter, Montgomery, Reid, & Jacobs, 1993; Bosinski et al., 1997). While there is no evidence that PCOS is related to the development of a transsexual, transgender, or gender-nonconforming identity, PCOS is associated with increased risk of diabetes, cardiac disease, high blood pressure, and ovarian and endometrial cancers (Cattrall & Healy, 2004). Signs and symptoms of PCOS should be evaluated prior to initiating testosterone therapy, as testosterone may affect many of these conditions. Testosterone can affect the developing fetus (*Physicians' Desk Reference,* 2010), and patients at risk of becoming pregnant require highly effective birth control.

Baseline laboratory values are important to both assess initial risk and evaluate possible future adverse events. Initial labs should be based on the risks of masculinizing hormone therapy outlined in Table 2, as well as individual patient risk factors, including family history. Suggested initial lab panels have been published (Feldman & Safer, 2009; Hembree et al., 2009). These can be modified for patients or health care systems with limited resources, and in otherwise healthy patients.

Clinical Monitoring During Hormone Therapy for Efficacy and Adverse Events

The purpose of clinical monitoring during hormone use is to assess the degree of feminization/masculinization and the possible presence of adverse effects of medication. However, as with the monitoring of any long-term medication, monitoring should take place in the context of comprehensive health care. Suggested clinical monitoring protocols have been published (Feldman & Safer, 2009; Hembree et al., 2009). Patients with comorbid medical conditions may need to be monitored more frequently. Healthy patients in geographically remote or resource-poor areas may be able to use alternative strategies, such as telehealth, or cooperation with local providers such as nurses and physician assistants. In the absence of other indications, health professionals may prioritize monitoring for those risks that are either likely to be increased by hormone therapy or possibly increased by hormone therapy but clinically serious in nature.

Efficacy and Risk Monitoring During Feminizing Hormone Therapy (MtF)

The best assessment of hormone efficacy is clinical response: Is a patient developing a feminized body while minimizing masculine characteristics, consistent with that patient's gender goals? In order to more rapidly predict the hormone dosages that will achieve clinical response, one can measure testosterone levels for suppression below the upper limit of the normal female range and estradiol levels within a premenopausal female range but well below supraphysiologic levels (Feldman & Safer, 2009; Hembree et al., 2009).

Monitoring for adverse events should include both clinical and laboratory evaluation. Follow-up should include careful assessment for signs of cardiovascular impairment and venous thromboembolism (VTE) through measurement of blood pressure, weight, and pulse; heart and lung exams; and examination of the extremities for peripheral edema, localized swelling, or pain (Feldman & Safer, 2009). Laboratory monitoring should be based on the risks of hormone therapy described above, a patient's individual comorbidities and risk factors, and the specific hormone regimen itself. Specific lab-monitoring protocols have been published (Feldman & Safer, 2009; Hembree et al., 2009).

Efficacy and Risk Monitoring During Masculinizing Hormone Therapy (FtM)

The best assessment of hormone efficacy is clinical response: Is a patient developing a masculinized body while minimizing feminine characteristics, consistent with that patient's gender goals? Clinicians can achieve a good clinical response with the least likelihood of adverse events by maintaining testosterone levels within the normal male range while avoiding supraphysiological

levels (Dahl et al., 2006; Hembree et al., 2009). For patients using intramuscular (IM) testosterone cypionate or enanthate, some clinicians check trough levels while others prefer midcycle levels (Dahl et al., 2006; Hembree et al., 2009; Tangpricha, Turner, Malabanan, & Holick, 2001; Tangpricha, Ducharme, Barber, & Chipkin, 2003).

Monitoring for adverse events should include both clinical and laboratory evaluation. Follow-up should include careful assessment for signs and symptoms of excessive weight gain, acne, uterine break-through bleeding, and cardiovascular impairment, as well as psychiatric symptoms in at-risk patients. Physical examinations should include measurement of blood pressure, weight, and pulse; and heart, lung, and skin exams (Feldman & Safer, 2009). Laboratory monitoring should be based on the risks of hormone therapy described above, a patient's individual comorbidities and risk factors, and the specific hormone regimen itself. Specific lab monitoring protocols have been published (Feldman & Safer, 2009; Hembree et al., 2009).

Hormone Regimens

To date, no controlled clinical trials of any feminizing/masculinizing hormone regimen have been conducted to evaluate safety or efficacy in producing physical transition. As a result, wide variation in doses and types of hormones have been published in the medical literature (Moore et al., 2003; Tangpricha et al., 2003; van Kesteren, Asscheman, Megens, & Gooren, 1997). In addition, access to particular medications may be limited by a patient's geographical location and/or social or econonomic situations. For these reasons, WPATH does not describe or endorse a particular feminizing/masculinizing hormone regimen. Rather, the medication classes and routes of administration used in most published regimens are broadly reviewed.

As outlined above, there are demonstrated safety differences in individual elements of various regimens. The Endocrine Society Guidelines (Hembree et al., 2009) and Feldman and Safer (2009) provide specific guidance regarding the types of hormones and suggested dosing to maintain levels within physiologic ranges for a patient's desired gender expression (based on goals of full feminization/masculinization). It is strongly recommend that hormone providers regularly review the literature for new information and use those medications that safely meet individual patient needs with available local resources.

Regimens for Feminizing Hormone Therapy (MtF)

Estrogen

Use of oral estrogen, and specifically ethinyl estradiol, appears to increase the risk of VTE. Because of this safety concern, ethinyl estradiol is not recommended for feminizing hormone therapy. Transdermal estrogen is recommended for those patients with risks factors for VTE. The risk of adverse events increases with higher doses, particular doses resulting in supraphysiologic levels (Hembree et al., 2009). Patients with co-morbid conditions that can be affected by estrogen should avoid oral estrogen if possible and be started at lower levels. Some patients may not be able to safely use the levels of estrogen needed to get the desired results. This possibility needs to be discussed with patients well in advance of starting hormone therapy.

Androgen-reducing medications ("anti-androgens")

A combination of estrogen and "anti-androgens" is the most commonly studied regimen for feminization. Androgen-reducing medications, from a variety of classes of drugs, have the effect of reducing either endogenous testosterone levels or testosterone activity, and thus diminishing masculine characteristics such as body hair. They minimize the dosage of estrogen needed to suppress testosterone, thereby reducing the risks associated with high-dose exogenous estrogen (Prior, Vigna, Watson, Diewold, & Robinow, 1986; Prior, Vigna, & Watson, 1989).

Common anti-androgens include the following:

- Spironolactone, an antihypertensive agent, directly inhibits testosterone secretion and androgen binding to the androgen receptor. Blood pressure and electrolytes need to be monitored because of the potential for hyperkalemia.

- Cyproterone acetate is a progestational compound with anti-androgenic properties. This medication is not approved in the United States because of concerns over potential hepatotoxicity, but it is widely used elsewhere (De Cuypere et al., 2005).

- GnRH agonists (e.g., goserelin, buserelin, triptorelin) are neurohormones that block the gonadtropin-releasing hormone receptor, thus blocking the release of follicle stimulating hormone and luteinizing hormone. This leads to highly effective gonadal blockade. However, these medications are expensive and only available as injectables or implants.

- 5-alpha reductase inhibitors (finasteride and dutasteride) block the conversion of testosterone to the more active agent, 5-alpha-dihydrotestosterone. These medications have beneficial effects on scalp hair loss, body hair growth, sebaceous glands, and skin consistency.

Cyproterone and spironolactone are the most commonly used anti-androgens and are likely the most cost-effective.

Progestins

With the exception of cyproterone, the inclusion of progestins in feminizing hormone therapy is controversial (Oriel, 2000). Because progestins play a role in mammary development on a cellular level, some clinicians believe that these agents are necessary for full breast development (Basson & Prior, 1998; Oriel, 2000). However, a clinical comparison of feminization regimens with and without progestins found that the addition of progestins neither enhanced breast growth nor lowered serum levels of free testosterone (Meyer et al., 1986). There are concerns regarding potential adverse effects of progestins, including depression, weight gain, and lipid changes (Meyer et al., 1986; Tangpricha et al., 2003). Progestins (especially medroxyprogesterone) are also suspected to increase breast cancer risk and cardiovascular risk in women (Rossouw et al., 2002). Micronized progesterone may be better tolerated and have a more favorable impact on the lipid profile than medroxyprogesterone does (de Lignières, 1999; Fitzpatrick, Pace, & Wiita, 2000).

Regimens for Masculinizing Hormone Therapy (FtM)

Testosterone

Testosterone generally can be given orally, transdermally, or parenterally (IM), although buccal and implantable preparations are also available. Oral testosterone undecanoate, available outside the United States, results in lower serum testosterone levels than nonoral preparations and has limited efficacy in suppressing menses (Feldman, 2005, April; Moore et al., 2003). Because intramuscular testosterone cypionate or enanthate are often administered every 2–4 weeks, some patients may notice cyclic variation in effects (e.g., fatigue and irritability at the end of the injection cycle, aggression or expansive mood at the beginning of the injection cycle), as well as more time outside the normal physiologic levels (Jockenhövel, 2004). This may be mitigated by using a lower but more frequent dosage schedule or by using a daily transdermal preparation (Dobs et al., 1999; Jockenhövel, 2004; Nieschlag et al., 2004). Intramuscular testosterone undecanoate (not currently available in the United States) maintains stable, physiologic testosterone levels over approximately 12 weeks and has been effective in both the setting of hypogonadism and in FtM individuals (Mueller, Kiesewetter, Binder, Beckmann, & Dittrich, 2007; Zitzmann, Saad, & Nieschlag, 2006). There is evidence that transdermal and intramuscular testosterone achieve similar masculinizing results, although the timeframe may be somewhat slower with transdermal preparations (Feldman, 2005, April). Especially as patients age, the goal is to use the lowest dose needed to maintain the desired clinical result, with appropriate precautions being made to maintain bone density.

Other agents

Progestins, most commonly medroxyprogesterone, can be used for a short period of time to assist with menstrual cessation early in hormone therapy. GnRH agonists can be used similarly, as well as for refractory uterine bleeding in patients without an underlying gynecological abnormality.

Bioidentical and Compounded Hormones

As discussion surrounding the use of bioidentical hormones in postmenopausal hormone replacement has heightened, interest has also increased in the use of similar compounds in feminizing/masculinizing hormone therapy. There is no evidence that custom compounded bioidentical hormones are safer or more effective than government agency-approved bioidentical hormones (Sood, Shuster, Smith, Vincent, & Jatoi, 2011). Therefore, it has been advised by the North American Menopause Society (2010) and others to assume that, whether the hormone is from a compounding pharmacy or not, if the active ingredients are similar, it should have a similar side-effect profile. WPATH concurs with this assessment.

IX
Reproductive Health

Many transgender, transsexual, and gender-nonconforming people will want to have children. Because feminizing/masculinizing hormone therapy limits fertility (Darney, 2008; Zhang, Gu, Wang, Cui, & Bremner, 1999), it is desirable for patients to make decisions concerning fertility before starting hormone therapy or undergoing surgery to remove/alter their reproductive organs. Cases are known of people who received hormone therapy and genital surgery and later regretted their inability to parent genetically related children (De Sutter, Kira, Verschoor, & Hotimsky, 2002).

Health care professionals—including mental health professionals recommending hormone therapy or surgery, hormone-prescribing physicians, and surgeons—should discuss reproductive options with patients prior to initiation of these medical treatments for gender dysphoria. These discussions should occur even if patients are not interested in these issues at the time of treatment, which may be more common for younger patients (De Sutter, 2009). Early discussions are desirable, but not always possible. If an individual has not had complete sex reassignment surgery, it may be possible to stop hormones long enough for natal hormones to recover, allowing

the production of mature gametes (Payer, Meyer, & Walker, 1979; Van den Broecke, Van der Elst, Liu, Hovatta, & Dhont, 2001).

Besides debate and opinion papers, very few research papers have been published on the reproductive health issues of individuals receiving different medical treatments for gender dysphoria. Another group who faces the need to preserve reproductive function in light of loss or damage to their gonads are people with malignancies that require removal of reproductive organs or use of damaging radiation or chemotherapy. Lessons learned from that group can be applied to people treated for gender dysphoria.

MtF patients, especially those who have not already reproduced, should be informed about sperm-preservation options and encouraged to consider banking their sperm prior to hormone therapy. In a study examining testes that were exposed to high-dose estrogen (Payer et al., 1979), findings suggest that stopping estrogen may allow the testes to recover. In an article reporting on the opinions of MtF individuals towards sperm freezing (De Sutter et al., 2002), the vast majority of 121 survey respondents felt that the availability of freezing sperm should be discussed and offered by the medical world. Sperm should be collected before hormone therapy or after stopping the therapy until the sperm count rises again. Cryopreservation should be discussed even if there is poor semen quality. In adults with azoospermia, a testicular biopsy with subsequent cryopreservation of biopsied material for sperm is possible, but may not be successful.

Reproductive options for FtM patients might include oocyte (egg) or embryo freezing. The frozen gametes and embryo could later be used with a surrogate woman to carry to pregnancy. Studies of women with polycystic ovarian disease suggest that the ovary can recover in part from the effects of high testosterone levels (Hunter & Sterrett, 2000). Stopping the testosterone briefly might allow for ovaries to recover enough to release eggs; success likely depends on the patient's age and duration of testosterone treatment. While not systematically studied, some FtM individuals are doing exactly that, and some have been able to become pregnant and deliver children (More, 1998).

Patients should be advised that these techniques are not available everywhere and can be very costly. Transsexual, transgender, and gender-nonconforming people should not be refused reproductive options for any reason.

A special group of individuals are prepubertal or pubertal adolescents who will never develop reproductive function in their natal sex due to blockers or cross-gender hormones. At this time there is no technique for preserving function from the gonads of these individuals.

X

Voice and Communication Therapy

Communication, both verbal and nonverbal, is an important aspect of human behavior and gender expression. Transsexual, transgender, and gender-nonconforming people might seek the assistance of a voice and communication specialist to develop vocal characteristics (e.g., pitch, intonation, resonance, speech rate, phrasing patterns) and non-verbal communication patterns (e.g., gestures, posture/movement, facial expressions) that facilitate comfort with their gender identity. Voice and communication therapy may help to alleviate gender dysphoria and be a positive and motivating step towards achieving one's goals for gender role expression.

Competency of Voice and Communication Specialists Working with Transsexual, Transgender, and Gender-Nonconforming Clients

Specialists may include speech-language pathologists, speech therapists, and speech-voice clinicians. In most countries the professional association for speech-language pathologists requires specific qualifications and credentials for membership. In some countries the government regulates practice through licensing, certification, or registration processes (American Speech-Language-Hearing Association, 2011; Canadian Association of Speech-Language Pathologists and Audiologists; Royal College of Speech Therapists, United Kingdom; Speech Pathology Australia).

The following are recommended minimum credentials for voice and communication specialists working with transsexual, transgender, and gender-nonconforming clients:

1. Specialized training and competence in the assessment and development of communication skills in transsexual, transgender, and gender-nonconforming clients.

2. A basic understanding of transgender health, including hormonal and surgical treatments for feminization/masculinization and trans-specific psychosocial issues as outlined in the *SOC*; and familiarity with basic sensitivity protocols such as the use of preferred gender pronoun and name (Canadian Association of Speech-Language Pathologists and Audiologists; Royal College of Speech Therapists, United Kingdom; Speech Pathology Australia).

3. Continuing education in the assessment and development of communication skills in transsexual, transgender, and gender-nonconforming clients. This may include attendance at professional meetings, workshops, or seminars; participation in research related to gender identity issues; independent study; or mentoring from an experienced, certified clinician.

Other professionals such as vocal coaches, theatre professionals, singing teachers, and movement experts may play a valuable adjunct role. Such professionals will ideally have experience working with, or be actively collaborating with, speech-language pathologists.

Assessment and Treatment Considerations

The overall purpose of voice and communication therapy is to help clients adapt their voice and communication in a way that is both safe and authentic, resulting in communication patterns that clients feel are congruent with their gender identity and that reflect their sense of self (Adler, Hirsch, & Mordaunt, 2006). It is essential that voice and communication specialists be sensitive to individual communication preferences. Communication—style, voice, choice of language, etc.—is personal. Individuals should not be counseled to adopt behaviors with which they are not comfortable or which do not feel authentic. Specialists can best serve their clients by taking the time to understand a person's gender concerns and goals for gender-role expression (American Speech-Language-Hearing Association, 2011; Canadian Association of Speech-Language Pathologists and Audiologists; Royal College of Speech Therapists, United Kingdom; Speech Pathology Australia).

Individuals may choose the communication behaviors that they wish to acquire in accordance with their gender identity. These decisions are also informed and supported by the knowledge of the voice and communication specialist and by the assessment data for a specific client (Hancock, Krissinger, & Owen, 2010). Assessment includes a client's self-evaluation and a specialist's evaluation of voice, resonance, articulation, spoken language, and non-verbal communication (Adler et al., 2006; Hancock et al., 2010).

Voice-and-communication treatment plans are developed by considering the available research evidence, the clinical knowledge and experience of the specialist, and the client's own goals and values (American Speech-Language-Hearing Association, 2011; Canadian Association of Speech-Language Pathologists and Audiologists; Royal College of Speech Therapists, United Kingdom; Speech Pathology Australia). Targets of treatment typically include pitch, intonation, loudness and stress patterns, voice quality, resonance, articulation, speech rate and phrasing, language, and nonverbal communication (Adler et al., 2006; Davies & Goldberg, 2006; de Bruin, Coerts, & Greven, 2000; Gelfer, 1999; McNeill, 2006; Oates & Dacakis, 1983). Treatment may involve individual and/or group sessions. The frequency and duration of treatment will vary according to a client's needs. Existing protocols for voice-and-communication treatment can be considered in

developing an individualized therapy plan (Carew, Dacakis, & Oates, 2007; Dacakis, 2000; Davies & Goldberg, 2006; Gelfer, 1999; McNeill, Wilson, Clark, & Deakin, 2008; Mount & Salmon, 1988).

Feminizing or masculinizing the voice involves non-habitual use of the voice production mechanism. Prevention measures are necessary to avoid the possibility of vocal misuse and long-term vocal damage. All voice and communication therapy services should therefore include a vocal health component (Adler et al., 2006).

Vocal Health Considerations After Voice Feminization Surgery

As noted in section XI, some transsexual, transgender, and gender-nonconforming people will undergo voice feminization surgery. (Voice deepening can be achieved through masculinizing hormone therapy, but feminizing hormones do not have an impact on the adult MtF voice.) There are varying degrees of satisfaction, safety, and long-term improvement in patients who have had such surgery. It is recommended that individuals undergoing voice feminization surgery also consult a voice and communication specialist to maximize the surgical outcome, help protect vocal health, and learn nonpitch related aspects of communication. Voice surgery procedures should include follow-up sessions with a voice and communication specialist who is licensed and/or credentialed by the board responsible for speech therapists/speech-language pathologists in that country (Kanagalingam et al., 2005; Neumann & Welzel, 2004).

XI
Surgery

Sex Reassignment Surgery Is Effective and Medically Necessary

Surgery – particularly genital surgery – is often the last and the most considered step in the treatment process for gender dysphoria. While many transsexual, transgender, and gender-nonconforming individuals find comfort with their gender identity, role, and expression without surgery, for many others surgery is essential and medically necessary to alleviate their gender dysphoria (Hage & Karim, 2000). For the latter group, relief from gender dysphoria cannot be achieved

without modification of their primary and/or secondary sex characteristics to establish greater congruence with their gender identity. Moreover, surgery can help patients feel more at ease in the presence of sex partners or in venues such as physicians' offices, swimming pools, or health clubs. In some settings, surgery might reduce risk of harm in the event of arrest or search by police or other authorities.

Follow-up studies have shown an undeniable beneficial effect of sex reassignment surgery on postoperative outcomes such as subjective well-being, cosmesis, and sexual function (De Cuypere et al., 2005; Gijs & Brewaeys, 2007; Klein & Gorzalka, 2009; Pfäfflin & Junge, 1998). Additional information on the outcomes of surgical treatments are summarized in Appendix D.

Ethical Questions Regarding Sex Reassignment Surgery

In ordinary surgical practice, pathological tissues are removed to restore disturbed functions, or alterations are made to body features to improve a patient's self image. Some people, including some health professionals, object on ethical grounds to surgery as a treatment for gender dysphoria, because these conditions are thought not to apply.

It is important that health professionals caring for patients with gender dysphoria feel comfortable about altering anatomically normal structures. In order to understand how surgery can alleviate the psychological discomfort and distress of individuals with gender dysphoria, professionals need to listen to these patients discuss their symptoms, dilemmas, and life histories. The resistance against performing surgery on the ethical basis of "above all do no harm" should be respected, discussed, and met with the opportunity to learn from patients themselves about the psychological distress of having gender dysphoria and the potential for harm caused by denying access to appropriate treatments.

Genital and breast/chest surgical treatments for gender dysphoria are not merely another set of elective procedures. Typical elective procedures involve only a private mutually consenting contract between a patient and a surgeon. Genital and breast/chest surgeries as medically necessary treatments for gender dysphoria are to be undertaken only after assessment of the patient by qualified mental health professionals, as outlined in section VII of the *SOC*. These surgeries may be performed once there is written documentation that this assessment has occurred and that the person has met the criteria for a specific surgical treatment. By following this procedure, mental health professionals, surgeons, and patients share responsibility for the decision to make irreversible changes to the body.

It is unethical to deny availability or eligibility for sex reassignment surgeries solely on the basis of blood seropositivity for blood-borne infections such as HIV or hepatitis C or B.

Relationship of Surgeons with Mental Health Professionals, Hormone-Prescribing Physicians (if Applicable), and Patients (Informed Consent)

The role of a surgeon in the treatment of gender dysphoria is not that of a mere technician. Rather, conscientious surgeons will have insight into each patient's history and the rationale that led to the referral for surgery. To that end, surgeons must talk at length with their patients and have close working relationships with other health professionals who have been actively involved in their clinical care.

Consultation is readily accomplished when a surgeon practices as part of an interdisciplinary health care team. In the absence of this, a surgeon must be confident that the referring mental health professional(s), and if applicable the physician who prescribes hormones, is/are competent in the assessment and treatment of gender dysphoria, because the surgeon is relying heavily on his/her/their expertise.

Once a surgeon is satisfied that the criteria for specific surgeries have been met (as outlined below), surgical treatment should be considered and a preoperative surgical consultation should take place. During this consultation, the procedure and postoperative course should be extensively discussed with the patient. Surgeons are responsible for discussing all of the following with patients seeking surgical treatments for gender dysphoria:

- The different surgical techniques available (with referral to colleagues who provide alternative options);
- The advantages and disadvantages of each technique;
- The limitations of a procedure to achieve "ideal" results; surgeons should provide a full range of before-and-after photographs of their own patients, including both successful and unsuccessful outcomes;
- The inherent risks and possible complications of the various techniques; surgeons should inform patients of their own complication rates with each procedure.

These discussions are the core of the informed consent process, which is both an ethical and legal requirement for any surgical procedure. Ensuring that patients have a realistic expectation of outcomes is important in achieving a result that will alleviate their gender dysphoria.

All of this information should be provided to patients in writing, in a language in which they are fluent, and in graphic illustrations. Patients should receive the information in advance (possibly

via the Internet) and be given ample time to review it carefully. The elements of informed consent should always be discussed face-to-face prior to the surgical intervention. Questions can then be answered and written informed consent can be provided by the patient. Because these surgeries are irreversibile, care should be taken to ensure that patients have sufficient time to absorb information fully before they are asked to provide informed consent. A minimum of 24 hours is suggested.

Surgeons should provide immediate aftercare and consultation with other physicians serving the patient in the future. Patients should work with their surgeon to develop an adequate aftercare plan for the surgery.

Overview of Surgical Procedures for the Treatment of Patients with Gender Dysphoria

For the Male-to-Female (MtF) Patient, Surgical Procedures May Include the Following:

1. Breast/chest surgery: augmentation mammoplasty (implants/lipofilling);

2. Genital surgery: penectomy, orchiectomy, vaginoplasty, clitoroplasty, vulvoplasty;

3. Nongenital, nonbreast surgical interventions: facial feminization surgery, liposuction, lipofilling, voice surgery, thyroid cartilage reduction, gluteal augmentation (implants/lipofilling), hair reconstruction, and various aesthetic procedures.

For the Female-to-Male (FtM) Patient, Surgical Procedures May Include the Following:

1. Breast/chest surgery: subcutaneous mastectomy, creation of a male chest;

2. Genital surgery: hysterectomy/salpingo-oophorectomy, reconstruction of the fixed part of the urethra, which can be combined with a metoidioplasty or with a phalloplasty (employing a pedicled or free vascularized flap), vaginectomy, scrotoplasty, and implantation of erection and/or testicular prostheses;

3. Nongenital, nonbreast surgical interventions: voice surgery (rare), liposuction, lipofilling, pectoral implants, and various aesthetic procedures.

Reconstructive Versus Aesthetic Surgery

The question of whether sex reassignment surgery should be considered "aesthetic" surgery or "reconstructive" surgery is pertinent not only from a philosophical point of view, but also from a financial point of view. Aesthetic or cosmetic surgery is mostly regarded as not medically necessary and therefore is typically paid for entirely by the patient. In contrast, reconstructive procedures are considered medically necessary—with unquestionable therapeutic results—and thus paid for partially or entirely by national health systems or insurance companies.

Unfortunately, in the field of plastic and reconstructive surgery (both in general and specifically for gender-related surgeries), there is no clear distinction between what is purely reconstructive and what is purely cosmetic. Most plastic surgery procedures actually are a mixture of both reconstructive and cosmetic components.

While most professionals agree that genital surgery and mastectomy cannot be considered purely cosmetic, opinions diverge as to what degree other surgical procedures (e.g., breast augmentation, facial feminization surgery) can be considered purely reconstructive. Although it may be much easier to see a phalloplasty or a vaginoplasty as an intervention to end lifelong suffering, for certain patients an intervention like a reduction rhinoplasty can have a radical and permanent effect on their quality of life, and therefore is much more medically necessary than for somebody without gender dysphoria.

Criteria for Surgeries

As for all of the *SOC*, the criteria for initiation of surgical treatments for gender dysphoria were developed to promote optimal patient care. While the *SOC* allow for an individualized approach to best meet a patient's health care needs, a criterion for all breast/chest and genital surgeries is documentation of persistent gender dysphoria by a qualified mental health professional. For some surgeries, additional criteria include preparation and treatment consisting of feminizing/masculinizing hormone therapy and one year of continuous living in a gender role that is congruent with one's gender identity.

These criteria are outlined below. Based on the available evidence and expert clinical consensus, different recommendations are made for different surgeries.

The *SOC* do not specify an order in which different surgeries should occur. The number and sequence of surgical procedures may vary from patient to patient, according to their clinical needs.

Criteria for Breast/Chest Surgery (One Referral)

Criteria for mastectomy and creation of a male chest in FtM patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Hormone therapy is not a prerequisite.

Criteria for breast augmentation (implants/lipofilling) in MtF patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Although not an explicit criterion, it is recommended that MtF patients undergo feminizing hormone therapy (minimum 12 months) prior to breast augmentation surgery. The purpose is to maximize breast growth in order to obtain better surgical (aesthetic) results.

Criteria for Genital Surgery (Two Referrals)

The criteria for genital surgery are specific to the type of surgery being requested.

Criteria for hysterectomy and salpingo-oophorectomy in FtM patients and for orchiectomy in MtF patients:

1. Persistent, well-documented gender dysphoria;

2. Capacity to make a fully informed decision and to consent for treatment;

3. Age of majority in a given country;

4. If significant medical or mental health concerns are present, they must be well controlled.

5. 12 continuous months of hormone therapy as appropriate to the patient's gender goals (unless hormones are not clinically indicated for the individual).

The aim of hormone therapy prior to gonadectomy is primarily to introduce a period of reversible estrogen or testosterone suppression, before the patient undergoes irreversible surgical intervention.

These criteria do not apply to patients who are having these procedures for medical indications other than gender dysphoria.

Criteria for metoidioplasty or phalloplasty in FtM patients and for vaginoplasty in MtF patients:

1. Persistent, well-documented gender dysphoria;

2. Capacity to make a fully informed decision and to consent for treatment;

3. Age of majority in a given country;

4. If significant medical or mental health concerns are present, they must be well controlled;

5. 12 continuous months of hormone therapy as appropriate to the patient's gender goals (unless hormones are not clinically indicated for the individual).

6. 12 continuous months of living in a gender role that is congruent with their gender identity.

Although not an explicit criterion, it is recommended that these patients also have regular visits with a mental health or other medical professional.

Rationale for a preoperative, 12-month experience of living in an identity-congruent gender role:

The criterion noted above for some types of genital surgeries—i.e., that patients engage in 12 continuous months of living in a gender role that is congruent with their gender identity—is based on expert clinical consensus that this experience provides ample opportunity for patients to experience and socially adjust in their desired gender role, before undergoing irreversible surgery. As noted in section VII, the social aspects of changing one's gender role are usually challenging—

often more so than the physical aspects. Changing gender role can have profound personal and social consequences, and the decision to do so should include an awareness of what the familial, interpersonal, educational, vocational, economic, and legal challenges are likely to be, so that people can function successfully in their gender role. Support from a qualified mental health professional and from peers can be invaluable in ensuring a successful gender role adaptation (Bockting, 2008).

The duration of 12 months allows for a range of different life experiences and events that may occur throughout the year (e.g., family events, holidays, vacations, season-specific work or school experiences). During this time, patients should present consistently, on a day-to-day basis and across all settings of life, in their desired gender role. This includes coming out to partners, family, friends, and community members (e.g., at school, work, other settings).

Health professionals should clearly document a patient's experience in the gender role in the medical chart, including the start date of living full time for those who are preparing for genital surgery. In some situations, if needed, health professionals may request verification that this criterion has been fulfilled: They may communicate with individuals who have related to the patient in an identity-congruent gender role, or request documentation of a legal name and/or gender marker change, if applicable.

Surgery for People with Psychotic Conditions and Other Serious Mental Illnesses

When patients with gender dysphoria are also diagnosed with severe psychiatric disorders and impaired reality testing (e.g., psychotic episodes, bipolar disorder, dissociative identity disorder, borderline personality disorder), an effort must be made to improve these conditions with psychotropic medications and/or psychotherapy before surgery is contemplated. (Dhejne et al., 2011). Reevaluation by a mental health professional qualified to assess and manage psychotic conditions should be conducted prior to surgery, describing the patient's mental status and readiness for surgery. It is preferable that this mental health professional be familiar with the patient. No surgery should be performed while a patient is actively psychotic (De Cuypere & Vercruysse, 2009).

Competency of Surgeons Performing Breast/Chest or Genital Surgery

Physicians who perform surgical treatments for gender dysphoria should be urologists, gynecologists, plastic surgeons, or general surgeons, and board-certified as such by the relevant national

and/or regional association. Surgeons should have specialized competence in genital reconstructive techniques as indicated by documented supervised training with a more experienced surgeon. Even experienced surgeons must be willing to have their surgical skills reviewed by their peers. An official audit of surgical outcomes and publication of these results would be greatly reassuring to both referring health professionals and patients. Surgeons should regularly attend professional meetings where new techniques are presented. The internet is often effectively used by patients to share information on their experience with surgeons and their teams.

Ideally, surgeons should be knowledgeable about more than one surgical technique for genital reconstruction so that they, in consultation with patients, can choose the ideal technique for each individual. Alternatively, if a surgeon is skilled in a single technique and this procedure is either not suitable for or desired by a patient, the surgeon should inform the patient about other procedures and offer referral to another appropriately skilled surgeon.

Breast/Chest Surgery Techniques and Complications

Although breast/chest appearance is an important secondary sex characteristic, breast presence or size is not involved in the legal definitions of sex and gender and is not necessary for reproduction. The performance of breast/chest operations for treatment of gender dysphoria should be considered with the same care as beginning hormone therapy, as both produce relatively irreversible changes to the body.

For the MtF patient, a breast augmentation (sometimes called "chest reconstruction") is not different from the procedure in a natal female patient. It is usually performed through implantation of breast prostheses and occasionally with the lipofilling technique. Infections and capsular fibrosis are rare complications of augmentation mammoplasty in MtF patients (Kanhai, Hage, Karim, & Mulder, 1999).

For the FtM patient, a mastectomy or "male chest contouring" procedure is available. For many FtM patients, this is the only surgery undertaken. When the amount of breast tissue removed requires skin removal, a scar will result and the patient should be so informed. Complications of subcutaneous mastectomy can include nipple necrosis, contour irregularities, and unsightly scarring (Monstrey et al., 2008).

Genital Surgery Techniques and Complications

Genital surgical procedures for the MtF patient may include orchiectomy, penectomy, vaginoplasty, clitoroplasty, and labiaplasty. Techniques include penile skin inversion, pedicled colosigmoid

transplant, and free skin grafts to line the neovagina. Sexual sensation is an important objective in vaginoplasty, along with creation of a functional vagina and acceptable cosmesis.

Surgical complications of MtF genital surgery may include complete or partial necrosis of the vagina and labia, fistulas from the bladder or bowel into the vagina, stenosis of the urethra, and vaginas that are either too short or too small for coitus. While the surgical techniques for creating a neovagina are functionally and aesthetically excellent, anorgasmia following the procedure has been reported, and a second stage labiaplasty may be needed for cosmesis (Klein & Gorzalka, 2009; Lawrence, 2006).

Genital surgical procedures for FtM patients may include hysterectomy, salpingo-oophorectomy, vaginectomy, metoidioplasty, scrotoplasty, urethroplasty, placement of testicular prostheses, and phalloplasty. For patients without former abdominal surgery, the laparoscopic technique for hysterectomy and salpingo-oophorectomy is recommended to avoid a lower-abdominal scar. Vaginal access may be difficult as most patients are nulliparous and have often not experienced penetrative intercourse. Current operative techniques for phalloplasty are varied. The choice of techniques may be restricted by anatomical or surgical considerations and by a client's financial considerations. If the objectives of phalloplasty are a neophallus of good appearance, standing micturition, sexual sensation, and/or coital ability, patients should be clearly informed that there are several separate stages of surgery and frequent technical difficulties, which may require additional operations. Even metoidioplasty, which in theory is a one-stage procedure for construction of a microphallus, often requires more than one operation. The objective of standing micturition with this technique can not always be ensured (Monstrey et al., 2009).

Complications of phalloplasty in FtMs may include frequent urinary tract stenoses and fistulas, and occasionally necrosis of the neophallus. Metoidioplasty results in a micropenis, without the capacity for standing urination. Phalloplasty, using a pedicled or a free vascularized flap, is a lengthy, multi-stage procedure with significant morbidity that includes frequent urinary complications and unavoidable donor site scarring. For this reason, many FtM patients never undergo genital surgery other than hysterectomy and salpingo-oophorectomy (Hage & De Graaf, 1993).

Even patients who develop severe surgical complications seldom regret having undergone surgery. The importance of surgery can be appreciated by the repeated finding that quality of surgical results is one of the best predictors of the overall outcome of sex reassignment (Lawrence, 2006).

Other Surgeries

Other surgeries for assisting in body feminization include reduction thyroid chondroplasty (reduction of the Adam's apple), voice modification surgery, suction-assisted lipoplasty (contour

modeling) of the waist, rhinoplasty (nose correction), facial bone reduction, face-lift, and blepharoplasty (rejuvenation of the eyelid). Other surgeries for assisting in body masculinization include liposuction, lipofilling, and pectoral implants. Voice surgery to obtain a deeper voice is rare but may be recommended in some cases, such as when hormone therapy has been ineffective.

Although these surgeries do not require referral by mental health professionals, such professionals can play an important role in assisting clients in making a fully informed decision about the timing and implications of such procedures in the context of the social transition.

Although most of these procedures are generally labeled "purely aesthetic," these same operations in an individual with severe gender dysphoria can be considered medically necessary, depending on the unique clinical situation of a given patient's condition and life situation. This ambiguity reflects reality in clinical situations, and allows for individual decisions as to the need and desirability of these procedures.

XII

Postoperative Care and Follow-Up

Long-term postoperative care and follow-up after surgical treatments for gender dysphoria are associated with good surgical and psychosocial outcomes (Monstrey et al., 2009). Follow-up is important to a patient's subsequent physical and mental health and to a surgeon's knowledge about the benefits and limitations of surgery. Surgeons who operate on patients coming from long distances should include personal follow-up in their care plan and attempt to ensure affordable local long-term aftercare in their patients' geographic region.

Postoperative patients may sometimes exclude themselves from follow-up by specialty providers, including the hormone-prescribing physician (for patients receiving hormones), not recognizing that these providers are often best able to prevent, diagnose, and treat medical conditions that are unique to hormonally and surgically treated patients. The need for follow-up equally extends to mental health professionals, who may have spent a longer period of time with the patient than any other professional and therefore are in an excellent position to assist in any postoperative adjustment difficulties. Health professionals should stress the importance of postoperative follow-up care with their patients and offer continuity of care.

Postoperative patients should undergo regular medical screening according to recommended guidelines for their age. This is discussed more in the next section.

XIII

Lifelong Preventive and Primary Care

Transsexual, transgender, and gender-nonconforming people need health care throughout their lives. For example, to avoid the negative secondary effects of having a gonadectomy at a relatively young age and/or receiving long-term, high-dose hormone therapy, patients need thorough medical care by providers experienced in primary care and transgender health. If one provider is not able to provide all services, ongoing communication among providers is essential.

Primary care and health maintenance issues should be addressed before, during, and after any possible changes in gender role and medical interventions to alleviate gender dysphoria. While hormone providers and surgeons play important roles in preventive care, every transsexual, transgender, and gender-nonconforming person should partner with a primary care provider for overall health care needs (Feldman, 2007).

General Preventive Health Care

Screening guidelines developed for the general population are appropriate for organ systems that are unlikely to be affected by feminizing/masculinizing hormone therapy. However, in areas such as cardiovascular risk factors, osteoporosis, and some cancers (breast, cervical, ovarian, uterine, and prostate), such general guidelines may either over- or underestimate the cost-effectiveness of screening individuals who are receiving hormone therapy.

Several resources provide detailed protocols for the primary care of patients undergoing feminizing/masculinizing hormone therapy, including therapy that is provided after sex reassignment surgeries (Center of Excellence for Transgender Health, UCSF, 2011; Feldman & Goldberg, 2006; Feldman, 2007; Gorton, Buth, & Spade, 2005). Clinicians should consult their national evidence-based guidelines and discuss screening with their patients in light of the effects of hormone therapy on their baseline risk.

Cancer Screening

Cancer screening of organ systems that are associated with sex can present particular medical and psychosocial challenges for transsexual, transgender, and gender-nonconforming patients and their health care providers. In the absence of large-scale prospective studies, providers are unlikely to have enough evidence to determine the appropriate type and frequency of cancer screenings for this population. Over-screening results in higher health care costs, high false positive rates, and often unnecessary exposure to radiation and/or diagnostic interventions such as biopsies. Under-screening results in diagnostic delay for potentially treatable cancers. Patients may find cancer screening gender affirming (such as mammograms for MtF patients) or both physically and emotionally painful (such as Pap smears offer continuity of care for FtM patients).

Urogenital Care

Gynecologic care may be necessary for transsexual, transgender, and gender-nonconforming people of both sexes. For FtM patients, such care is needed predominantly for individuals who have not had genital surgery. For MtF patients, such care is needed after genital surgery. While many surgeons counsel patients regarding postoperative urogenital care, primary care clinicians and gynecologists should also be familiar with the special genital concerns of this population.

All MtF patients should receive counseling regarding genital hygiene, sexuality, and prevention of sexually transmitted infections; those who have had genital surgery should also be counseled on the need for regular vaginal dilation or penetrative intercourse in order to maintain vaginal depth and width (van Trotsenburg, 2009). Due to the anatomy of the male pelvis, the axis and the dimensions of the neovagina differ substantially from those of a biologic vagina. This anatomic difference can affect intercourse if not understood by MtF patients and their partners (van Trotsenburg, 2009).

Lower urinary tract infections occur frequently in MtF patients who have had surgery because of the reconstructive requirements of the shortened urethra. In addition, these patients may suffer from functional disorders of the lower urinary tract; such disorders may be caused by damage of the autonomous nerve supply of the bladder floor during dissection between the rectum and the bladder, and by a change of the position of the bladder itself. A dysfunctional bladder (e.g., overactive bladder, stress or urge urinary incontinence) may occur after sex reassignment surgery (Hoebeke et al., 2005; Kuhn, Hiltebrand, & Birkhauser, 2007).

Most FtM patients do not undergo vaginectomy (colpectomy). For patients who take masculinizing hormones, despite considerable conversion of testosterone to estrogens, atrophic changes of the vaginal lining can be observed regularly and may lead to pruritus or burning. Examination can be

both physically and emotionally painful, but lack of treatment can seriously aggravate the situation. Gynecologists treating the genital complaints of FtM patients should be aware of the sensitivity that patients with a male gender identity and masculine gender expression might have around having genitals typically associated with the female sex.

XIV

Applicability of the *Standards of Care* to People Living in Institutional Environments

The *SOC* in their entirety apply to all transsexual, transgender, and gender-nonconforming people, irrespective of their housing situation. People should not be discriminated against in their access to appropriate health care based on where they live, including institutional environments such as prisons or long-/intermediate-term health care facilities (Brown, 2009). Health care for transsexual, transgender, and gender-nonconforming people living in an institutional environment should mirror that which would be available to them if they were living in a non-institutional setting within the same community.

All elements of assessment and treatment as described in the *SOC* can be provided to people living in institutions (Brown, 2009). Access to these medically necessary treatments should not be denied on the basis of institutionalization or housing arrangements. If the in-house expertise of health professionals in the direct or indirect employ of the institution does not exist to assess and/or treat people with gender dysphoria, it is appropriate to obtain outside consultation from professionals who are knowledgeable about this specialized area of health care.

People with gender dysphoria in institutions may also have coexisting mental health conditions (Cole et al., 1997). These conditions should be evaluated and treated appropriately.

People who enter an institution on an appropriate regimen of hormone therapy should be continued on the same, or similar, therapies and monitored according to the *SOC*. A "freeze frame" approach is not considered appropriate care in most situations *(Kosilek v. Massachusetts Department of Corrections/Maloney,* C.A. No. 92–12820-MLW, 2002). People with gender dysphoria who are deemed appropriate for hormone therapy (following the *SOC*) should be started on such therapy. The consequences of abrupt withdrawal of hormones or lack of initiation of hormone therapy when medically necessary include a high likelihood of negative outcomes such as surgical self-treatment by autocastration, depressed mood, dysphoria, and/or suicidality (Brown, 2010).

Reasonable accommodations to the institutional environment can be made in the delivery of care consistent with the *SOC*, if such accommodations do not jeopardize the delivery of medically necessary care to people with gender dysphoria. An example of a reasonable accommodation is the use of injectable hormones, if not medically contraindicated, in an environment where diversion of oral preparations is highly likely (Brown, 2009). Denial of needed changes in gender role or access to treatments, including sex reassignment surgery, on the basis of residence in an institution are not reasonable accommodations under the *SOC* (Brown, 2010).

Housing and shower/bathroom facilities for transsexual, transgender, and gender-nonconforming people living in institutions should take into account their gender identity and role, physical status, dignity, and personal safety. Placement in a single-sex housing unit, ward, or pod on the sole basis of the appearance of the external genitalia may not be appropriate and may place the individual at risk for victimization (Brown, 2009).

Institutions where transsexual, transgender, and gender-nonconforming people reside and receive health care should monitor for a tolerant and positive climate to ensure that residents are not under attack by staff or other residents.

XV

Applicability of the *Standards of Care* to People With Disorders of Sex Development

Terminology

The term *disorder of sex development* (DSD) refers to a somatic condition of atypical development of the reproductive tract (Hughes, Houk, Ahmed, Lee, & LWPES/ESPE Consensus Group, 2006). DSDs include the condition that used to be called *intersexuality*. Although the terminology was changed to DSD during an international consensus conference in 2005 (Hughes et al., 2006), disagreement about language use remains. Some people object strongly to the "disorder" label, preferring instead to view these congenital conditions as a matter of diversity (Diamond, 2009) and to continue using the terms *intersex* or *intersexuality*. In the *SOC*, WPATH uses the term DSD in an objective and value-free manner, with the goal of ensuring that health professionals recognize this medical term and use it to access relevant literature as the field progresses. WPATH remains

open to new terminology that will further illuminate the experience of members of this diverse population and lead to improvements in health care access and delivery.

Rationale for Addition to the *SOC*

Previously, individuals with a DSD who also met the *DSM-IV-TR's* behavioral criteria for Gender Identity Disorder (American Psychiatric Association, 2000) were excluded from that general diagnosis. Instead, they were categorized as having a "Gender Identity Disorder - Not Otherwise Specified." They were also excluded from the WPATH *Standards of Care*.

The current proposal for *DSM-5* (www.dsm5.org) is to replace the term *gender identity disorder* with *gender dysphoria*. Moreover, the proposed changes to the *DSM* consider gender dysphoric people with a DSD to have a subtype of gender dysphoria. This proposed categorization—which explicitly differentiates between gender dysphoric individuals with and without a DSD—is justified: In people with a DSD, gender dysphoria differs in its phenomenological presentation, epidemiology, life trajectories, and etiology (Meyer-Bahlburg, 2009).

Adults with a DSD and gender dysphoria have increasingly come to the attention of health professionals. Accordingly, a brief discussion of their care is included in this version of the *SOC*.

Health History Considerations

Health professionals assisting patients with both a DSD and gender dysphoria need to be aware that the medical context in which such patients have grown up is typically very different from that of people without a DSD.

Some people are recognized as having a DSD through the observation of gender-atypical genitals at birth. (Increasingly this observation is made during the prenatal period by way of imaging procedures such as ultrasound.) These infants then undergo extensive medical diagnostic procedures. After consultation among the family and health professionals—during which the specific diagnosis, physical and hormonal findings, and feedback from long-term outcome studies (Cohen-Kettenis, 2005; Dessens, Slijper, & Drop, 2005; Jurgensen, Hiort, Holterhus, & Thyen, 2007; Mazur, 2005; Meyer-Bahlburg, 2005; Stikkelbroeck et al., 2003; Wisniewski, Migeon, Malouf, & Gearhart, 2004) are considered—the newborn is assigned a sex, either male or female.

Other individuals with a DSD come to the attention of health professionals around the age of puberty through the observation of atypical development of secondary sex characteristics. This observation also leads to a specific medical evaluation.

The type of DSD and severity of the condition has significant implications for decisions about a patient's initial sex assignment, subsequent genital surgery, and other medical and psychosocial care (Meyer-Bahlburg, 2009). For instance, the degree of prenatal androgen exposure in individuals with a DSD has been correlated with the degree of masculinization of gender-related *behavior* (that is, *gender role and expression*); however, the correlation is only moderate, and considerable behavioral variability remains unaccounted for by prenatal androgen exposure (Jurgensen et al., 2007; Meyer-Bahlburg, Dolezal, Baker, Ehrhardt, & New, 2006). Notably, a similar correlation of prenatal hormone exposure with gender *identity* has not been demonstrated (e.g., Meyer-Bahlburg et al., 2004). This is underlined by the fact that people with the same (core) gender identity can vary widely in the degree of masculinization of their gender-related behavior.

Assessment and Treatment of Gender Dysphoria in People with Disorders of Sex Development

Very rarely are individuals with a DSD identified as having gender dysphoria *before* a DSD diagnosis has been made. Even so, a DSD diagnosis is typically apparent with an appropriate history and basic physical exam—both of which are part of a medical evaluation for the appropriateness of hormone therapy or surgical interventions for gender dysphoria. Mental health professionals should ask their clients presenting with gender dysphoria to have a physical exam, particularly if they are not currently seeing a primary care (or other health care) provider.

Most people with a DSD who are born with genital ambiguity do not develop gender dysphoria (e.g., Meyer-Bahlburg, Dolezal, et al., 2004; Wisniewski et al., 2004). However, some people with a DSD will develop chronic gender dysphoria and even undergo a change in their birth-assigned sex and/or their gender role (Meyer-Bahlburg, 2005; Wilson, 1999; Zucker, 1999). If there are persistent and strong indications that gender dysphoria is present, a comprehensive evaluation by clinicians skilled in the assessment and treatment of gender dysphoria is essential, irrespective of the patient's age. Detailed recommendations have been published for conducting such an assessment and for making treatment decisions to address gender dysphoria in the context of a DSD (Meyer-Bahlburg, 2011). Only after thorough assessment should steps be taken in the direction of changing a patient's birth-assigned sex or gender role.

Clinicians assisting these patients with treatment options to alleviate gender dysphoria may profit from the insights gained from providing care to patients without a DSD (Cohen-Kettenis, 2010).

However, certain criteria for treatment (e.g., age, duration of experience with living in the desired gender role) are usually not routinely applied to people with a DSD; rather, the criteria are interpreted in light of a patient's specific situation (Meyer-Bahlburg, 2011). In the context of a DSD, changes in birth-assigned sex and gender role have been made at any age between early elementary-school age and middle adulthood. Even genital surgery may be performed much earlier in these patients than in gender dysphoric individuals without a DSD if the surgery is well justified by the diagnosis, by the evidence-based gender-identity prognosis for the given syndrome and syndrome severity, and by the patient's wishes.

One reason for these treatment differences is that genital surgery in individuals with a DSD is quite common in infancy and adolescence. Infertility may already be present due to either early gonadal failure or to gonadectomy because of a malignancy risk. Even so, it is advisable for patients with a DSD to undergo a full social transition to another gender role only if there is a long-standing history of gender-atypical behavior, and if gender dysphoria and/or the desire to change one's gender role has been strong and persistent for a considerable period of time. Six months is the time period of full symptom expression required for the application of the gender dysphoria diagnosis proposed for *DSM-5* (Meyer-Bahlburg, 2011).

Additional Resources

The gender-relevant medical histories of people with a DSD are often complex. Their histories may include a great variety of inborn genetic, endocrine, and somatic atypicalities, as well as various hormonal, surgical, and other medical treatments. For this reason, many additional issues need to be considered in the psychosocial and medical care of such patients, regardless of the presence of gender dysphoria. Consideration of these issues is beyond what can be covered in the *SOC*. The interested reader is referred to existing publications (e.g., Cohen-Kettenis & Pfäfflin, 2003; Meyer-Bahlburg, 2002, 2008). Some families and patients also find it useful to consult or work with community support groups.

There is a very substantial medical literature on the medical management of patients with a DSD. Much of this literature has been produced by high-level specialists in pediatric endocrinology and urology, with input from specialized mental health professionals, especially in the area of gender. Recent international consensus conferences have addressed evidence-based care guidelines (including issues of gender and of genital surgery) for DSD in general (Hughes et al., 2006) and specifically for Congenital Adrenal Hyperplasia (Joint LWPES/ESPE CAH Working Group et al., 2002; Speiser et al., 2010). Others have addressed the research needs for DSD in general (Meyer-Bahlburg & Blizzard, 2004) and for selected syndromes such as 46,XXY (Simpson et al., 2003).

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APPENDIX A
GLOSSARY

Terminology in the area of health care for transsexual, transgender, and gender-nonconforming people is rapidly evolving; new terms are being introduced, and the definitions of existing terms are changing. Thus, there is often misunderstanding, debate, or disagreement about language in this field. Terms that may be unfamiliar or that have specific meanings in the *SOC* are defined below for the purpose of this document only. Others may adopt these definitions, but WPATH acknowledges that these terms may be defined differently in different cultures, communities, and contexts.

WPATH also acknowledges that many terms used in relation to this population are not ideal. For example, the terms *transsexual* and *transvestite*—and, some would argue, the more recent term *transgender*—have been applied to people in an objectifying fashion. Yet such terms have been more or less adopted by many people who are making their best effort to make themselves understood. By continuing to use these terms, WPATH intends only to ensure that concepts and processes are comprehensible, in order to facilitate the delivery of quality health care to transsexual, transgender, and gender-nonconforming people. WPATH remains open to new terminology that will further illuminate the experience of members of this diverse population and lead to improvements in health care access and delivery.

Bioidentical hormones: Hormones that are *structurally* identical to those found in the human body (ACOG Committee of Gynecologic Practice, 2005). The hormones used in bioidentical hormone therapy (BHT) are generally derived from plant sources and are structurally similar to endogenous human hormones, but they need to be commercially processed to become bioidentical.

Bioidentical compounded hormone therapy (BCHT): Use of hormones that are prepared, mixed, assembled, packaged, or labeled as a drug by a pharmacist and custom-made for a patient according to a physician's specifications. Government drug agency approval is not possible for each compounded product made for an individual consumer.

Cross-dressing (transvestism): Wearing clothing and adopting a gender role presentation that, in a given culture, is more typical of the other sex.

Disorders of sex development (DSD): Congenital conditions in which the development of chromosomal, gonadal, or anatomic sex is atypical. Some people strongly object to the "disorder" label and instead view these conditions as a matter of diversity (Diamond, 2009), preferring the terms *intersex* and *intersexuality*.

Female-to-Male (FtM): Adjective to describe individuals assigned female at birth who are changing or who have changed their body and/or gender role from birth-assigned female to a more masculine body or role.

Gender dysphoria: Distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics) (Fisk, 1974; Knudson, De Cuypere, & Bockting, 2010b).

Gender identity: A person's intrinsic sense of being male (a boy or a man), female (a girl or woman), or an alternative gender (e.g., boygirl, girlboy, transgender, genderqueer, eunuch) (Bockting, 1999; Stoller, 1964).

Gender identity disorder: Formal diagnosis set forth by the *Diagnostic Statistical Manual of Mental Disorders, 4th Edition, Text Rev (DSM IV-TR)* (American Psychiatric Association, 2000). Gender identity disorder is characterized by a strong and persistent cross-gender identification and a persistent discomfort with one's sex or sense of inappropriateness in the gender role of that sex, causing clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Gender-nonconforming: Adjective to describe individuals whose gender identity, role, or expression differs from what is normative for their assigned sex in a given culture and historical period.

Gender role or expression: Characteristics in personality, appearance, and behavior that in a given culture and historical period are designated as masculine or feminine (that is, more typical of the male or female social role) (Ruble, Martin, & Berenbaum, 2006). While most individuals present socially in clearly masculine or feminine gender roles, some people present in an alternative gender role such as genderqueer or specifically transgender. All people tend to incorporate both masculine and feminine characteristics in their gender expression in varying ways and to varying degrees (Bockting, 2008).

Genderqueer: Identity label that may be used by individuals whose gender identity and/or role does not conform to a binary understanding of gender as limited to the categories of man or woman, male or female (Bockting, 2008).

Internalized transphobia: Discomfort with one's own transgender feelings or identity as a result of internalizing society's normative gender expectations.

Male-to-Female (MtF): Adjective to describe individuals assigned male at birth who are changing or who have changed their body and/or gender role from birth-assigned male to a more feminine body or role.

Natural hormones: Hormones that are derived from natural *sources* such as plants or animals. Natural hormones may or may not be bioidentical.

Sex: Sex is assigned at birth as male or female, usually based on the appearance of the external genitalia. When the external genitalia are ambiguous, other components of sex (internal genitalia, chromosomal and hormonal sex) are considered in order to assign sex (Grumbach, Hughes, & Conte, 2003; MacLaughlin & Donahoe, 2004; Money & Ehrhardt, 1972; Vilain, 2000). For most people, gender identity and expression are consistent with their sex assigned at birth; for transsexual, transgender, and gender-nonconforming individuals, gender identity or expression differ from their sex assigned at birth.

Sex reassignment surgery (gender affirmation surgery): Surgery to change primary and/or secondary sex characteristics to affirm a person's gender identity. Sex reassignment surgery can be an important part of medically necessary treatment to alleviate gender dysphoria.

Transgender: Adjective to describe a diverse group of individuals who cross or transcend culturally defined categories of gender. The gender identity of transgender people differs to varying degrees from the sex they were assigned at birth (Bockting, 1999).

Transition: Period of time when individuals change from the gender role associated with their sex assigned at birth to a different gender role. For many people, this involves learning how to live socially in another gender role; for others this means finding a gender role and expression that are most comfortable for them. Transition may or may not include feminization or masculinization of the body through hormones or other medical procedures. The nature and duration of transition are variable and individualized.

Transsexual: Adjective (often applied by the medical profession) to describe individuals who seek to change or who have changed their primary and/or secondary sex characteristics through femininizing or masculinizing medical interventions (hormones and/or surgery), typically accompanied by a permanent change in gender role.

APPENDIX B
OVERVIEW OF MEDICAL RISKS OF HORMONE THERAPY

The risks outlined below are based on two comprehensive, evidence-based literature reviews of masculinizing/feminizing hormone therapy (Feldman & Safer, 2009; Hembree et al., 2009), along with a large cohort study (Asscheman et al., 2011). These reviews can serve as detailed references for providers, along with other widely recognized, published clinical materials (e.g., Dahl et al., 2006; Ettner et al., 2007).

Risks of Feminizing Hormone Therapy (MtF)

Likely Increased Risk:

Venous thromboembolic disease

- Estrogen use increases the risk of venous thromboembolic events (VTE), particularly in patients who are over age 40, smokers, highly sedentary, obese, and who have underlying thrombophilic disorders.
- This risk is increased with the additional use of third generation progestins.
- This risk is decreased with use of the transdermal (versus oral) route of estradiol administration, which is recommended for patients at higher risk of VTE.

Cardiovascular, cerebrovascular disease

- Estrogen use increases the risk of cardiovascular events in patients over age 50 with underlying cardiovascular risk factors. Additional progestin use may increase this risk.

Lipids

- Oral estrogen use may markedly increase triglycerides in patients, increasing the risk of pancreatitis and cardiovascular events.
- Different routes of administration will have different metabolic effects on levels of HDL cholesterol, LDL cholesterol and lipoprotein(a).
- In general, clinical evidence suggests that MtF patients with pre-existing lipid disorders may benefit from the use of transdermal rather than oral estrogen.

Liver/gallbladder

- Estrogen and cyproterone acetate use may be associated with transient liver enzyme elevations and, rarely, clinical hepatotoxicity.
- Estrogen use increases the risk of cholelithiasis (gall stones) and subsequent cholecystectomy.

Possible Increased Risk:

Type 2 diabetes mellitus

- Feminizing hormone therapy, particularly estrogen, may increase the risk of type 2 diabetes, particularly among patients with a family history of diabetes or other risk factors for this disease.

Hypertension

- Estrogen use may increase blood pressure, but the effect on incidence of overt hypertension is unknown.
- Spironolactone reduces blood pressure and is recommended for at-risk or hypertensive patients desiring feminization.

Prolactinoma

- Estrogen use increases the risk of hyperprolactinemia among MtF patients in the first year of treatment, but this risk is unlikely thereafter.
- High-dose estrogen use may promote the clinical appearance of preexisting but clinically unapparent prolactinoma.

Inconclusive or No Increased Risk:

Items in this category include those that may present risk, but for which the evidence is so minimal that no clear conclusion can be reached.

Breast cancer

- MtF persons who have taken feminizing hormones do experience breast cancer, but it is unknown how their degree of risk compares to that of persons born with female genitalia.
- Longer duration of feminizing hormone exposure (i.e., number of years taking estrogen preparations), family history of breast cancer, obesity (BMI >35), and the use of progestins likely influence the level of risk.

Other Side Effects of Feminizing Therapy:

The following effects may be considered minor or even desired, depending on the patient, but are clearly associated with feminizing hormone therapy.

Fertility and sexual function

- Feminizing hormone therapy may impair fertility.
- Feminizing hormone therapy may decrease libido.
- Feminizing hormone therapy reduces nocturnal erections, with variable impact on sexually stimulated erections.

Risks of Anti-Androgen Medications:

Feminizing hormone regimens often include a variety of agents that affect testosterone production or action. These include GnRH agonists, progestins (including cyproterone acetate), spironolactone, and 5-alpha reductase inhibitors. An extensive discussion of the specific risks of these agents is beyond the scope of the *SOC*. However, both spironolactone and cyproterone acetate are widely used and deserve some comment.

Cyproterone acetate is a progestational compound with anti-androgenic properties (Gooren, 2005; Levy et al., 2003). Although widely used in Europe, it is not approved for use in the United States because of concerns about hepatotoxicity (Thole, Manso, Salgueiro, Revuelta, & Hidalgo, 2004). Spironolactone is commonly used as an anti-androgen in feminizing hormone therapy, particularly in regions where cyproterone is not approved for use (Dahl et al., 2006; Moore et al., 2003; Tangpricha et al., 2003). Spironolactone has a long history of use in treating hypertension and congestive heart failure. Its common side effects include hyperkalemia, dizziness, and gastrointestinal symptoms (*Physicians' Desk Reference*, 2007).

Risks of Masculinizing Hormone Therapy (FtM)

Likely Increased Risk:

Polycythemia

- Masculinizing hormone therapy involving testosterone or other androgenic steroids increases the risk of polycythemia (hematocrit > 50%), particularly in patients with other risk factors.
- Transdermal administration and adaptation of dosage may reduce this risk.

Weight gain/visceral fat

- Masculinizing hormone therapy can result in modest weight gain, with an increase in visceral fat.

Possible Increased Risk:

Lipids

- Testosterone therapy decreases HDL, but variably affects LDL and triglycerides.
- Supraphysiologic (beyond normal male range) serum levels of testosterone, often found with extended intramuscular dosing, may worsen lipid profiles, whereas transdermal administration appears to be more lipid neutral.
- Patients with underlying polycystic ovarian syndrome or dyslipidemia may be at increased risk of worsening dyslipidemia with testosterone therapy.

Liver

- Transient elevations in liver enzymes may occur with testosterone therapy.
- Hepatic dysfunction and malignancies have been noted with oral methyltestosterone. However, methyltestosterone is no longer available in most countries and should no longer be used.

Psychiatric

Masculinizing therapy involving testosterone or other androgenic steroids may increase the risk of hypomanic, manic, or psychotic symptoms in patients with underlying psychiatric disorders that include such symptoms. This adverse event appears to be associated with higher doses or supraphysiologic blood levels of testosterone.

Inconclusive or No Increased Risk:

Items in this category include those that may present risk, but for which the evidence is so minimal that no clear conclusion can be reached.

Osteoporosis

- Testosterone therapy maintains or increases bone mineral density among FtM patients prior to oophorectomy, at least in the first three years of treatment.
- There is an increased risk of bone density loss after oophorectomy, particularly if testosterone therapy is interrupted or insufficient. This includes patients utilizing solely oral testosterone.

Cardiovascular

- Masculinizing hormone therapy at normal physiologic doses does not appear to increase the risk of cardiovascular events among healthy patients.
- Masculinizing hormone therapy may increase the risk of cardiovascular disease in patients with underlying risks factors.

Hypertension

- Masculinizing hormone therapy at normal physiologic doses may increase blood pressure but does not appear to increase the risk of hypertension.
- Patients with risk factors for hypertension, such as weight gain, family history, or polycystic ovarian syndrome, may be at increased risk.

Type 2 diabetes mellitus

- Testosterone therapy does not appear to increase the risk of type 2 diabetes among FtM patients overall, unless other risk factors are present.
- Testosterone therapy may further increase the risk of type 2 diabetes in patients with other risk factors, such as significant weight gain, family history, and polycystic ovarian syndrome. There are no data that suggest or show an increase in risk in those with risk factors for dyslipidemia.

Breast cancer

- Testosterone therapy in FtM patients does not increase the risk of breast cancer.

Cervical cancer

- Testosterone therapy in FtM patients does not increase the risk of cervical cancer, although it may increase the risk of minimally abnormal Pap smears due to atrophic changes.

Ovarian cancer

- Analogous to persons born with female genitalia with elevated androgen levels, testosterone therapy in FtM patients may increase the risk of ovarian cancer, although evidence is limited.

Endometrial (uterine) cancer

- Testosterone therapy in FtM patients may increase the risk of endometrial cancer, although evidence is limited.

Other Side Effects of Masculinizing Therapy:

The following effects may be considered minor or even desired, depending on the patient, but are clearly associated with masculinization.

Fertility and sexual function

- Testosterone therapy in FtM patients reduces fertility, although the degree and reversibility are unknown.

- Testosterone therapy can induce permanent anatomic changes in the developing embryo or fetus.
- Testosterone therapy induces clitoral enlargement and increases libido.

Acne, androgenic alopecia

Acne and varying degrees of male pattern hair loss (androgenic alopecia) are common side effects of masculinizing hormone therapy.

APPENDIX C
SUMMARY OF CRITERIA FOR HORMONE THERAPY AND SURGERIES

As for all previous versions of the *SOC*, the criteria put forth in the *SOC* for hormone therapy and surgical treatments for gender dysphoria are clinical guidelines; individual health professionals and programs may modify them. Clinical departures from the *SOC* may come about because of a patient's unique anatomic, social, or psychological situation; an experienced health professional's evolving method of handling a common situation; a research protocol; lack of resources in various parts of the world; or the need for specific harm-reduction strategies. These departures should be recognized as such, explained to the patient, and documented through informed consent for quality patient care and legal protection. This documentation is also valuable to accumulate new data, which can be retrospectively examined to allow for health care—and the *SOC*—to evolve.

Criteria for Feminizing/Masculinizing Hormone Therapy (One Referral or Chart Documentation of Psychosocial Assessment)

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to give consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* for children and adolescents);
4. If significant medical or mental concerns are present, they must be reasonably well controlled.

Criteria for Breast/Chest Surgery (One Referral)

Mastectomy and Creation of a Male Chest in FtM Patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to give consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Hormone therapy is not a prerequisite.

Breast Augmentation (Implants/Lipofilling) in MtF Patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to give consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Although not an explicit criterion, it is recommended that MtF patients undergo feminizing hormone therapy (minimum 12 months) prior to breast augmentation surgery. The purpose is to maximize breast growth in order to obtain better surgical (aesthetic) results.

Criteria for Genital Surgery (Two Referrals)

Hysterectomy and Salpingo-Oophorectomy in FtM Patients and Orchiectomy in MtF Patients:

1. Persistent, well documented gender dysphoria;
2. Capacity to make a fully informed decision and to give consent for treatment;

3. Age of majority in a given country;

4. If significant medical or mental health concerns are present, they must be well controlled;

5. 12 continuous months of hormone therapy as appropriate to the patient's gender goals (unless hormones are not clinically indicated for the individual).

The aim of hormone therapy prior to gonadectomy is primarily to introduce a period of reversible estrogen or testosterone suppression, before a patient undergoes irreversible surgical intervention.

These criteria do not apply to patients who are having these surgical procedures for medical indications other than gender dysphoria.

Metoidioplasty or Phalloplasty in FtM Patients and Vaginoplasty in MtF Patients:

1. Persistent, well documented gender dysphoria;

2. Capacity to make a fully informed decision and to give consent for treatment;

3. Age of majority in a given country;

4. If significant medical or mental health concerns are present, they must be well controlled;

5. 12 continuous months of hormone therapy as appropriate to the patient's gender goals (unless hormones are not clinically indicated for the individual);

6. 12 continuous months of living in a gender role that is congruent with their gender identity.

Although not an explicit criterion, it is recommended that these patients also have regular visits with a mental health or other medical professional.

The criterion noted above for some types of genital surgeries—that is, that patients engage in 12 continuous months of living in a gender role that is congruent with their gender identity—is based on expert clinical consensus that this experience provides ample opportunity for patients to experience and socially adjust in their desired gender role, before undergoing irreversible surgery.

APPENDIX D
EVIDENCE FOR CLINICAL OUTCOMES OF THERAPEUTIC APPROACHES

One of the real supports for any new therapy is an outcome analysis. Because of the controversial nature of sex reassignment surgery, this type of analysis has been very important. Almost all of the outcome studies in this area have been retrospective.

One of the first studies to examine the post-treatment psychosocial outcomes of transsexual patients was done in 1979 at Johns Hopkins University School of Medicine and Hospital (USA) (J. K. Meyer & Reter, 1979). This study focused on patients' occupational, educational, marital, and domiciliary stability. The results revealed several significant changes with treatment. These changes were not seen as positive; rather, they showed that many individuals who had entered the treatment program were no better off or were worse off in many measures after participation in the program. These findings resulted in closure of the treatment program at that hospital/medical school (Abramowitz, 1986).

Subsequently, a significant number of health professionals called for a standard for eligibility for sex reassignment surgery. This led to the formulation of the original *Standards of Care* of the Harry Benjamin International Gender Dysphoria Association (now WPATH) in 1979.

In 1981, Pauly published results from a large retrospective study of people who had undergone sex reassignment surgery. Participants in that study had much better outcomes: Among 83 FtM patients, 80.7% had a satisfactory outcome (i.e., patient self report of "improved social and emotional adjustment"), 6.0% unsatisfactory. Among 283 MtF patients, 71.4% had a satisfactory outcome, 8.1% unsatisfactory. This study included patients who were treated before the publication and use of the *Standards of Care*.

Since the *Standards of Care* have been in place, there has been a steady increase in patient satisfaction and decrease in dissatisfaction with the outcome of sex reassignment surgery. Studies conducted after 1996 focused on patients who were treated according to the *Standards of Care*. The findings of Rehman and colleagues (1999) and Krege and colleagues (2001) are typical of this body of work; none of the patients in these studies regretted having had surgery, and most reported being satisfied with the cosmetic and functional results of the surgery. Even patients who develop severe surgical complications seldom regret having undergone surgery. Quality of surgical results is one of the best predictors of the overall outcome of sex reassignment (Lawrence, 2003). The vast majority of follow-up studies have shown an undeniable beneficial effect of sex reassignment surgery on postoperative outcomes such as subjective well being, cosmesis, and sexual function (De Cuypere et al., 2005; Garaffa, Christopher, & Ralph, 2010; Klein & Gorzalka, 2009), although the specific magnitude of benefit is uncertain from

the currently available evidence. One study (Emory, Cole, Avery, Meyer, & Meyer, 2003) even showed improvement in patient income.

One troubling report (Newfield et al., 2006) documented lower scores on quality of life (measured with the SF-36) for FtM patients than for the general population. A weakness of that study is that it recruited its 384 participants by a general email rather than a systematic approach, and the degree and type of treatment were not recorded. Study participants who were taking testosterone had typically being doing so for less than 5 years. Reported quality of life was higher for patients who had undergone breast/chest surgery than for those who had not ($p<.001$). (A similar analysis was not done for genital surgery.) In other work, Kuhn and colleagues (2009) used the King's Health Questionnaire to assess the quality of life of 55 transsexual patients at 15 years after surgery. Scores were compared to those of 20 healthy female control patients who had undergone abdominal/pelvic surgery in the past. Quality of life scores for transsexual patients were the same or better than those of control patients for some subscales (emotions, sleep, incontinence, symptom severity, and role limitation), but worse in other domains (general health, physical limitation, and personal limitation).

Two long-term observational studies, both retrospective, compared the mortality and psychiatric morbidity of transsexual adults to those of general population samples (Asscheman et al., 2011; Dhejne et al., 2011). An analysis of data from the Swedish National Board of Health and Welfare information registry found that individuals who had received sex reassignment surgery (191 MtF and 133 FtM) had significantly higher rates of mortality, suicide, suicidal behavior, and psychiatric morbidity than those for a nontranssexual control group matched on age, immigrant status, prior psychiatric morbidity, and birth sex (Dhejne et al., 2011). Similarly, a study in the Netherlands reported a higher total mortality rate, including incidence of suicide, in both pre- and post-surgery transsexual patients (966 MtF and 365 MtF) than in the general population of that country (Asscheman et al., 2011). Neither of these studies questioned the efficacy of sex reassignment; indeed, both lacked an adequate comparison group of transsexuals who either did not receive treatment or who received treatment other than genital surgery. Moreover, transsexual people in these studies were treated as far back as the 1970s. However, these findings do emphasize the need to have good long-term psychological and psychiatric care available for this population. More studies are needed that focus on the outcomes of current assessment and treatment approaches for gender dysphoria.

It is difficult to determine the effectiveness of hormones alone in the relief of gender dysphoria. Most studies evaluating the effectiveness of masculinizing/feminizing hormone therapy on gender dysphoria have been conducted with patients who have also undergone sex reassignment surgery. Favorable effects of therapies that included both hormones and surgery were reported in a comprehensive review of over 3000 patients in 79 studies (mostly observational) conducted between 1961 and 1991 (Eldh, Berg, & Gustafsson, 1997; Gijs & Brewaeys, 2007; Murad et al., 2010; Pfäfflin & Junge, 1998). Patients operated on after 1986 did better than those before 1986; this reflects significant improvement in surgical complications (Eldh et al., 1997). Most patients have reported improved psychosocial outcomes, ranging between 87% for MtF patients and 97% for FtM patients (Green & Fleming, 1990).

Similar improvements were found in a Swedish study in which "almost all patients were satisfied with sex reassignment at 5 years, and 86% were assessed by clinicians at follow-up as stable or improved in global functioning" (Johansson, Sundbom, Höjerback, & Bodlund, 2010). Weaknesses of these earlier studies are their retrospective design and use of different criteria to evaluate outcomes.

A prospective study conducted in the Netherlands evaluated 325 consecutive adult and adolescent subjects seeking sex reassignment (Smith, Van Goozen, Kuiper, & Cohen-Kettenis, 2005). Patients who underwent sex reassignment therapy (both hormonal and surgical intervention) showed improvements in their mean gender dysphoria scores, measured by the Utrecht Gender Dysphoria Scale. Scores for body dissatisfaction and psychological function also improved in most categories. Fewer than 2% of patients expressed regret after therapy. This is the largest prospective study to affirm the results from retrospective studies that a combination of hormone therapy and surgery improves gender dysphoria and other areas of psychosocial functioning. There is a need for further research on the effects of hormone therapy without surgery, and without the goal of maximum physical feminization or masculinization.

Overall, studies have been reporting a steady improvement in outcomes as the field becomes more advanced. Outcome research has mainly focused on the outcome of sex reassignment surgery. In current practice there is a range of identity, role, and physical adaptations that could use additional follow-up or outcome research (Institute of Medicine, 2011).

APPENDIX E
DEVELOPMENT PROCESS FOR THE *STANDARDS OF CARE,* VERSION 7

The process of developing *Standards of Care, Version 7* began when an initial *SOC* "work group" was established in 2006. Members were invited to examine specific sections of *SOC, Version 6*. For each section, they were asked to review the relevant literature, identify where research was lacking and needed, and recommend potential revisions to the *SOC* as warranted by new evidence. Invited papers were submitted by the following authors: Aaron Devor, Walter Bockting, George Brown, Michael Brownstein, Peggy Cohen-Kettenis, Griet DeCuypere, Petra DeSutter, Jamie Feldman, Lin Fraser, Arlene Istar Lev, Stephen Levine, Walter Meyer, Heino Meyer-Bahlburg, Stan Monstrey, Loren Schechter, Mick van Trotsenburg, Sam Winter, and Ken Zucker. Some of these authors chose to add co-authors to assist them in their task.

Initial drafts of these papers were due June 1, 2007. Most were completed by September 2007, with the rest completed by the end of 2007. These manuscripts were then submitted to the *International*

Journal of Transgenderism (IJT). Each underwent the regular *IJT* peer review process. The final papers were published in Volume 11 (1–4) in 2009, making them available for discussion and debate.

After these articles were published, an *SOC* Revision Committee was established by the WPATH Board of Directors in 2010. The Revision Committee was first charged with debating and discussing the *IJT* background papers through a Google website. A subgroup of the Revision Committee was appointed by the Board of Directors to serve as the Writing Group. This group was charged with preparing the first draft of *SOC, Version 7* and continuing to work on revisions for consideration by the broader Revision Committee. The Board also appointed an International Advisory Group of transsexual, transgender, and gender-nonconforming individuals to give input on the revision.

A technical writer was hired to (1) review all of the recommendations for revision—both the original recommendations as outlined in the *IJT* articles and additional recommendations that emanated from the online discussion—and (2) create a survey to solicit further input on these potential revisions. From the survey results, the Writing Group was able to discern where these experts stood in terms of areas of agreement and areas in need of more discussion and debate. The technical writer then (3) created a very rough first draft of *SOC, Version 7* for the Writing Group to consider and build on.

The Writing Group met on March 4 and 5, 2011 in a face-to-face expert consultation meeting. They reviewed all recommended changes and debated and came to consensus on various controversial areas. Decisions were made based on the best available science and expert consensus. These decisions were incorporated into the draft, and additional sections were written by the Writing Group with the assistance of the technical writer.

The draft that emerged from the consultation meeting was then circulated among the Writing Group and finalized with the help of the technical writer. Once this initial draft was finalized, it was circulated among the broader *SOC* Revision Committee and the International Advisory Group. Discussion was opened up on the Google website and a conference call was held to resolve issues. Feedback from these groups was considered by the Writing Group, who then made further revisions. Two additional drafts were created and posted on the Google website for consideration by the broader *SOC* Revision Committee and the International Advisory Group. Upon completion of these three iterations of review and revision, the final document was presented to the WPATH Board of Directors for approval. The Board of Directors approved this version on September 14, 2011.

Funding

The *Standards of Care* revision process was made possible through a generous grant from the Tawani Foundation and a gift from an anonymous donor. These funds supported the following:

1. Costs of a professional technical writer;

2. Process of soliciting international input on proposed changes from gender identity professionals and the transgender community;

3. Working meeting of the Writing Group;

4. Process of gathering additional feedback and arriving at final expert consensus from the professional and transgender communities, the *Standards of Care, Version 7,* Revision Committee, and WPATH Board of Directors;

5. Costs of printing and distributing *Standards of Care, Version 7,* and posting a free downloadable copy on the WPATH website;

6. Plenary session to launch the *Standards of Care, Version 7,* at the 2011 WPATH Biennial Symposium in Atlanta, Georgia, USA.

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Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline

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*Cosponsoring Associations: American Association of Clinical Endocrinologists, American Society of Andrology, European Society for Pediatric Endocrinology, European Society of Endocrinology, Pediatric Endocrine Society, and World Professional Association for Transgender Health.

Objective: To update the "Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline," published by the Endocrine Society in 2009.

Participants: The participants include an Endocrine Society–appointed task force of nine experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The task force commissioned two systematic reviews and used the best available evidence from other published systematic reviews and individual studies.

Consensus Process: Group meetings, conference calls, and e-mail communications enabled consensus. Endocrine Society committees, members and cosponsoring organizations reviewed and commented on preliminary drafts of the guidelines.

Conclusion: Gender affirmation is multidisciplinary treatment in which endocrinologists play an important role. Gender-dysphoric/gender-incongruent persons seek and/or are referred to endocrinologists to develop the physical characteristics of the affirmed gender. They require a safe and effective hormone regimen that will (1) suppress endogenous sex hormone secretion determined by the person's genetic/gonadal sex and (2) maintain sex hormone levels within the normal range for the person's affirmed gender. Hormone treatment is not recommended for prepubertal gender-dysphoric/gender-incongruent persons. Those clinicians who recommend gender-affirming endocrine treatments—appropriately trained diagnosing clinicians (required), a mental health provider for adolescents (required) and mental health

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Abbreviations: BMD, bone mineral density; DSD, disorder/difference of sex development; DSM, Diagnostic and Statistical Manual of Mental Disorders; GD, gender dysphoria; GnRH, gonadotropin-releasing hormone; ICD, International Statistical Classification of Diseases and Related Health Problems; MHP, mental health professional; VTE, venous thromboembolism.

professional for adults (recommended)—should be knowledgeable about the diagnostic criteria and criteria for gender-affirming treatment, have sufficient training and experience in assessing psychopathology, and be willing to participate in the ongoing care throughout the endocrine transition. We recommend treating gender-dysphoric/gender-incongruent adolescents who have entered puberty at Tanner Stage G2/B2 by suppression with gonadotropin-releasing hormone agonists. Clinicians may add gender-affirming hormones after a multidisciplinary team has confirmed the persistence of gender dysphoria/gender incongruence and sufficient mental capacity to give informed consent to this partially irreversible treatment. Most adolescents have this capacity by age 16 years old. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to age 16 years, although there is minimal published experience treating prior to 13.5 to 14 years of age. For the care of peripubertal youths and older adolescents, we recommend that an expert multidisciplinary team comprised of medical professionals and mental health professionals manage this treatment. The treating physician must confirm the criteria for treatment used by the referring mental health practitioner and collaborate with them in decisions about gender-affirming surgery in older adolescents. For adult gender-dysphoric/gender-incongruent persons, the treating clinicians (collectively) should have expertise in transgender-specific diagnostic criteria, mental health, primary care, hormone treatment, and surgery, as needed by the patient. We suggest maintaining physiologic levels of gender-appropriate hormones and monitoring for known risks and complications. When high doses of sex steroids are required to suppress endogenous sex steroids and/or in advanced age, clinicians may consider surgically removing natal gonads along with reducing sex steroid treatment. Clinicians should monitor both transgender males (female to male) and transgender females (male to female) for reproductive organ cancer risk when surgical removal is incomplete. Additionally, clinicians should persistently monitor adverse effects of sex steroids. For gender-affirming surgeries in adults, the treating physician must collaborate with and confirm the criteria for treatment used by the referring physician. Clinicians should avoid harming individuals (via hormone treatment) who have conditions other than gender dysphoria/gender incongruence and who may not benefit from the physical changes associated with this treatment. (***J Clin Endocrinol Metab*** **102: 3869–3903, 2017)**

Summary of Recommendations

1.0 Evaluation of youth and adults

1.1. We advise that only trained mental health professionals (MHPs) who meet the following criteria should diagnose gender dysphoria (GD)/gender incongruence in adults: (1) competence in using the Diagnostic and Statistical Manual of Mental Disorders (DSM) and/or the International Statistical Classification of Diseases and Related Health Problems (ICD) for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)

1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or the ICD for diagnostic purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)

1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).

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1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 |⊕⊕◯◯)

1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 |⊕⊕⊕◯)

2.0 Treatment of adolescents

2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment, and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 |⊕⊕◯◯)

2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty. (2 |⊕⊕◯◯)

2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 |⊕⊕◯◯)

2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years. (1 |⊕⊕◯◯).

2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 |⊕◯◯◯)

2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment. (2 |⊕⊕◯◯)

3.0 Hormonal therapy for transgender adults

3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and the criteria for the endocrine phase of gender transition before beginning treatment. (1 |⊕⊕⊕◯)

3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment. (1 |⊕⊕⊕◯)

3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 |⊕⊕◯◯)

3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 |⊕◯◯◯)

4.0 Adverse outcome prevention and long-term care

4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every 3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 |⊕⊕◯◯)

4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 |⊕⊕◯◯)

4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 |⊕⊕◯◯)

4.4. We recommend that clinicians obtain bone mineral density (BMD) measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 |⊕⊕◯◯)

4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for non-transgender females. (2 |⊕⊕◯◯)

4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 |⊕◯◯◯)

4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

5.0 Surgery for sex reassignment and gender confirmation

5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically necessary and would benefit the patient's overall health and/or well-being. (1 |⊕⊕◯◯)

5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)

5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)

5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 |⊕◯◯◯)

5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 |⊕⊕◯◯).

5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 |⊕◯◯◯)

Changes Since the Previous Guideline

Both the current guideline and the one published in 2009 contain similar sections. Listed here are the sections contained in the current guideline and the corresponding number of recommendations: Introduction, Evaluation of Youth and Adults (5), Treatment of Adolescents (6), Hormonal Therapy for Transgender Adults (4), Adverse Outcomes Prevention and Long-term Care (7), and Surgery for Sex Reassignment and Gender Confirmation (6). The current introduction updates the diagnostic classification of "gender dysphoria/gender incongruence." It also reviews the development of "gender identity" and summarizes its natural development. The section on clinical evaluation of both youth and adults, defines in detail the professional qualifications required of those who diagnose and treat both adolescents and adults. We advise that decisions regarding the social transition of prepubertal youth are made with the assistance of a mental health professional or similarly experienced professional. We recommend against puberty blocking followed by gender-affirming hormone treatment of prepubertal children. Clinicians should inform pubertal children, adolescents, and adults seeking gender-confirming treatment of their options for fertility preservation. Prior to treatment, clinicians should evaluate the presence of medical conditions that may be worsened by hormone depletion and/or treatment. A multidisciplinary team, preferably composed of medical and mental health professionals, should monitor treatments. Clinicians evaluating transgender adults for endocrine treatment should confirm the diagnosis of persistent gender dysphoria/gender incongruence. Physicians should educate transgender persons regarding the time course of steroid-induced physical changes. Treatment should include periodic monitoring of hormone levels and metabolic parameters, as well as assessments of bone density and the impact upon prostate, gonads, and uterus. We also make recommendations for transgender persons who plan genital gender-affirming surgery.

Method of Development of Evidence-Based Clinical Practice Guidelines

The Clinical Guidelines Subcommittee (CGS) of the Endocrine Society deemed the diagnosis and treatment of individuals with GD/gender incongruence a priority area for revision and appointed a task force to formulate evidence-based recommendations. The task force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation group, an international group with expertise in the development and implementation of evidence-based guidelines (1). A detailed description of the grading scheme has been published elsewhere (2). The task force used the best available research evidence to develop the recommendations. The task force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of the recommendation, strong recommendations use the phrase "we recommend" and the number 1, and weak recommendations use the phrase "we suggest" and the number 2. Cross-filled circles indicate the quality of the evidence, such that ⊕◯◯◯ denotes very low–quality evidence; ⊕⊕◯◯, low quality; ⊕⊕⊕◯, moderate quality; and ⊕⊕⊕⊕, high quality. The task force has confidence that persons who receive care according to the strong recommendations will derive, on average, more benefit than harm. Weak recommendations require more careful consideration of the person's circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the

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values that the task force considered in making the recommendation. In some instances, there are remarks in which the task force offers technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the task force and their preferences; therefore, one should consider these remarks as suggestions.

In this guideline, the task force made several statements to emphasize the importance of shared decision-making, general preventive care measures, and basic principles of the treatment of transgender persons. They labeled these "Ungraded Good Practice Statement." Direct evidence for these statements was either unavailable or not systematically appraised and considered out of the scope of this guideline. The intention of these statements is to draw attention to these principles.

The Endocrine Society maintains a rigorous conflict-of-interest review process for developing clinical practice guidelines. All task force members must declare any potential conflicts of interest by completing a conflict-of-interest form. The CGS reviews all conflicts of interest before the Society's Council approves the members to participate on the task force and periodically during the development of the guideline. All others participating in the guideline's development must also disclose any conflicts of interest in the matter under study, and most of these participants must be without any conflicts of interest. The CGS and the task force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from commercial interests; grants; research support; consulting fees; salary; ownership interests [*e.g.*, stocks and stock options (excluding diversified mutual funds)]; honoraria and other payments for participation in speakers' bureaus, advisory boards, or boards of directors; and all other financial benefits. Completed forms are available through the Endocrine Society office.

The Endocrine Society provided the funding for this guideline; the task force received no funding or remuneration from commercial or other entities.

Commissioned Systematic Review

The task force commissioned two systematic reviews to support this guideline. The first one aimed to summarize the available evidence on the effect of sex steroid use in transgender individuals on lipids and cardiovascular outcomes. The review identified 29 eligible studies at moderate risk of bias. In transgender males (female to male), sex steroid therapy was associated with a statistically significant increase in serum triglycerides and low-density lipoprotein cholesterol levels. High-density lipoprotein cholesterol levels decreased significantly across all follow-up time periods. In transgender females (male to female), serum triglycerides were significantly higher without any changes in other parameters. Few myocardial infarction, stroke, venous thromboembolism (VTE), and death events were reported. These events were more frequent in transgender females. However, the quality of the evidence was low. The second review summarized the available evidence regarding the effect of sex steroids on bone health in transgender individuals and identified 13 studies. In transgender males, there was no statistically significant difference in the lumbar spine, femoral neck, or total hip BMD at 12 and 24 months compared with baseline values before initiating masculinizing hormone therapy. In transgender females, there was a statistically significant increase in lumbar spine BMD at 12 months and 24 months compared with baseline values before initiation of feminizing hormone therapy. There was minimal information on fracture rates. The quality of evidence was also low.

Introduction

Throughout recorded history (in the absence of an endocrine disorder) some men and women have experienced confusion and anguish resulting from rigid, forced conformity to sexual dimorphism. In modern history, there have been numerous ongoing biological, psychological, cultural, political, and sociological debates over various aspects of gender variance. The 20th century marked the emergence of a social awakening for men and women with the belief that they are "trapped" in the wrong body (3). Magnus Hirschfeld and Harry Benjamin, among others, pioneered the medical responses to those who sought relief from and a resolution to their profound discomfort. Although the term transsexual became widely known after Benjamin wrote "The Transsexual Phenomenon" (4), it was Hirschfeld who coined the term "transsexual" in 1923 to describe people who want to live a life that corresponds with their experienced gender vs their designated gender (5). Magnus Hirschfeld (6) and others (4, 7) have described other types of trans phenomena besides transsexualism. These early researchers proposed that the gender identity of these people was located somewhere along a unidimensional continuum. This continuum ranged from all male through "something in between" to all female. Yet such a classification does not take into account that people may have gender identities outside this continuum. For instance, some experience themselves as having both a male and female gender identity, whereas others completely renounce any gender classification (8, 9). There are also reports of individuals experiencing a continuous and rapid involuntary alternation between a male and female identity (10) or men who do not experience themselves as men but do not want to live as women (11, 12). In some countries, (*e.g.*, Nepal, Bangladesh, and Australia), these nonmale or nonfemale genders are officially recognized (13). Specific treatment protocols, however, have not yet been developed for these groups.

Instead of the term transsexualism, the current classification system of the American Psychiatric Association uses the term gender dysphoria in its diagnosis of persons who are not satisfied with their designated gender (14). The current version of the World Health Organization's ICD-10 still uses the term transsexualism when diagnosing adolescents and adults. However, for the ICD-11, the World Health Organization has proposed using the term "gender incongruence" (15).

Treating persons with GD/gender incongruence (15) was previously limited to relatively ineffective elixirs or creams. However, more effective endocrinology-based treatments became possible with the availability of testosterone in 1935 and diethylstilbestrol in 1938. Reports of individuals with GD/gender incongruence who were treated with hormones and gender-affirming surgery appeared in the press during the second half of the 20th century. The Harry Benjamin International Gender Dysphoria Association was founded in September 1979 and is now called the World Professional Association for Transgender Health (WPATH). WPATH published its first Standards of Care in 1979. These standards have since been regularly updated, providing guidance for treating persons with GD/gender incongruence (16).

Prior to 1975, few peer-reviewed articles were published concerning endocrine treatment of transgender persons. Since then, more than two thousand articles about various aspects of transgender care have appeared.

It is the purpose of this guideline to make detailed recommendations and suggestions, based on existing medical literature and clinical experience, that will enable treating physicians to maximize benefit and minimize risk when caring for individuals diagnosed with GD/gender incongruence.

In the future, we need more rigorous evaluations of the effectiveness and safety of endocrine and surgical protocols. Specifically, endocrine treatment protocols for GD/gender incongruence should include the careful assessment of the following: (1) the effects of prolonged delay of puberty in adolescents on bone health, gonadal function, and the brain (including effects on cognitive, emotional, social, and sexual development); (2) the effects of treatment in adults on sex hormone levels; (3) the requirement for and the effects of progestins and other agents used to suppress endogenous sex steroids during treatment; and (4) the risks and benefits of gender-affirming hormone treatment in older transgender people.

To successfully establish and enact these protocols, a commitment of mental health and endocrine investigators is required to collaborate in long-term, large-scale studies across countries that use the same diagnostic and inclusion criteria, medications, assay methods, and response assessment tools (*e.g.*, the European Network for the Investigation of Gender Incongruence) (17, 18).

Terminology and its use vary and continue to evolve. Table 1 contains the definitions of terms as they are used throughout this guideline.

Biological Determinants of Gender Identity Development

One's self-awareness as male or female changes gradually during infant life and childhood. This process of cognitive and affective learning evolves with interactions with parents, peers, and environment. A fairly accurate timetable exists outlining the steps in this process (19). Normative psychological literature, however, does not address if and when gender identity becomes crystallized and what factors contribute to the development of a gender identity that is not congruent with the gender of rearing. Results of studies from a variety of biomedical disciplines—genetic, endocrine, and neuroanatomic—support the concept that gender identity and/or gender expression (20) likely reflect a complex interplay of biological, environmental, and cultural factors (21, 22).

With respect to endocrine considerations, studies have failed to find differences in circulating levels of sex steroids between transgender and nontransgender individuals (23). However, studies in individuals with a disorder/difference of sex development (DSD) have informed our understanding of the role that hormones may play in gender identity outcome, even though most persons with GD/gender incongruence do not have a DSD. For example, although most 46,XX adult individuals with virilizing congenital adrenal hyperplasia caused by mutations in *CYP21A2* reported a female gender identity, the prevalence of GD/gender incongruence was much greater in this group than in the general population without a DSD. This supports the concept that there is a role for prenatal/postnatal androgens in gender development (24–26), although some studies indicate that prenatal androgens are more likely to affect gender behavior and sexual orientation rather than gender identity *per se* (27, 28).

Researchers have made similar observations regarding the potential role of androgens in the development of gender identity in other individuals with DSD. For example, a review of two groups of 46,XY persons, each with androgen synthesis deficiencies and female raised, reported transgender male (female-to-male) gender role changes in 56% to 63% and 39% to 64% of patients, respectively (29). Also, in 46,XY female-raised individuals with cloacal

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Table 1. Definitions of Terms Used in This Guideline

Biological sex, biological male or female: These terms refer to physical aspects of maleness and femaleness. As these may not be in line with each other (*e.g.*, a person with XY chromosomes may have female-appearing genitalia), the terms biological sex and biological male or female are imprecise and should be avoided.
Cisgender: This means not transgender. An alternative way to describe individuals who are not transgender is "non-transgender people."
Gender-affirming (hormone) treatment: See "gender reassignment"
Gender dysphoria: This is the distress and unease experienced if gender identity and designated gender are not completely congruent (see Table 2). In 2013, the American Psychiatric Association released the fifth edition of the DSM-5, which replaced "gender identity disorder" with "gender dysphoria" and changed the criteria for diagnosis.
Gender expression: This refers to external manifestations of gender, expressed through one's name, pronouns, clothing, haircut, behavior, voice, or body characteristics. Typically, transgender people seek to make their gender expression align with their gender identity, rather than their designated gender.
Gender identity/experienced gender: This refers to one's internal, deeply held sense of gender. For transgender people, their gender identity does not match their sex designated at birth. Most people have a gender identity of man or woman (or boy or girl). For some people, their gender identity does not fit neatly into one of those two choices. Unlike gender expression (see below), gender identity is not visible to others.
Gender identity disorder: This is the term used for GD/gender incongruence in previous versions of DSM (see "gender dysphoria"). The ICD-10 still uses the term for diagnosing child diagnoses, but the upcoming ICD-11 has proposed using "gender incongruence of childhood."
Gender incongruence: This is an umbrella term used when the gender identity and/or gender expression differs from what is typically associated with the designated gender. Gender incongruence is also the proposed name of the gender identity–related diagnoses in ICD-11. Not all individuals with gender incongruence have gender dysphoria or seek treatment.
Gender variance: See "gender incongruence"
Gender reassignment: This refers to the treatment procedure for those who want to adapt their bodies to the experienced gender by means of hormones and/or surgery. This is also called gender-confirming or gender-affirming treatment.
Gender-reassignment surgery (gender-confirming/gender-affirming surgery): These terms refer only to the surgical part of gender-confirming/gender-affirming treatment.
Gender role: This refers to behaviors, attitudes, and personality traits that a society (in a given culture and historical period) designates as masculine or feminine and/or that society associates with or considers typical of the social role of men or women.
Sex designated at birth: This refers to sex assigned at birth, usually based on genital anatomy.
Sex: This refers to attributes that characterize biological maleness or femaleness. The best known attributes include the sex-determining genes, the sex chromosomes, the H-Y antigen, the gonads, sex hormones, internal and external genitalia, and secondary sex characteristics.
Sexual orientation: This term describes an individual's enduring physical and emotional attraction to another person. Gender identity and sexual orientation are not the same. Irrespective of their gender identity, transgender people may be attracted to women (gynephilic), attracted to men (androphilic), bisexual, asexual, or queer.
Transgender: This is an umbrella term for people whose gender identity and/or gender expression differs from what is typically associated with their sex designated at birth. Not all transgender individuals seek treatment.
Transgender male (also: trans man, female-to-male, transgender male): This refers to individuals assigned female at birth but who identify and live as men.
Transgender woman (also: trans woman, male-to female, transgender female): This refers to individuals assigned male at birth but who identify and live as women.
Transition: This refers to the process during which transgender persons change their physical, social, and/or legal characteristics consistent with the affirmed gender identity. Prepubertal children may choose to transition socially.
Transsexual: This is an older term that originated in the medical and psychological communities to refer to individuals who have permanently transitioned through medical interventions or desired to do so.

exstrophy and penile agenesis, the occurrence of transgender male changes was significantly more prevalent than in the general population (30, 31). However, the fact that a high percentage of individuals with the same conditions did not change gender suggests that cultural factors may play a role as well.

With respect to genetics and gender identity, several studies have suggested heritability of GD/gender incongruence (32, 33). In particular, a study by Heylens *et al.* (33) demonstrated a 39.1% concordance rate for gender identity disorder (based on the DSM-IV criteria) in 23 monozygotic twin pairs but no concordance in 21 same-sex dizygotic or seven opposite-sex twin pairs. Although numerous investigators have sought to identify specific genes associated with GD/gender incongruence, such studies have been inconsistent and without strong statistical significance (34–38).

Studies focusing on brain structure suggest that the brain phenotypes of people with GD/gender incongruence differ in various ways from control males and females, but that there is not a complete sex reversal in brain structures (39).

In summary, although there is much that is still unknown with respect to gender identity and its expression, compelling studies support the concept that biologic factors, in addition to environmental factors, contribute to this fundamental aspect of human development.

Natural History of Children With GD/Gender Incongruence

With current knowledge, we cannot predict the psychosexual outcome for any specific child. Prospective follow-up studies show that childhood GD/gender incongruence does not invariably persist into adolescence and adulthood (so-called "desisters"). Combining all outcome studies to date, the GD/gender incongruence of a minority of prepubertal children appears to persist in adolescence (20, 40). In adolescence, a significant number of these desisters identify as homosexual or bisexual. It may be that children who only showed some gender nonconforming characteristics have been included in the follow-up studies, because the DSM-IV text revision criteria for a diagnosis were rather broad. However, the persistence of GD/gender incongruence into adolescence is more likely if it had been extreme in childhood (41, 42). With the newer, stricter criteria of the DSM-5 (Table 2), persistence rates may well be different in future studies.

1.0 Evaluation of Youth and Adults

Gender-affirming treatment is a multidisciplinary effort. After evaluation, education, and diagnosis, treatment may include mental health care, hormone therapy, and/or surgical therapy. Together with an MHP, hormone-prescribing clinicians should examine the psychosocial impact of the potential changes on people's lives, including mental health, friends, family, jobs, and their role in society. Transgender individuals should be encouraged to experience living in the new gender role and assess whether this improves their quality of life. Although the focus of this guideline is gender-affirming hormone therapy, collaboration with appropriate professionals responsible for each aspect of treatment maximizes a successful outcome.

Diagnostic assessment and mental health care

GD/gender incongruence may be accompanied with psychological or psychiatric problems (43–51). It is therefore necessary that clinicians who prescribe hormones and are involved in diagnosis and psychosocial assessment meet the following criteria: (1) are competent in using the DSM and/or the ICD for diagnostic purposes, (2) are able to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) are trained in diagnosing psychiatric conditions, (4) undertake or refer for appropriate treatment, (5) are able to do a psychosocial assessment of the patient's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) regularly attend relevant professional meetings.

Because of the psychological vulnerability of many individuals with GD/gender incongruence, it is important that mental health care is available before, during, and sometimes also after transitioning. For children and adolescents, an MHP who has training/experience in child and adolescent gender development (as well as child and adolescent psychopathology) should make the diagnosis, because assessing GD/gender incongruence in children and adolescents is often extremely complex.

During assessment, the clinician obtains information from the individual seeking gender-affirming treatment. In the case

Table 2. DSM-5 Criteria for Gender Dysphoria in Adolescents and Adults

A. A marked incongruence between one's experienced/expressed gender and natal gender of at least 6 mo in duration, as manifested by at least two of the following:
   1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
   2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
   3. A strong desire for the primary and/or secondary sex characteristics of the other gender
   4. A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
   5. A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)
   6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender)

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:
   1. The condition exists with a disorder of sex development.
   2. The condition is posttransitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (*e.g.*, penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

Reference: American Psychiatric Association (14).

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of adolescents, the clinician also obtains information from the parents or guardians regarding various aspects of the child's general and psychosexual development and current functioning. On the basis of this information, the clinician:

- decides whether the individual fulfills criteria for treatment (see Tables 2 and 3) for GD/gender incongruence (DSM-5) or transsexualism (DSM-5 and/or ICD-10);
- informs the individual about the possibilities and limitations of various kinds of treatment (hormonal/surgical and nonhormonal), and if medical treatment is desired, provides correct information to prevent unrealistically high expectations;
- assesses whether medical interventions may result in unfavorable psychological and social outcomes.

In cases in which severe psychopathology, circumstances, or both seriously interfere with the diagnostic work or make satisfactory treatment unlikely, clinicians should assist the adolescent in managing these other issues. Literature on postoperative regret suggests that besides poor quality of surgery, severe psychiatric comorbidity and lack of support may interfere with positive outcomes (52–56).

For adolescents, the diagnostic procedure usually includes a complete psychodiagnostic assessment (57) and an assessment of the decision-making capability of the youth. An evaluation to assess the family's ability to endure stress, give support, and deal with the complexities of the adolescent's situation should be part of the diagnostic phase (58).

Social transitioning

A change in gender expression and role (which may involve living part time or full time in another gender role that is consistent with one's gender identity) may test the person's resolve, the capacity to function in the affirmed gender, and the adequacy of social, economic, and psychological supports. It assists both the individual and the clinician in their judgments about how to proceed (16). During social transitioning, the person's feelings about the social transformation (including coping with the responses of others) is a major focus of the counseling. The optimal timing for social transitioning may differ between individuals. Sometimes people wait until they start gender-affirming hormone treatment to make social transitioning easier, but individuals increasingly start social transitioning long before they receive medically supervised, gender-affirming hormone treatment.

Criteria

Adolescents and adults seeking gender-affirming hormone treatment and surgery should satisfy certain criteria before proceeding (16). Criteria for gender-affirming hormone therapy for adults are in Table 4, and criteria for gender-affirming hormone therapy for adolescents are in Table 5. Follow-up studies in adults meeting these criteria indicate a high satisfaction rate with treatment (59). However, the quality of evidence is usually low. A few follow-up studies on adolescents who fulfilled these criteria also indicated good treatment results (60–63).

Recommendations for Those Involved in the Gender-Affirming Hormone Treatment of Individuals With GD/Gender Incongruence

1.1. We advise that only trained MHPs who meet the following criteria should diagnose GD/gender incongruence in adults: (1) competence in using the DSM and/or the ICD for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)

1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or ICD for diagnostic

Table 3. ICD-10 Criteria for Transsexualism

Transsexualism (F64.0) has three criteria:
1. The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatments.
2. The transsexual identity has been present persistently for at least 2 y.
3. The disorder is not a symptom of another mental disorder or a genetic, DSD, or chromosomal abnormality.

Table 4. Criteria for Gender-Affirming Hormone Therapy for Adults

1. Persistent, well-documented gender dysphoria/gender incongruence
2. The capacity to make a fully informed decision and to consent for treatment
3. The age of majority in a given country (if younger, follow the criteria for adolescents)
4. Mental health concerns, if present, must be reasonably well controlled

Reproduced from World Professional Association for Transgender Health (16).

purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)

Evidence

Individuals with gender identity issues may have psychological or psychiatric problems (43–48, 50, 51, 64, 65). It is therefore necessary that clinicians making the diagnosis are able to make a distinction between GD/gender incongruence and conditions that have similar features. Examples of conditions with similar features are body dysmorphic disorder, body identity integrity disorder (a condition in which individuals have a sense that their anatomical configuration as an able-bodied person is somehow wrong or inappropriate) (66), or certain forms of eunuchism (in which a person is preoccupied with or engages in castration and/or penectomy for

Table 5. Criteria for Gender-Affirming Hormone Therapy for Adolescents

Adolescents are eligible for GnRH agonist treatment if:

1. A qualified MHP has confirmed that:
- the adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed),
- gender dysphoria worsened with the onset of puberty,
- any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment,
- the adolescent has sufficient mental capacity to give informed consent to this (reversible) treatment,

2. And the adolescent:
- has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility,
- has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,

3. And a pediatric endocrinologist or other clinician experienced in pubertal assessment
- agrees with the indication for GnRH agonist treatment,
- has confirmed that puberty has started in the adolescent (Tanner stage ≥G2/B2),
- has confirmed that there are no medical contraindications to GnRH agonist treatment.

Adolescents are eligible for subsequent sex hormone treatment if:

1. A qualified MHP has confirmed:
- the persistence of gender dysphoria,
- any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start sex hormone treatment,
- the adolescent has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment,

2. And the adolescent:
- has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility),
- has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,

3. And a pediatric endocrinologist or other clinician experienced in pubertal induction:
- agrees with the indication for sex hormone treatment,
- has confirmed that there are no medical contraindications to sex hormone treatment.

Reproduced from World Professional Association for Transgender Health (16).

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reasons that are not gender identity related) (11). Clinicians should also be able to diagnose psychiatric conditions accurately and ensure that these conditions are treated appropriately, particularly when the conditions may complicate treatment, affect the outcome of gender-affirming treatment, or be affected by hormone use.

Values and preferences

The task force placed a very high value on avoiding harm from hormone treatment in individuals who have conditions other than GD/gender incongruence and who may not benefit from the physical changes associated with this treatment and placed a low value on any potential benefit these persons believe they may derive from hormone treatment. This justifies the good practice statement.

1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).

1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 |⊕⊕◯◯)

Evidence

In most children diagnosed with GD/gender incongruence, it did not persist into adolescence. The percentages differed among studies, probably dependent on which version of the DSM clinicians used, the patient's age, the recruitment criteria, and perhaps cultural factors. However, the large majority (about 85%) of prepubertal children with a childhood diagnosis did not remain GD/gender incongruent in adolescence (20). If children have completely socially transitioned, they may have great difficulty in returning to the original gender role upon entering puberty (40). Social transition is associated with the persistence of GD/gender incongruence as a child progresses into adolescence. It may be that the presence of GD/gender incongruence in prepubertal children is the earliest sign that a child is destined to be transgender as an adolescent/adult (20). However, social transition (in addition to GD/gender incongruence) has been found to contribute to the likelihood of persistence.

This recommendation, however, does not imply that children should be discouraged from showing gender-variant behaviors or should be punished for exhibiting such behaviors. In individual cases, an early complete social transition may result in a more favorable outcome, but there are currently no criteria to identify the GD/gender-incongruent children to whom this applies. At the present time, clinical experience suggests that persistence of GD/gender incongruence can only be reliably assessed after the first signs of puberty.

Values and preferences

The task force placed a high value on avoiding harm with gender-affirming hormone therapy in prepubertal children with GD/gender incongruence. This justifies the strong recommendation in the face of low-quality evidence.

1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 |⊕⊕⊕◯)

Remarks

Persons considering hormone use for gender affirmation need adequate information about this treatment in general and about fertility effects of hormone treatment in particular to make an informed and balanced decision (67, 68). Because young adolescents may not feel qualified to make decisions about fertility and may not fully understand the potential effects of hormonal interventions, consent and protocol education should include parents, the referring MHP(s), and other members of the adolescent's support group. To our knowledge, there are no formally evaluated decision aids available to assist in the discussion and decision regarding the future fertility of adolescents or adults beginning gender-affirming treatment.

Treating early pubertal youth with GnRH analogs will temporarily impair spermatogenesis and oocyte maturation. Given that an increasing number of transgender youth want to preserve fertility potential, delaying or temporarily discontinuing GnRH analogs to promote gamete maturation is an option. This option is often not preferred, because mature sperm production is associated with later stages of puberty and with the significant development of secondary sex characteristics.

For those designated male at birth with GD/gender incongruence and who are in early puberty, sperm production and the development of the reproductive tract are insufficient for the cryopreservation of sperm. However, prolonged pubertal suppression using GnRH analogs is reversible and clinicians should inform these individuals that sperm production can be initiated following prolonged gonadotropin suppression. This can be accomplished by spontaneous gonadotropin recovery after

cessation of GnRH analogs or by gonadotropin treatment and will probably be associated with physical manifestations of testosterone production, as stated above. Note that there are no data in this population concerning the time required for sufficient spermatogenesis to collect enough sperm for later fertility. In males treated for precocious puberty, spermarche was reported 0.7 to 3 years after cessation of GnRH analogs (69). In adult men with gonadotropin deficiency, sperm are noted in seminal fluid by 6 to 12 months of gonadotropin treatment. However, sperm numbers when partners of these patients conceive are far below the "normal range" (70, 71).

In girls, no studies have reported long-term, adverse effects of pubertal suppression on ovarian function after treatment cessation (72, 73). Clinicians should inform adolescents that no data are available regarding either time to spontaneous ovulation after cessation of GnRH analogs or the response to ovulation induction following prolonged gonadotropin suppression.

In males with GD/gender incongruence, when medical treatment is started in a later phase of puberty or in adulthood, spermatogenesis is sufficient for cryopreservation and storage of sperm. *In vitro* spermatogenesis is currently under investigation. Restoration of spermatogenesis after prolonged estrogen treatment has not been studied.

In females with GD/gender incongruence, the effect of prolonged treatment with exogenous testosterone on ovarian function is uncertain. There have been reports of an increased incidence of polycystic ovaries in transgender males, both prior to and as a result of androgen treatment (74–77), although these reports were not confirmed by others (78). Pregnancy has been reported in transgender males who have had prolonged androgen treatment and have discontinued testosterone but have not had genital surgery (79, 80). A reproductive endocrine gynecologist can counsel patients before gender-affirming hormone treatment or surgery regarding potential fertility options (81). Techniques for cryopreservation of oocytes, embryos, and ovarian tissue continue to improve, and oocyte maturation of immature tissue is being studied (82).

2.0 Treatment of Adolescents

During the past decade, clinicians have progressively acknowledged the suffering of young adolescents with GD/gender incongruence. In some forms of GD/gender incongruence, psychological interventions may be useful and sufficient. However, for many adolescents with GD/gender incongruence, the pubertal physical changes are unbearable. As early medical intervention may prevent psychological harm, various clinics have decided to start treating young adolescents with GD/gender incongruence with puberty-suppressing medication (a GnRH analog). As compared with starting gender-affirming treatment long after the first phases of puberty, a benefit of pubertal suppression at early puberty may be a better psychological and physical outcome.

In girls, the first physical sign of puberty is the budding of the breasts followed by an increase in breast and fat tissue. Breast development is also associated with the pubertal growth spurt, and menarche occurs ~2 years later. In boys, the first physical change is testicular growth. A testicular volume ≥4 mL is seen as consistent with the initiation of physical puberty. At the beginning of puberty, estradiol and testosterone levels are still low and are best measured in the early morning with an ultrasensitive assay. From a testicular volume of 10 mL, daytime testosterone levels increase, leading to virilization (83). Note that pubic hair and/or axillary hair/odor may not reflect the onset of gonadarche; instead, it may reflect adrenarche alone.

2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment (Table 5), and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 ⊕⊕◯◯)

2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty (Tanner stages G2/B2). (2 ⊕⊕◯◯)

Evidence

Pubertal suppression can expand the diagnostic phase by a long period, giving the subject more time to explore options and to live in the experienced gender before making a decision to proceed with gender-affirming sex hormone treatments and/or surgery, some of which is irreversible (84, 85). Pubertal suppression is fully reversible, enabling full pubertal development in the natal gender, after cessation of treatment, if appropriate. The experience of full endogenous puberty is an undesirable condition for the GD/gender-incongruent individual and may seriously interfere with healthy psychological functioning and well-being. Treating GD/gender-incongruent adolescents entering puberty with GnRH analogs has been shown to improve psychological functioning in several domains (86).

Another reason to start blocking pubertal hormones early in puberty is that the physical outcome is improved compared with initiating physical transition after puberty has been completed (60, 62). Looking like a man or woman when living as the opposite sex creates difficult

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barriers with enormous life-long disadvantages. We therefore advise starting suppression in early puberty to prevent the irreversible development of undesirable secondary sex characteristics. However, adolescents with GD/gender incongruence should experience the first changes of their endogenous spontaneous puberty, because their emotional reaction to these first physical changes has diagnostic value in establishing the persistence of GD/gender incongruence (85). Thus, Tanner stage 2 is the optimal time to start pubertal suppression. However, pubertal suppression treatment in early puberty will limit the growth of the penis and scrotum, which will have a potential effect on future surgical treatments (87).

Clinicians can also use pubertal suppression in adolescents in later pubertal stages to stop menses in transgender males and prevent facial hair growth in transgender females. However, in contrast to the effects in early pubertal adolescents, physical sex characteristics (such as more advanced breast development in transgender boys and lowering of the voice and outgrowth of the jaw and brow in transgender girls) are not reversible.

Values and preferences

These recommendations place a high value on avoiding an unsatisfactory physical outcome when secondary sex characteristics have become manifest and irreversible, a higher value on psychological well-being, and a lower value on avoiding potential harm from early pubertal suppression.

Remarks

Table 6 lists the Tanner stages of breast and male genital development. Careful documentation of hallmarks of pubertal development will ensure precise timing when initiating pubertal suppression once puberty has started. Clinicians can use pubertal LH and sex steroid levels to confirm that puberty has progressed sufficiently before starting pubertal suppression (88). Reference ranges for sex steroids by Tanner stage may vary depending on the assay used. Ultrasensitive sex steroid and gonadotropin assays will help clinicians document early pubertal changes.

Irreversible and, for GD/gender-incongruent adolescents, undesirable sex characteristics in female puberty are breasts, female body habitus, and, in some cases, relative short stature. In male puberty, they are a prominent Adam's apple; low voice; male bone configuration, such as a large jaw, big feet and hands, and tall stature; and male hair pattern on the face and extremities.

2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 l⊕⊕○○)

Evidence

Clinicians can suppress pubertal development and gonadal function most effectively via gonadotropin suppression using GnRH analogs. GnRH analogs are long-acting agonists that suppress gonadotropins by GnRH receptor desensitization after an initial increase of gonadotropins during ~10 days after the first and (to a lesser degree) the second injection (89). Antagonists immediately suppress pituitary gonadotropin secretion (90, 91). Long-acting GnRH analogs are the currently preferred treatment option. Clinicians may consider long-acting GnRH antagonists when evidence on their safety and efficacy in adolescents becomes available.

During GnRH analog treatment, slight development of secondary sex characteristics may regress, and in a later phase of pubertal development, it will stop. In girls, breast tissue will become atrophic, and menses will stop. In boys, virilization will stop, and testicular volume may decrease (92).

An advantage of using GnRH analogs is the reversibility of the intervention. If, after extensive exploration of his/her transition wish, the individual no longer desires transition, they can discontinue pubertal suppression. In subjects with

Table 6. Tanner Stages of Breast Development and Male External Genitalia

The description of Tanner stages for breast development:
1. Prepubertal
2. Breast and papilla elevated as small mound; areolar diameter increased
3. Breast and areola enlarged, no contour separation
4. Areola and papilla form secondary mound
5. Mature; nipple projects, areola part of general breast contour

For penis and testes:
1. Prepubertal, testicular volume <4 mL
2. Slight enlargement of penis; enlarged scrotum, pink, texture altered, testes 4–6 mL
3. Penis longer, testes larger (8–12 mL)
4. Penis and glans larger, including increase in breadth; testes larger (12–15 mL), scrotum dark
5. Penis adult size; testicular volume > 15 ml

Adapted from Lawrence (56).

precocious puberty, spontaneous pubertal development has been shown to resume after patients discontinue taking GnRH analogs (93).

Recommendations 2.1 to 2.3 are supported by a prospective follow-up study from The Netherlands. This report assessed mental health outcomes in 55 transgender adolescents/young adults (22 transgender females and 33 transgender males) at three time points: (1) before the start of GnRH agonist (average age of 14.8 years at start of treatment), (2) at initiation of gender-affirming hormones (average age of 16.7 years at start of treatment), and (3) 1 year after "gender-reassignment surgery" (average age of 20.7 years) (63). Despite a decrease in depression and an improvement in general mental health functioning, GD/gender incongruence persisted through pubertal suppression, as previously reported (86). However, following sex hormone treatment and gender-reassignment surgery, GD/gender incongruence was resolved and psychological functioning steadily improved (63). Furthermore, well-being was similar to or better than that reported by age-matched young adults from the general population, and none of the study participants regretted treatment. This study represents the first long-term follow-up of individuals managed according to currently existing clinical practice guidelines for transgender youth, and it underscores the benefit of the multidisciplinary approach pioneered in The Netherlands; however, further studies are needed.

Side effects

The primary risks of pubertal suppression in GD/gender-incongruent adolescents may include adverse effects on bone mineralization (which can theoretically be reversed with sex hormone treatment), compromised fertility if the person subsequently is treated with sex hormones, and unknown effects on brain development. Few data are available on the effect of GnRH analogs on BMD in adolescents with GD/gender incongruence. Initial data in GD/gender-incongruent subjects demonstrated no change of absolute areal BMD during 2 years of GnRH analog therapy but a decrease in BMD z scores (85). A recent study also suggested suboptimal bone mineral accrual during GnRH analog treatment. The study reported a decrease in areal BMD z scores and of bone mineral apparent density z scores (which takes the size of the bone into account) in 19 transgender males treated with GnRH analogs from a mean age of 15.0 years (standard deviation = 2.0 years) for a median duration of 1.5 years (0.3 to 5.2 years) and in 15 transgender females treated from 14.9 (±1.9) years for 1.3 years (0.5 to 3.8 years), although not all changes were statistically significant (94). There was incomplete catch-up at age 22 years after sex hormone treatment from age 16.6 (±1.4) years for a median duration of 5.8 years (3.0 to 8.0 years) in transgender females and from age 16.4 (±2.3) years for 5.4 years (2.8 to 7.8 years) in transgender males. Little is known about more prolonged use of GnRH analogs. Researchers reported normal BMD z scores at age 35 years in one individual who used GnRH analogs from age 13.7 years until age 18.6 years before initiating sex hormone treatment (65).

Additional data are available from individuals with late puberty or GnRH analog treatment of other indications. Some studies reported that men with constitutionally delayed puberty have decreased BMD in adulthood (95). However, other studies reported that these men have normal BMD (96, 97). Treating adults with GnRH analogs results in a decrease of BMD (98). In children with central precocious puberty, treatment with GnRH analogs has been found to result in a decrease of BMD during treatment by some (99) but not others (100). Studies have reported normal BMD after discontinuing therapy (69, 72, 73, 101, 102). In adolescents treated with growth hormone who are small for gestational age and have normal pubertal timing, 2-year GnRH analog treatments did not adversely affect BMD (103). Calcium supplementation may be beneficial in optimizing bone health in GnRH analog–treated individuals (104). There are no studies of vitamin D supplementation in this context, but clinicians should offer supplements to vitamin D–deficient adolescents. Physical activity, especially during growth, is important for bone mass in healthy individuals (103) and is therefore likely to be beneficial for bone health in GnRH analog–treated subjects.

GnRH analogs did not induce a change in body mass index standard deviation score in GD/gender-incongruent adolescents (94) but caused an increase in fat mass and decrease in lean body mass percentage (92). Studies in girls treated for precocious puberty also reported a stable body mass index standard deviation score during treatment (72) and body mass index and body composition comparable to controls after treatment (73).

Arterial hypertension has been reported as an adverse effect in a few girls treated with GnRH analogs for precocious/early puberty (105, 106). Blood pressure monitoring before and during treatment is recommended.

Individuals may also experience hot flashes, fatigue, and mood alterations as a consequence of pubertal suppression. There is no consensus on treatment of these side effects in this context.

It is recommended that any use of pubertal blockers (and subsequent use of sex hormones, as detailed below) include a discussion about implications for fertility (see recommendation 1.3). Transgender adolescents may

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want to preserve fertility, which may be otherwise compromised if puberty is suppressed at an early stage and the individual completes phenotypic transition with the use of sex hormones.

Limited data are available regarding the effects of GnRH analogs on brain development. A single cross-sectional study demonstrated no compromise of executive function (107), but animal data suggest there may be an effect of GnRH analogs on cognitive function (108).

Values and preferences

Our recommendation of GnRH analogs places a higher value on the superior efficacy, safety, and reversibility of the pubertal hormone suppression achieved (as compared with the alternatives) and a relatively lower value on limiting the cost of therapy. Of the available alternatives, depot and oral progestin preparations are effective. Experience with this treatment dates back prior to the emergence of GnRH analogs for treating precocious puberty in papers from the 1960s and early 1970s (109–112). These compounds are usually safe, but some side effects have been reported (113–115). Only two recent studies involved transgender youth (116, 117). One of these studies described the use of oral lynestrenol monotherapy followed by the addition of testosterone treatment in transgender boys who were at Tanner stage B4 or further at the start of treatment (117). They found lynestrenol safe, but gonadotropins were not fully suppressed. The study reported metrorrhagia in approximately half of the individuals, mainly in the first 6 months. Acne, headache, hot flashes, and fatigue were other frequent side effects. Another progestin that has been studied in the United States is medroxyprogesterone. This agent is not as effective as GnRH analogs in lowering endogenous sex hormones either and may be associated with other side effects (116). Progestin preparations may be an acceptable treatment for persons without access to GnRH analogs or with a needle phobia. If GnRH analog treatment is not available (insurance denial, prohibitive cost, or other reasons), postpubertal, transgender female adolescents may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see adult section).

Remarks

Measurements of gonadotropin and sex steroid levels give precise information about gonadal axis suppression, although there is insufficient evidence for any specific short-term monitoring scheme in children treated with GnRH analogs (88). If the gonadal axis is not completely suppressed—as evidenced by (for example) menses, erections, or progressive hair growth—the interval of GnRH analog treatment can be shortened or the dose increased. During treatment, adolescents should be monitored for negative effects of delaying puberty, including a halted growth spurt and impaired bone mineral accretion. Table 7 illustrates a suggested clinical protocol.

Anthropometric measurements and X-rays of the left hand to monitor bone age are informative for evaluating growth. To assess BMD, clinicians can perform dual-energy X-ray absorptiometry scans.

2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule (see Table 8) after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years (Table 5). (1 |⊕⊕◯◯)

2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 |⊕◯◯◯)

2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment (Table 9). (2 |⊕⊕◯◯)

Table 7. Baseline and Follow-Up Protocol During Suppression of Puberty

Every 3–6 mo
Anthropometry: height, weight, sitting height, blood pressure, Tanner stages
Every 6–12 mo
Laboratory: LH, FSH, E2/T, 25OH vitamin D
Every 1–2 y
Bone density using DXA
Bone age on X-ray of the left hand (if clinically indicated)

Adapted from Hembree *et al.* (118).

Abbreviations: DXA, dual-energy X-ray absorptiometry; E2, estradiol; FSH, follicle stimulating hormone; LH, luteinizing hormone; T, testosterone;

Table 8. Protocol Induction of Puberty

Induction of female puberty with oral 17β-estradiol, increasing the dose every 6 mo:
- 5 μg/kg/d
- 10 μg/kg/d
- 15 μg/kg/d
- 20 μg/kg/d
- Adult dose = 2–6 mg/d
- *In postpubertal transgender female adolescents, the dose of 17β-estradiol can be increased more rapidly:*
  - 1 mg/d for 6 mo
  - 2 mg/d

Induction of female puberty with transdermal 17β-estradiol, increasing the dose every 6 mo (new patch is placed every 3.5 d):
- 6.25–12.5 μg/24 h (cut 25-μg patch into quarters, then halves)
- 25 μg/24 h
- 37.5 μg/24 h
- Adult dose = 50–200 μg/24 h
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological estradiol levels (see Table 15).*

Induction of male puberty with testosterone esters increasing the dose every 6 mo (IM or SC):
- 25 mg/m^2/2 wk (or alternatively, half this dose weekly, or double the dose every 4 wk)
- 50 mg/m^2/2 wk
- 75 mg/m^2/2 wk
- 100 mg/m^2/2 wk
- Adult dose = 100–200 mg every 2 wk
- *In postpubertal transgender male adolescents the dose of testosterone esters can be increased more rapidly:*
  - 75 mg/2 wk for 6 mo
  - 125 mg/2 wk
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological testosterone levels (see Table 14).*

Adapted from Hembree *et al.* (118).

Abbreviations: IM, intramuscularly; SC, subcutaneously.

Evidence

Adolescents develop competence in decision making at their own pace. Ideally, the supervising medical professionals should individually assess this competence, although no objective tools to make such an assessment are currently available.

Many adolescents have achieved a reasonable level of competence by age 15 to 16 years (119), and in many countries 16-year-olds are legally competent with regard to medical decision making (120). However, others believe that although some capacities are generally achieved before age 16 years, other abilities (such as good risk assessment) do not develop until well after 18 years (121). They suggest that health care procedures should be divided along a matrix of relative risk, so that younger adolescents can be allowed to decide about low-risk procedures, such as most diagnostic tests and common therapies, but not about high-risk procedures, such as most surgical procedures (121).

Currently available data from transgender adolescents support treatment with sex hormones starting at age 16 years (63, 122). However, some patients may incur potential risks by waiting until age 16 years. These include the potential risk to bone health if puberty is suppressed

Table 9. Baseline and Follow-up Protocol During Induction of Puberty

Every 3–6 mo
- •Anthropometry: height, weight, sitting height, blood pressure, Tanner stages

Every 6–12 mo
- •In transgender males: hemoglobin/hematocrit, lipids, testosterone, 25OH vitamin D
- •In transgender females: prolactin, estradiol, 25OH vitamin D

Every 1–2 y
- •BMD using DXA
- •Bone age on X-ray of the left hand (if clinically indicated)

BMD should be monitored into adulthood (until the age of 25–30 y or until peak bone mass has been reached).
For recommendations on monitoring once pubertal induction has been completed, see Tables 14 and 15.

Adapted from Hembree *et al.* (118).

Abbreviation: DXA, dual-energy X-ray absorptiometry.

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for 6 to 7 years before initiating sex hormones (*e.g.*, if someone reached Tanner stage 2 at age 9-10 years old). Additionally, there may be concerns about inappropriate height and potential harm to mental health (emotional and social isolation) if initiation of secondary sex characteristics must wait until the person has reached 16 years of age. However, only minimal data supporting earlier use of gender-affirming hormones in transgender adolescents currently exist (63). Clearly, long-term studies are needed to determine the optimal age of sex hormone treatment in GD/gender-incongruent adolescents.

The MHP who has followed the adolescent during GnRH analog treatment plays an essential role in assessing whether the adolescent is eligible to start sex hormone therapy and capable of consenting to this treatment (Table 5). Support of the family/environment is essential. Prior to the start of sex hormones, clinicians should discuss the implications for fertility (see recommendation 1.5). Throughout pubertal induction, an MHP and a pediatric endocrinologist (or other clinician competent in the evaluation and induction of pubertal development) should monitor the adolescent. In addition to monitoring therapy, it is also important to pay attention to general adolescent health issues, including healthy life style choices, such as not smoking, contraception, and appropriate vaccinations (*e.g.*, human papillomavirus).

For the induction of puberty, clinicians can use a similar dose scheme for hypogonadal adolescents with GD/gender incongruence as they use in other individuals with hypogonadism, carefully monitoring for desired and undesired effects (Table 8). In transgender female adolescents, transdermal 17β-estradiol may be an alternative for oral 17β-estradiol. It is increasingly used for pubertal induction in hypogonadal females. However, the absence of low-dose estrogen patches may be a problem. As a result, individuals may need to cut patches to size themselves to achieve appropriate dosing (123). In transgender male adolescents, clinicians can give testosterone injections intramuscularly or subcutaneously (124, 125).

When puberty is initiated with a gradually increasing schedule of sex steroid doses, the initial levels will not be high enough to suppress endogenous sex steroid secretion. Gonadotropin secretion and endogenous production of testosterone may resume and interfere with the effectiveness of estrogen treatment, in transgender female adolescents (126, 127). Therefore, continuation of GnRH analog treatment is advised until gonadectomy. Given that GD/gender-incongruent adolescents may opt not to have gonadectomy, long-term studies are necessary to examine the potential risks of prolonged GnRH analog treatment. Alternatively, in transgender male adolescents, GnRH analog treatment can be discontinued once an adult dose of testosterone has been reached and the individual is well virilized. If uterine bleeding occurs, a progestin can be added. However, the combined use of a GnRH analog (for ovarian suppression) and testosterone may enable phenotypic transition with a lower dose of testosterone in comparison with testosterone alone. If there is a wish or need to discontinue GnRH analog treatment in transgender female adolescents, they may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see section 3.0 "Hormonal Therapy for Transgender Adults").

Values and preferences

The recommendation to initiate pubertal induction only when the individual has sufficient mental capacity (roughly age 16 years) to give informed consent for this partly irreversible treatment places a higher value on the ability of the adolescent to fully understand and oversee the partially irreversible consequences of sex hormone treatment and to give informed consent. It places a lower value on the possible negative effects of delayed puberty. We may not currently have the means to weigh adequately the potential benefits of waiting until around age 16 years to initiate sex hormones vs the potential risks/harm to BMD and the sense of social isolation from having the timing of puberty be so out of sync with peers (128).

Remarks

Before starting sex hormone treatment, effects on fertility and options for fertility preservation should be discussed. Adult height may be a concern in transgender adolescents. In a transgender female adolescent, clinicians may consider higher doses of estrogen or a more rapid tempo of dose escalation during pubertal induction. There are no established treatments yet to augment adult height in a transgender male adolescent with open epiphyses during pubertal induction. It is not uncommon for transgender adolescents to present for clinical services after having completed or nearly completed puberty. In such cases, induction of puberty with sex hormones can be done more rapidly (see Table 8). Additionally, an adult dose of testosterone in transgender male adolescents may suffice to suppress the gonadal axis without the need to use a separate agent. At the appropriate time, the multidisciplinary team should adequately prepare the adolescent for transition to adult care.

3.0 Hormonal Therapy for Transgender Adults

The two major goals of hormonal therapy are (1) to reduce endogenous sex hormone levels, and thus reduce

the secondary sex characteristics of the individual's designated gender, and (2) to replace endogenous sex hormone levels consistent with the individual's gender identity by using the principles of hormone replacement treatment of hypogonadal patients. The timing of these two goals and the age at which to begin treatment with the sex hormones of the chosen gender is codetermined in collaboration with both the person pursuing transition and the health care providers. The treatment team should include a medical provider knowledgeable in transgender hormone therapy, an MHP knowledgeable in GD/gender incongruence and the mental health concerns of transition, and a primary care provider able to provide care appropriate for transgender individuals. The physical changes induced by this sex hormone transition are usually accompanied by an improvement in mental well-being (129, 130).

3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and the criteria for the endocrine phase of gender transition before beginning treatment. (1 |⊕⊕⊕◯)

3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment (Table 10). (1 |⊕⊕⊕◯)

3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 |⊕⊕◯◯)

Evidence

It is the responsibility of the treating clinician to confirm that the person fulfills criteria for treatment. The treating clinician should become familiar with the terms and criteria presented in Tables 1–5 and take a thorough history from the patient in collaboration with the other members of the treatment team. The treating clinician must ensure that the desire for transition is appropriate; the consequences, risks, and benefits of treatment are well understood; and the desire for transition persists. They also need to discuss fertility preservation options (see recommendation 1.3) (67, 68).

Transgender males

Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males (Appendix A) (113, 114, 131–134). Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism (135). Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range (this is dependent on the specific assay, but is typically 320 to 1000 ng/dL) (Table 11) (136). Sustained supraphysiologic levels of testosterone increase the risk of adverse reactions (see section 4.0 "Adverse Outcome Prevention and Long-Term Care") and should be avoided.

Similar to androgen therapy in hypogonadal men, testosterone treatment in transgender males results in increased muscle mass and decreased fat mass, increased facial hair and acne, male pattern baldness in those genetically predisposed, and increased sexual desire (137).

Table 10. Medical Risks Associated With Sex Hormone Therapy

Transgender female: estrogen
Very high risk of adverse outcomes:
•Thromboembolic disease
Moderate risk of adverse outcomes:
•Macroprolactinoma
•Breast cancer
•Coronary artery disease
•Cerebrovascular disease
•Cholelithiasis
•Hypertriglyceridemia
Transgender male: testosterone
Very high risk of adverse outcomes:
•Erythrocytosis (hematocrit > 50%)
Moderate risk of adverse outcomes:
•Severe liver dysfunction (transaminases > threefold upper limit of normal)
•Coronary artery disease
•Cerebrovascular disease
•Hypertension
•Breast or uterine cancer

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Table 11. Hormone Regimens in Transgender Persons

Transgender females[a]	
Estrogen	
Oral	
Estradiol	2.0–6.0 mg/d
Transdermal	
Estradiol transdermal patch (New patch placed every 3–5 d)	0.025–0.2 mg/d
Parenteral	
Estradiol valerate or cypionate	5–30 mg IM every 2 wk 2–10 mg IM every week
Anti-androgens	
Spironolactone	100–300 mg/d
Cyproterone acetate[b]	25–50 mg/d
GnRH agonist	3.75 mg SQ (SC) monthly 11.25 mg SQ (SC) 3-monthly
Transgender males	
Testosterone	
Parenteral testosterone	
Testosterone enanthate or cypionate	100–200 mg SQ (IM) every 2 wk or SQ (SC) 50% per week
Testosterone undecanoate[c]	1000 mg every 12 wk
Transdermal testosterone	
Testosterone gel 1.6%[d]	50–100 mg/d
Testosterone transdermal patch	2.5–7.5 mg/d

Abbreviations: IM, intramuscularly; SQ, sequentially; SC, subcutaneously.

[a]Estrogens used with or without antiandrogens or GnRH agonist.

[b]Not available in the United States.

[c]One thousand milligrams initially followed by an injection at 6 wk then at 12-wk intervals.

[d]Avoid cutaneous transfer to other individuals.

In transgender males, testosterone will result in clitoromegaly, temporary or permanent decreased fertility, deepening of the voice, cessation of menses (usually), and a significant increase in body hair, particularly on the face, chest, and abdomen. Cessation of menses may occur within a few months with testosterone treatment alone, although high doses of testosterone may be required. If uterine bleeding continues, clinicians may consider the addition of a progestational agent or endometrial ablation (138). Clinicians may also administer GnRH analogs or depot medroxyprogesterone to stop menses prior to testosterone treatment.

Transgender females

The hormone regimen for transgender females is more complex than the transgender male regimen (Appendix B). Treatment with physiologic doses of estrogen alone is insufficient to suppress testosterone levels into the normal range for females (139). Most published clinical studies report the need for adjunctive therapy to achieve testosterone levels in the female range (21, 113, 114, 132–134, 139, 140).

Multiple adjunctive medications are available, such as progestins with antiandrogen activity and GnRH agonists (141). Spironolactone works by directly blocking androgens during their interaction with the androgen receptor (114, 133, 142). It may also have estrogenic activity (143). Cyproterone acetate, a progestational compound with antiandrogenic properties (113, 132, 144), is widely used in Europe. 5α-Reductase inhibitors do not reduce testosterone levels and have adverse effects (145).

Dittrich *et al.* (141) reported that monthly doses of the GnRH agonist goserelin acetate in combination with estrogen were effective in reducing testosterone levels with a low incidence of adverse reactions in 60 transgender females. Leuprolide and transdermal estrogen were as effective as cyproterone and transdermal estrogen in a comparative retrospective study (146).

Patients can take estrogen as oral conjugated estrogens, oral 17β-estradiol, or transdermal 17β-estradiol. Among estrogen options, the increased risk of thromboembolic events associated with estrogens in general seems most concerning with ethinyl estradiol specifically (134, 140, 141), which is why we specifically suggest that it not be used in any transgender treatment plan. Data distinguishing among other estrogen options are less well established although there is some thought that oral routes of administration are more thrombogenic due to the "first pass effect" than are transdermal and parenteral routes, and that the risk of thromboembolic events is dose-dependent. Injectable estrogen and sublingual

estrogen may benefit from avoiding the first pass effect, but they can result in more rapid peaks with greater overall periodicity and thus are more difficult to monitor (147, 148). However, there are no data demonstrating that increased periodicity is harmful otherwise.

Clinicians can use serum estradiol levels to monitor oral, transdermal, and intramuscular estradiol. Blood tests cannot monitor conjugated estrogens or synthetic estrogen use. Clinicians should measure serum estradiol and serum testosterone and maintain them at the level for premenopausal females (100 to 200 pg/mL and <50 ng/dL, respectively). The transdermal preparations and injectable estradiol cypionate or valerate preparations may confer an advantage in older transgender females who may be at higher risk for thromboembolic disease (149).

Values

Our recommendation to maintain levels of gender-affirming hormones in the normal adult range places a high value on the avoidance of the long-term complications of pharmacologic doses. Those patients receiving endocrine treatment who have relative contraindications to hormones should have an in-depth discussion with their physician to balance the risks and benefits of therapy.

Remarks

Clinicians should inform all endocrine-treated individuals of all risks and benefits of gender-affirming hormones prior to initiating therapy. Clinicians should strongly encourage tobacco use cessation in transgender females to avoid increased risk of VTE and cardiovascular complications. We strongly discourage the unsupervised use of hormone therapy (150).

Not all individuals with GD/gender incongruence seek treatment as described (*e.g.*, male-to-eunuchs and individuals seeking partial transition). Tailoring current protocols to the individual may be done within the context of accepted safety guidelines using a multidisciplinary approach including mental health. No evidence-based protocols are available for these groups (151). We need prospective studies to better understand treatment options for these persons.

3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 ⊕◯◯◯)

Evidence

Transgender males

Physical changes that are expected to occur during the first 1 to 6 months of testosterone therapy include cessation of menses, increased sexual desire, increased facial and body hair, increased oiliness of skin, increased muscle, and redistribution of fat mass. Changes that occur within the first year of testosterone therapy include deepening of the voice (152, 153), clitoromegaly, and male pattern hair loss (in some cases) (114, 144, 154, 155) (Table 12).

Transgender females

Physical changes that may occur in transgender females in the first 3 to 12 months of estrogen and antiandrogen therapy include decreased sexual desire, decreased spontaneous erections, decreased facial and body hair (usually mild), decreased oiliness of skin, increased breast tissue growth, and redistribution of fat mass (114, 139, 149, 154, 155, 161) (Table 13). Breast development is generally maximal at 2 years after initiating hormones (114, 139, 149, 155). Over a long period of time, the prostate gland and testicles will undergo atrophy.

Although the time course of breast development in transgender females has been studied (150), precise information about other changes induced by sex hormones is lacking (141). There is a great deal of variability among individuals, as evidenced during pubertal development. We all know that a major concern for transgender females is breast development. If we work with estrogens, the result will be often not what the transgender female expects.

Alternatively, there are transgender females who report an anecdotal improved breast development, mood, or sexual desire with the use of progestogens. However, there have been no well-designed studies of the role of progestogens in feminizing hormone regimens, so the question is still open.

Our knowledge concerning the natural history and effects of different cross-sex hormone therapies on breast

Table 12. Masculinizing Effects in Transgender Males

Effect	Onset	Maximum
Skin oiliness/acne	1–6 mo	1–2 y
Facial/body hair growth	6–12 mo	4–5 y
Scalp hair loss	6–12 mo	—[a]
Increased muscle mass/strength	6–12 mo	2–5 y
Fat redistribution	1–6 mo	2–5 y
Cessation of menses	1–6 mo	—[b]
Clitoral enlargement	1–6 mo	1–2 y
Vaginal atrophy	1–6 mo	1–2 y
Deepening of voice	6–12 mo	1–2 y

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157), Wierckx *et al.* (158).

[a] Prevention and treatment as recommended for biological men.

[b] Menorrhagia requires diagnosis and treatment by a gynecologist.

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Table 13. Feminizing Effects in Transgender Females

Effect	Onset	Maximum
Redistribution of body fat	3–6 mo	2–3 y
Decrease in muscle mass and strength	3–6 mo	1–2 y
Softening of skin/decreased oiliness	3–6 mo	Unknown
Decreased sexual desire	1–3 mo	3–6 mo
Decreased spontaneous erections	1–3 mo	3–6 mo
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 mo	2–3 y
Decreased testicular volume	3–6 mo	2–3 y
Decreased sperm production	Unknown	>3 y
Decreased terminal hair growth	6–12 mo	>3 y[a]
Scalp hair	Variable	—[b]
Voice changes	None	—[c]

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157).

[a]Complete removal of male sexual hair requires electrolysis or laser treatment or both.

[b]Familial scalp hair loss may occur if estrogens are stopped.

[c]Treatment by speech pathologists for voice training is most effective.

development in transgender females is extremely sparse and based on the low quality of evidence. Current evidence does not indicate that progestogens enhance breast development in transgender females, nor does evidence prove the absence of such an effect. This prevents us from drawing any firm conclusion at this moment and demonstrates the need for further research to clarify these important clinical questions (162).

Values and preferences

Transgender persons have very high expectations regarding the physical changes of hormone treatment and are aware that body changes can be enhanced by surgical procedures (*e.g.*, breast, face, and body habitus). Clear expectations for the extent and timing of sex hormone–induced changes may prevent the potential harm and expense of unnecessary procedures.

4.0 Adverse Outcome Prevention and Long-Term Care

Hormone therapy for transgender males and females confers many of the same risks associated with sex hormone replacement therapy in nontransgender persons. The risks arise from and are worsened by inadvertent or intentional use of supraphysiologic doses of sex hormones, as well as use of inadequate doses of sex hormones to maintain normal physiology (131, 139).

4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every 3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 ⊕⊕◯◯)

Evidence

Pretreatment screening and appropriate regular medical monitoring are recommended for both transgender males and females during the endocrine transition and periodically thereafter (26, 155). Clinicians should monitor weight and blood pressure, conduct physical exams, and assess routine health questions, such as tobacco use, symptoms of depression, and risk of adverse events such as deep vein thrombosis/pulmonary embolism and other adverse effects of sex steroids.

Transgender males

Table 14 contains a standard monitoring plan for transgender males on testosterone therapy (154, 159). Key issues include maintaining testosterone levels in the physiologic normal male range and avoiding adverse events resulting from excess testosterone therapy, particularly erythrocytosis, sleep apnea, hypertension, excessive weight gain, salt retention, lipid changes, and excessive or cystic acne (135).

Because oral 17-alkylated testosterone is not recommended, serious hepatic toxicity is not anticipated with parenteral or transdermal testosterone use (163, 164). Past concerns regarding liver toxicity with testosterone have been alleviated with subsequent reports that indicate the risk of serious liver disease is minimal (144, 165, 166).

Transgender females

Table 15 contains a standard monitoring plan for transgender females on estrogens, gonadotropin suppression, or antiandrogens (160). Key issues include avoiding supraphysiologic doses or blood levels of estrogen that may lead to increased risk for thromboembolic disease, liver dysfunction, and hypertension. Clinicians should monitor serum estradiol levels using laboratories participating in external quality control, as measurements of estradiol in blood can be very challenging (167).

VTE may be a serious complication. A study reported a 20-fold increase in venous thromboembolic disease in a large cohort of Dutch transgender subjects (161). This increase may have been associated with the use of the synthetic estrogen, ethinyl estradiol (149). The incidence decreased when clinicians stopped administering ethinyl estradiol (161). Thus, the use of synthetic estrogens and conjugated estrogens is undesirable because of the inability to regulate doses by measuring serum levels and the risk of thromboembolic disease. In a German gender clinic, deep vein thrombosis occurred in 1 of 60 of transgender females treated with a GnRH analog and oral

Table 14. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Male

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
2. Measure serum testosterone every 3 mo until levels are in the normal physiologic male range:[a]
   a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is 400–700 ng/dL to 400 ng/dL. Alternatively, measure peak and trough levels to ensure levels remain in the normal male range.
   b. For parenteral testosterone undecanoate, testosterone should be measured just before the following injection. If the level is <400 ng/dL, adjust dosing interval.
   c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 h after application).
3. Measure hematocrit or hemoglobin at baseline and every 3 mo for the first year and then one to two times a year. Monitor weight, blood pressure, and lipids at regular intervals.
4. Screening for osteoporosis should be conducted in those who stop testosterone treatment, are not compliant with hormone therapy, or who develop risks for bone loss.
5. If cervical tissue is present, monitoring as recommended by the American College of Obstetricians and Gynecologists.
6. Ovariectomy can be considered after completion of hormone transition.
7. Conduct sub- and periareolar annual breast examinations if mastectomy performed. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

[a] Adapted from Lapauw *et al.* (154) and Ott *et al.* (159).

estradiol (141). The patient who developed a deep vein thrombosis was found to have a homozygous C677 T mutation in the methylenetetrahydrofolate reductase gene. In an Austrian gender clinic, administering gender-affirming hormones to 162 transgender females and 89 transgender males was not associated with VTE, despite an 8.0% and 5.6% incidence of thrombophilia (159). A more recent multinational study reported only 10 cases of VTE from a cohort of 1073 subjects (168). Thrombophilia screening of transgender persons initiating hormone treatment should be restricted to those with a personal or family history of VTE (159). Monitoring D-dimer levels during treatment is not recommended (169).

4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 l⊕⊕◯◯)

Evidence

Estrogen therapy can increase the growth of pituitary lactrotroph cells. There have been several reports of prolactinomas occurring after long-term, high-dose estrogen therapy (170–173). Up to 20% of transgender females treated with estrogens may have elevations in prolactin levels associated with enlargement of the pituitary gland (156). In most cases, the serum prolactin levels will return to the normal range with a reduction or discontinuation of the estrogen therapy or discontinuation of cyproterone acetate (157, 174, 175).

The onset and time course of hyperprolactinemia during estrogen treatment are not known. Clinicians should measure prolactin levels at baseline and then at least annually during the transition period and every 2 years thereafter. Given that only a few case studies reported prolactinomas, and prolactinomas were not reported in large cohorts of estrogen-treated persons, the risk is likely to be very low. Because the major presenting findings of microprolactinomas (hypogonadism and sometimes gynecomastia) are not apparent in transgender females, clinicians may perform radiologic examinations of the pituitary in those patients whose prolactin levels persistently increase despite stable or reduced estrogen levels. Some transgender individuals receive psychotropic medications that can increase prolactin levels (174).

Table 15. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Female

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of feminization and for development of adverse reactions.
2. Measure serum testosterone and estradiol every 3 mo.
   a. Serum testosterone levels should be <50 ng/dL.
   b. Serum estradiol should not exceed the peak physiologic range: 100–200 pg/mL.
3. For individuals on spironolactone, serum electrolytes, particularly potassium, should be monitored every 3 mo in the first year and annually thereafter.
4. Routine cancer screening is recommended, as in nontransgender individuals (all tissues present).
5. Consider BMD testing at baseline (160). In individuals at low risk, screening for osteoporosis should be conducted at age 60 years or in those who are not compliant with hormone therapy.

This table presents strong recommendations and does not include lower level recommendations.

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4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 |⊕⊕◯◯)

Evidence

Transgender males

Administering testosterone to transgender males results in a more atherogenic lipid profile with lowered high-density lipoprotein cholesterol and higher triglyceride and low-density lipoprotein cholesterol values (176–179). Studies of the effect of testosterone on insulin sensitivity have mixed results (178, 180). A randomized, open-label uncontrolled safety study of transgender males treated with testosterone undecanoate demonstrated no insulin resistance after 1 year (181, 182). Numerous studies have demonstrated the effects of sex hormone treatment on the cardiovascular system (160, 179, 183, 184). Long-term studies from The Netherlands found no increased risk for cardiovascular mortality (161). Likewise, a meta-analysis of 19 randomized trials in nontransgender males on testosterone replacement showed no increased incidence of cardiovascular events (185). A systematic review of the literature found that data were insufficient (due to very low–quality evidence) to allow a meaningful assessment of patient-important outcomes, such as death, stroke, myocardial infarction, or VTE in transgender males (176). Future research is needed to ascertain the potential harm of hormonal therapies (176). Clinicians should manage cardiovascular risk factors as they emerge according to established guidelines (186).

Transgender females

A prospective study of transgender females found favorable changes in lipid parameters with increased high-density lipoprotein and decreased low-density lipoprotein concentrations (178). However, increased weight, blood pressure, and markers of insulin resistance attenuated these favorable lipid changes. In a meta-analysis, only serum triglycerides were higher at ≥24 months without changes in other parameters (187). The largest cohort of transgender females (mean age 41 years, followed for a mean of 10 years) showed no increase in cardiovascular mortality despite a 32% rate of tobacco use (161).

Thus, there is limited evidence to determine whether estrogen is protective or detrimental on lipid and glucose metabolism in transgender females (176). With aging, there is usually an increase of body weight. Therefore, as with nontransgender individuals, clinicians should monitor and manage glucose and lipid metabolism and blood pressure regularly according to established guidelines (186).

4.4. We recommend that clinicians obtain BMD measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 |⊕⊕◯◯)

Evidence

Transgender males

Baseline bone mineral measurements in transgender males are generally in the expected range for their pretreatment gender (188). However, adequate dosing of testosterone is important to maintain bone mass in transgender males (189, 190). In one study (190), serum LH levels were inversely related to BMD, suggesting that low levels of sex hormones were associated with bone loss. Thus, LH levels in the normal range may serve as an indicator of the adequacy of sex steroid administration to preserve bone mass. The protective effect of testosterone may be mediated by peripheral conversion to estradiol, both systemically and locally in the bone.

Transgender females

A baseline study of BMD reported T scores less than −2.5 in 16% of transgender females (191). In aging males, studies suggest that serum estradiol more positively correlates with BMD than does testosterone (192, 193) and is more important for peak bone mass (194). Estrogen preserves BMD in transgender females who continue on estrogen and antiandrogen therapies (188, 190, 191, 195, 196).

Fracture data in transgender males and females are not available. Transgender persons who have undergone gonadectomy may choose not to continue consistent sex steroid treatment after hormonal and surgical sex reassignment, thereby becoming at risk for bone loss. There have been no studies to determine whether clinicians should use the sex assigned at birth or affirmed gender for assessing osteoporosis (*e.g.*, when using the FRAX tool). Although some researchers use the sex assigned at birth (with the assumption that bone mass has usually peaked for transgender people who initiate hormones in early adulthood), this should be assessed on a case-by-case basis until there are more data available. This assumption will be further complicated by the increasing prevalence of transgender people who undergo hormonal transition at a pubertal age or soon after puberty. Sex for comparison within risk assessment tools may be based on the age at which hormones were initiated and the length of exposure to hormones. In some cases, it may be

reasonable to assess risk using both the male and female calculators and using an intermediate value. Because all subjects underwent normal pubertal development, with known effects on bone size, reference values for birth sex were used for all participants (154).

4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for those designated female at birth. (2 |⊕⊕◯◯)

4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 |⊕◯◯◯)

Evidence

Studies have reported a few cases of breast cancer in transgender females (197–200). A Dutch study of 1800 transgender females followed for a mean of 15 years (range of 1 30 years) found one case of breast cancer. The Women's Health Initiative study reported that females taking conjugated equine estrogen without progesterone for 7 years did not have an increased risk of breast cancer as compared with females taking placebo (137).

In transgender males, a large retrospective study conducted at the U.S. Veterans Affairs medical health system identified seven breast cancers (194). The authors reported that this was not above the expected rate of breast cancers in cisgender females in this cohort. Furthermore, they did report one breast cancer that developed in a transgender male patient after mastectomy, supporting the fact that breast cancer can occur even after mastectomy. Indeed, there have been case reports of breast cancer developing in subareolar tissue in transgender males, which occurred after mastectomy (201, 202).

Women with primary hypogonadism (Turner syndrome) treated with estrogen replacement exhibited a significantly decreased incidence of breast cancer as compared with national standardized incidence ratios (203, 204). These studies suggest that estrogen therapy does not increase the risk of breast cancer in the short term (<20 to 30 years). We need long-term studies to determine the actual risk, as well as the role of screening mammograms. Regular examinations and gynecologic advice should determine monitoring for breast cancer.

Prostate cancer is very rare before the age of 40, especially with androgen deprivation therapy (205). Childhood or pubertal castration results in regression of the prostate and adult castration reverses benign prostate hypertrophy (206). Although van Kesteren *et al.* (207) reported that estrogen therapy does not induce hypertrophy or premalignant changes in the prostates of transgender females, studies have reported cases of benign prostatic hyperplasia in transgender females treated with estrogens for 20 to 25 years (208, 209). Studies have also reported a few cases of prostate carcinoma in transgender females (210–214).

Transgender females may feel uncomfortable scheduling regular prostate examinations. Gynecologists are not trained to screen for prostate cancer or to monitor prostate growth. Thus, it may be reasonable for transgender females who transitioned after age 20 years to have annual screening digital rectal examinations after age 50 years and prostate-specific antigen tests consistent with U.S. Preventive Services Task Force Guidelines (215).

4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

Evidence

Although aromatization of testosterone to estradiol in transgender males has been suggested as a risk factor for endometrial cancer (216), no cases have been reported. When transgender males undergo hysterectomy, the uterus is small and there is endometrial atrophy (217, 218). Studies have reported cases of ovarian cancer (219, 220). Although there is limited evidence for increased risk of reproductive tract cancers in transgender males, health care providers should determine the medical necessity of a laparoscopic total hysterectomy as part of a gender-affirming surgery to prevent reproductive tract cancer (221).

Values

Given the discomfort that transgender males experience accessing gynecologic care, our recommendation for the medical necessity of total hysterectomy and oophorectomy places a high value on eliminating the risks of female reproductive tract disease and cancer and a lower value on avoiding the risks of these surgical procedures (related to the surgery and to the potential undesirable health consequences of oophorectomy) and their associated costs.

Remarks

The sexual orientation and type of sexual practices will determine the need and types of gynecologic care required following transition. Additionally, in certain countries, the approval required to change the sex in a birth certificate for transgender males may be dependent on having a complete hysterectomy. Clinicians should help patients research nonmedical administrative criteria and

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provide counseling. If individuals decide not to undergo hysterectomy, screening for cervical cancer is the same as all other females.

5.0 Surgery for Sex Reassignment and Gender Confirmation

For many transgender adults, genital gender-affirming surgery may be the necessary step toward achieving their ultimate goal of living successfully in their desired gender role. The type of surgery falls into two main categories: (1) those that directly affect fertility and (2) those that do not. Those that change fertility (previously called sex reassignment surgery) include genital surgery to remove the penis and gonads in the male and removal of the uterus and gonads in the female. The surgeries that effect fertility are often governed by the legal system of the state or country in which they are performed. Other gender-conforming surgeries that do not directly affect fertility are not so tightly governed.

Gender-affirming surgical techniques have improved markedly during the past 10 years. Reconstructive genital surgery that preserves neurologic sensation is now the standard. The satisfaction rate with surgical reassignment of sex is now very high (187). Additionally, the mental health of the individual seems to be improved by participating in a treatment program that defines a pathway of gender-affirming treatment that includes hormones and surgery (130, 144) (Table 16).

Surgery that affects fertility is irreversible. The World Professional Association for Transgender Health Standards of Care (222) emphasizes that the "threshold of 18 should not be seen as an indication in itself for active intervention." If the social transition has not been satisfactory, if the person is not satisfied with or is ambivalent about the effects of sex hormone treatment, or if the person is ambivalent about surgery then the individual should not be referred for surgery (223, 224).

Gender-affirming genital surgeries for transgender females that affect fertility include gonadectomy, penectomy, and creation of a neovagina (225, 226). Surgeons often invert the skin of the penis to form the wall of the vagina, and several literatures reviews have reported on outcomes (227). Sometimes there is inadequate tissue to form a full neovagina, so clinicians have revisited using intestine and found it to be successful (87, 228, 229). Some newer vaginoplasty techniques may involve autologuous oral epithelial cells (230, 231).

The scrotum becomes the labia majora. Surgeons use reconstructive surgery to fashion the clitoris and its hood, preserving the neurovascular bundle at the tip of the penis as the neurosensory supply to the clitoris. Some surgeons are also creating a sensate pedicled-spot adding a G spot to the neovagina to increase sensation (232). Most recently, plastic surgeons have developed techniques to fashion labia minora. To further complete the feminization, uterine transplants have been proposed and even attempted (233).

Neovaginal prolapse, rectovaginal fistula, delayed healing, vaginal stenosis, and other complications do sometimes occur (234, 235). Clinicians should strongly remind the transgender person to use their dilators to maintain the depth and width of the vagina throughout the postoperative period. Genital sexual responsivity and other aspects of sexual function are usually preserved following genital gender-affirming surgery (236, 237).

Ancillary surgeries for more feminine or masculine appearance are not within the scope of this guideline. Voice therapy by a speech language pathologist is available to transform speech patterns to the affirmed gender (148). Spontaneous voice deepening occurs during testosterone treatment of transgender males (152, 238). No studies have compared the effectiveness of speech therapy, laryngeal surgery, or combined treatment.

Breast surgery is a good example of gender-confirming surgery that does not affect fertility. In all females, breast size exhibits a very broad spectrum. For transgender females to make the best informed decision, clinicians should delay breast augmentation surgery until the patient has completed at least 2 years of estrogen therapy, because the breasts continue to grow during that time (141, 155).

Another major procedure is the removal of facial and masculine-appearing body hair using either electrolysis or

Table 16. Criteria for Gender-Affirming Surgery, Which Affects Fertility

1. Persistent, well-documented gender dysphoria
2. Legal age of majority in the given country
3. Having continuously and responsibly used gender-affirming hormones for 12 mo (if there is no medical contraindication to receiving such therapy)
4. Successful continuous full-time living in the new gender role for 12 mo
5. If significant medical or mental health concerns are present, they must be well controlled
6. Demonstrable knowledge of all practical aspects of surgery (*e.g.*, cost, required lengths of hospitalizations, likely complications, postsurgical rehabilitation)

laser treatments. Other feminizing surgeries, such as that to feminize the face, are now becoming more popular (239–241).

In transgender males, clinicians usually delay gender-affirming genital surgeries until after a few years of androgen therapy. Those surgeries that affect fertility in this group include oophorectomy, vaginectomy, and complete hysterectomy. Surgeons can safely perform them vaginally with laparoscopy. These are sometimes done in conjunction with the creation of a neopenis. The cosmetic appearance of a neopenis is now very good, but the surgery is multistage and very expensive (242, 243). Radial forearm flap seems to be the most satisfactory procedure (228, 244). Other flaps also exist (245). Surgeons can make neopenile erections possible by reinervation of the flap and subsequent contraction of the muscle, leading to stiffening of the neopenis (246, 247), but results are inconsistent (248). Surgeons can also stiffen the penis by imbedding some mechanical device (*e.g.*, a rod or some inflatable apparatus) (249, 250). Because of these limitations, the creation of a neopenis has often been less than satisfactory. Recently, penis transplants are being proposed (233).

In fact, most transgender males do not have any external genital surgery because of the lack of access, high cost, and significant potential complications. Some choose a metaoidioplasty that brings forward the clitoris, thereby allowing them to void in a standing position without wetting themselves (251, 252). Surgeons can create the scrotum from the labia majora with good cosmetic effect and can implant testicular prostheses (253).

The most important masculinizing surgery for the transgender male is mastectomy, and it does not affect fertility. Breast size only partially regresses with androgen therapy (155). In adults, discussions about mastectomy usually take place after androgen therapy has started. Because some transgender male adolescents present after significant breast development has occurred, they may also consider mastectomy 2 years after they begin androgen therapy and before age 18 years. Clinicians should individualize treatment based on the physical and mental health status of the individual. There are now newer approaches to mastectomy with better outcomes (254, 255). These often involve chest contouring (256). Mastectomy is often necessary for living comfortably in the new gender (256).

5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically necessary and would benefit the patient's overall health and/or well-being. (1 |⊕⊕◯◯)

5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)

5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)

5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 |⊕◯◯◯)

5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 |⊕⊕◯◯).

5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 |⊕◯◯◯)

Evidence

Owing to the lack of controlled studies, incomplete follow-up, and lack of valid assessment measures, evaluating various surgical approaches and techniques is difficult. However, one systematic review including a large numbers of studies reported satisfactory cosmetic and functional results for vaginoplasty/neovagina construction (257). For transgender males, the outcomes are less certain. However, the problems are now better understood (258). Several postoperative studies report significant long-term psychological and psychiatric pathology (259–261). One study showed satisfaction with breasts, genitals, and femininity increased significantly and showed the importance of surgical treatment as a key therapeutic option for transgender females (262). Another analysis demonstrated that, despite the young average age at death following surgery and the relatively larger number of individuals with somatic morbidity, the study does not allow for determination of

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causal relationships between, for example, specific types of hormonal or surgical treatment received and somatic morbidity and mortality (263). Reversal surgery in regretful male-to-female transsexuals after sexual reassignment surgery represents a complex, multistage procedure with satisfactory outcomes. Further insight into the characteristics of persons who regret their decision postoperatively would facilitate better future selection of applicants eligible for sexual reassignment surgery. We need more studies with appropriate controls that examine long-term quality of life, psychosocial outcomes, and psychiatric outcomes to determine the long-term benefits of surgical treatment.

When a transgender individual decides to have gender-affirming surgery, both the hormone prescribing clinician and the MHP must certify that the patient satisfies criteria for gender-affirming surgery (Table 16).

There is some concern that estrogen therapy may cause an increased risk for venous thrombosis during or following surgery (176). For this reason, the surgeon and the hormone-prescribing clinician should collaborate in making a decision about the use of hormones before and following surgery. One study suggests that preoperative factors (such as compliance) are less important for patient satisfaction than are the physical postoperative results (56). However, other studies and clinical experience dictate that individuals who do not follow medical instructions and do not work with their physicians toward a common goal do not achieve treatment goals (264) and experience higher rates of postoperative infections and other complications (265, 266). It is also important that the person requesting surgery feels comfortable with the anatomical changes that have occurred during hormone therapy. Dissatisfaction with social and physical outcomes during the hormone transition may be a contraindication to surgery (223).

An endocrinologist or experienced medical provider should monitor transgender individuals after surgery. Those who undergo gonadectomy will require hormone replacement therapy, surveillance, or both to prevent adverse effects of chronic hormone deficiency.

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RESEARCH ARTICLE

Parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria

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Abstract

Purpose

In on-line forums, parents have reported that their children seemed to experience a sudden or rapid onset of gender dysphoria, appearing for the first time during puberty or even after its completion. Parents describe that the onset of gender dysphoria seemed to occur in the context of belonging to a peer group where one, multiple, or even all of the friends have become gender dysphoric and transgender-identified during the same timeframe. Parents also report that their children exhibited an increase in social media/internet use prior to disclosure of a transgender identity. Recently, clinicians have reported that post-puberty presentations of gender dysphoria in natal females that appear to be rapid in onset is a phenomenon that they are seeing more and more in their clinic. Academics have raised questions about the role of social media in the development of gender dysphoria. The purpose of this study was to collect data about parents' observations, experiences, and perspectives about their adolescent and young adult (AYA) children showing signs of an apparent sudden or rapid onset of gender dysphoria that began during or after puberty, and develop hypotheses about factors that may contribute to the onset and/or expression of gender dysphoria among this demographic group.

Methods

For this descriptive, exploratory study, recruitment information with a link to a 90-question survey, consisting of multiple-choice, Likert-type and open-ended questions was placed on three websites where parents had reported sudden or rapid onsets of gender dysphoria occurring in their teen or young adult children. The study's eligibility criteria included parental response that their child had a sudden or rapid onset of gender dysphoria and parental indication that their child's gender dysphoria began during or after puberty. To maximize the chances of finding cases meeting eligibility criteria, the three websites (4thwavenow, transgender trend, and youthtranscriticalprofessionals) were selected for targeted recruitment. Website moderators and potential participants were encouraged to share the recruitment information and link to the survey with any individuals or communities that they thought

risk of participant recognition through linkage of details. As participants' identifiers were not collected it is not possible to contact participants and ask for their consent to disclose at this time. For any questions about restriction on data sharing, please contact PPHS at the Icahn School of Medicine at Mount Sinai (IRB@mssm.edu).

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Competing interests: Lisa Littman, MD, MPH, provides public health consulting on topics unrelated to this research. She is a member of several professional organizations including the American College of Preventive Medicine (ACPM), the American Public Health Association (APHA), the Society for Adolescent Health and Medicine (SAHM), the Society of Family Planning (SFP), the International Academy of Sex Research (IASR), and the World Professional Association for Transgender Health (WPATH).

might include eligible participants to expand the reach of the project through snowball sampling techniques. Data were collected anonymously via SurveyMonkey. Quantitative findings are presented as frequencies, percentages, ranges, means and/or medians. Open-ended responses from two questions were targeted for qualitative analysis of themes.

Results

There were 256 parent-completed surveys that met study criteria. The AYA children described were predominantly natal female (82.8%) with a mean age of 16.4 years at the time of survey completion and a mean age of 15.2 when they announced a transgender-identification. Per parent report, 41% of the AYAs had expressed a non-heterosexual sexual orientation before identifying as transgender. Many (62.5%) of the AYAs had reportedly been diagnosed with at least one mental health disorder or neurodevelopmental disability prior to the onset of their gender dysphoria (range of the number of pre-existing diagnoses 0–7). In 36.8% of the friendship groups described, parent participants indicated that the majority of the members became transgender-identified. Parents reported subjective declines in their AYAs' mental health (47.2%) and in parent-child relationships (57.3%) since the AYA "came out" and that AYAs expressed a range of behaviors that included: expressing distrust of non-transgender people (22.7%); stopping spending time with non-transgender friends (25.0%); trying to isolate themselves from their families (49.4%), and only trusting information about gender dysphoria from transgender sources (46.6%). Most (86.7%) of the parents reported that, along with the sudden or rapid onset of gender dysphoria, their child either had an increase in their social media/internet use, belonged to a friend group in which one or multiple friends became transgender-identified during a similar timeframe, or both

Conclusion

This descriptive, exploratory study of parent reports provides valuable detailed information that allows for the generation of hypotheses about factors that may contribute to the onset and/or expression of gender dysphoria among AYAs. Emerging hypotheses include the possibility of a potential new subcategory of gender dysphoria (referred to as rapid-onset gender dysphoria) that has not yet been clinically validated and the possibility of social influences and maladaptive coping mechanisms. Parent-child conflict may also explain some of the findings. More research that includes data collection from AYAs, parents, clinicians and third party informants is needed to further explore the roles of social influence, maladaptive coping mechanisms, parental approaches, and family dynamics in the development and duration of gender dysphoria in adolescents and young adults.

Introduction

In recent years, a number of parents have begun reporting in online discussion groups such as 4thwavenow in the US (https://4thwavenow.com) and Transgender Trend in the UK (https://www.transgendertrend.com) that their adolescent and young adult (AYA) children, who have had no histories of childhood gender identity issues, experienced a perceived sudden or rapid

onset of gender dysphoria. Parents have described clusters of gender dysphoria in pre-existing friend groups with multiple or even all members of a friend group becoming gender dysphoric and transgender-identified in a pattern that seems statistically unlikely based on previous research [1–8]. Parents describe a process of immersion in social media, such as "binge-watching" YouTube transition videos and excessive use of Tumblr, immediately preceding their child becoming gender dysphoric [1–2, 9]. These types of presentations have not been described in the research literature for gender dysphoria [1–10] and raise the question of whether social influences may be contributing to or even driving these occurrences of gender dysphoria in some populations of adolescents and young adults. (Note: The terminology of "natal sex", including the terms "natal female" and "natal male", will be used throughout this article. Natal sex refers to an individual's sex as it was observed and documented at the time of birth. Some researchers also use the terminology "assigned at birth".)

Background

Gender dysphoria in adolescents

Gender dysphoria (GD) is defined as an individual's persistent discomfort with their biological sex or assigned gender [11]. Two types of gender dysphoria studied include early-onset gender dysphoria, where the symptoms of gender dysphoria begin in early childhood, and late-onset gender dysphoria, where the symptoms begin after puberty [11]. Late-onset gender dysphoria that occurs during adolescence is now called adolescent-onset gender dysphoria. The majority of adolescents who present for care for gender dysphoria are individuals who experienced early-onset gender dysphoria that persisted or worsened with puberty although an atypical presentation has been described where adolescents who did not experience childhood symptoms present with new symptoms in adolescence [7, 12]. Adolescent-onset of gender dysphoria has only recently been reported in the literature for natal females [5,10, 13–14]. In fact, prior to 2012, there were little to no research studies about adolescent females with gender dysphoria first beginning in adolescence [10]. Thus, far more is known about adolescents with early-onset gender dysphoria than adolescents with adolescent-onset gender dysphoria [6, 15]. Although not all research studies on gender dysphoric adolescents exclude those with adolescent-onset gender dysphoria [10], it is important to note that most of the studies on adolescents, particularly those about gender dysphoria persistence and desistance rates and outcomes for the use of puberty suppression, cross-sex hormones, and surgery only included subjects whose gender dysphoria began in childhood and subjects with adolescent-onset gender dysphoria would not have met inclusion criteria for these studies [16–24]. Therefore, most of the research on adolescents with gender dysphoria to date is not generalizable to adolescents experiencing adolescent-onset gender dysphoria [16–24] and the outcomes for individuals with adolescent-onset gender dysphoria, including persistence and desistence rates and outcomes for treatments, are currently unknown.

As recently as 2012, there were only two clinics (one in Canada and one in the Netherlands) that had gathered enough data to provide empirical information about the main issues for gender dysphoric adolescents [25]. Both institutions concluded that the management of adolescent-onset gender dysphoria is more complicated than the management of early-onset gender dysphoria and that individuals with adolescent-onset are more likely to have significant psychopathology [25]. The presentation of gender dysphoria can occur in the context of severe psychiatric disorders, developmental difficulties, or as part of large-scale identity issues and, for these patients, medical transition might not be advisable [13]. The APA Task Force on the Treatment of Gender Identity Disorder notes that adolescents with gender dysphoria "should be screened carefully to detect the emergence of the desire for sex reassignment in the context

of trauma as well as for any disorder (such as schizophrenia, mania, psychotic depression) that may produce gender confusion. When present, such psychopathology must be addressed and taken into account prior to assisting the adolescent's decision as to whether or not to pursue sex reassignment or actually assisting the adolescent with the gender transition." [25].

Demographic and clinical changes for gender dysphoria

Although, by 2013, there was research documenting that a significant number of natal males experienced gender dysphoria that began during or after puberty, there was little information about this type of presentation for natal females [5]. Starting in the mid-2000s there has been a substantial change in demographics of patients presenting for care with most notably an increase in adolescent females and an inversion of the sex ratio from one favoring natal males to one favoring natal females [26–28]. And now, some clinicians have noted that they are seeing increasingly in their clinic, the phenomenon of natal females expressing a post-puberty rapid onset of gender dysphoria [14]. Some researchers have suggested that increased visibility of transgender people in the media, availability of information online, with a partial reduction of stigma may explain some of the increases in numbers of patients seeking care [27], but these factors would not explain the reversal of the sex ratio, disproportionate increase in adolescent natal females, and the new phenomenon of natal females experiencing gender dysphoria that begins during or after puberty. If there were cultural changes that made it more acceptable for natal females to seek transition [27], that would not explain why the reversal of the sex ratio reported for adolescents has not been reported for older adult populations [26]. There are many unanswered questions about potential causes for the recent demographic and clinical changes for gender dysphoric individuals.

Social and peer influences

Parental reports (on social media) of friend clusters exhibiting signs of gender dysphoria [1–4] and increased exposure to social media/internet preceding a child's announcement of a transgender identity [1–2, 9] raise the possibility of social and peer influences. In developmental psychology research, impacts of peers and other social influences on an individual's development are sometimes described using the terms peer contagion and social contagion, respectively. The use of "contagion" in this context is distinct from the term's use in the study of infectious disease, and furthermore its use as an established academic concept throughout this article is not meant in any way to characterize the developmental process, outcome, or behavior as a disease or disease-like state, or to convey any value judgement. Social contagion [29] is the spread of affect or behaviors through a population. Peer contagion, in particular, is the process where an individual and peer mutually influence each other in a way that promotes emotions and behaviors that can potentially have negative effects on their development [30]. Peer contagion has been associated with depressive symptoms, disordered eating, aggression, bullying, and drug use [30–31]. Internalizing symptoms such as depression can be spread via the mechanisms of co-rumination, which entails the repetitive discussion of problems, excessive reassurance seeking (ERS), and negative feedback [30, 32–34]. Deviancy training, which was first described for rule breaking, delinquency, and aggression, is the process whereby attitudes and behaviors associated with problem behaviors are promoted with positive reinforcement by peers [35, 36].

Peer contagion has been shown to be a factor in several aspects of eating disorders. There are examples in the eating disorder and anorexia nervosa literature of how both internalizing symptoms and behaviors have been shared and spread via peer influences [37–41] which may have relevance to considerations of a rapid onset of gender dysphoria occurring in AYAs. Friendship cliques can set the norms for preoccupation with one's body, one's body image,

and techniques for weight loss, and can predict an individual's body image concerns and eating behaviors [37–39]. Peer influence is intensified in inpatient and outpatient treatment settings for patients with anorexia and counter-therapeutic subcultures that actively promote the beliefs and behaviors of anorexia nervosa have been observed [39–41]. In these settings, there is a group dynamic where the "best" anorexics (those who are thinnest, most resistant to gaining weight, and who have experienced the most medical complications from their disease) are admired, validated, and seen as authentic while the patients who want to recover from anorexia and cooperate with medical treatment are maligned, ridiculed, and marginalized [39–41]. Additionally, behaviors associated with deceiving parents and doctors about eating and weight loss, referred to as the "anorexic tricks," are shared by patients in a manner akin to deviancy training [39–41]. Online environments provide ample opportunity for excessive reassurance seeking, co-rumination, positive and negative feedback, and deviancy training from peers who subscribe to unhealthy, self-harming behaviors. The pro-eating disorder sites provide motivation for extreme weight loss (sometimes calling the motivational content "thinspiration")[42–44]. Such sites promote validation of eating disorder as an identity, and offer "tips and tricks" for weight loss and for deceiving parents and doctors so that individuals may continue their weight-loss activities [42–44]. If similar mechanisms are at work in the context of gender dysphoria, this greatly complicates the evaluation and treatment of impacted AYAs.

In the past decade, there has been an increase in visibility, social media, and user-generated online content about transgender issues and transition [45], which may act as a double-edged sword. On the one hand, an increase in visibility has given a voice to individuals who would have been under-diagnosed and undertreated in the past [45]. On the other hand, it is plausible that online content may encourage vulnerable individuals to believe that nonspecific symptoms and vague feelings should be interpreted as gender dysphoria stemming from a transgender condition. Recently, leading international academic and clinical commentators have raised the question about the role of social media and online content in the development of gender dysphoria [46]. Concern has been raised that adolescents may come to believe that transition is the only solution to their individual situations, that exposure to internet content that is uncritically positive about transition may intensify these beliefs, and that those teens may pressure doctors for immediate medical treatment [25]. There are many examples on popular sites such as Reddit (www.reddit.com with subreddit ask/r/transgender) and Tumblr (www.tumblr.com) where online advice promotes the idea that nonspecific symptoms should be considered to be gender dysphoria, conveys an urgency to transition, and instructs individuals how to deceive parents, doctors, and therapists to obtain hormones quickly [47]. Fig 1 includes examples of online advice from Reddit and Tumblr.

Purpose

Rapid presentations of adolescent-onset gender dysphoria occurring in clusters of pre-existing friend groups are not consistent with current knowledge about gender dysphoria and have not been described in the scientific literature to date [1–8]. The purpose of this descriptive, exploratory research is to (1) collect data about parents' observations, experiences, and perspectives about their AYA children showing signs of a rapid onset of gender dysphoria that began during or after puberty, and (2) develop hypotheses about factors that may contribute to the onset and/or expression of gender dysphoria among this demographic group.

Materials and methods

The Icahn School of Medicine at Mount Sinai, Program for the Protection of Human Subjects provided approval of research for this project (HS#: 16–00744).

Instructions on lying	• "TL;DR find out what they want to hear if they're gonna give you T and then tell them just that. It's about getting treatment, not about being true to those around you. It's not their business and a lot of time doctors will screw stuff up for you."[a] • "…Get a story ready in your head, and as suggested keep the lie to a minimum. And only for stuff that can't be verified. Like how you were feeling, but was too afraid to tell anyone including your family."[b] • "I'd also look up the DSM for the diagnostic criteria for transgender and make sure your story fits it, assuming your psych follows it."[c]
Urgency to transition	• "…If you don't do it when you are young. You'll be miserable and unhappy with your body for the rest of your life."[d]
Vague and nonspecific symptoms called signs of GD	• "Signs of indirect gender dysphoria: 1. Continual difficulty with simply getting through the day. 2. A sense of misalignment, disconnect, or estrangement from your own emotions. 3. A feeling of just going through the motions in everyday life, as if you're always reading from a script. 4. A seeming pointlessness to your life, and no sense of any real meaning or ultimate purpose. 5. Knowing you're somehow different from everyone else, and wishing you could be normal like them…"[e]
	a. https://www.reddit.com/r/asktransgender/comments/2nt8gi/having_a_psych_eval_soon/#bottom-comments b. https://www.reddit.com/r/asktransgender/comments/4agf76/is_it_best_to_be_completely_honest_or_lie_a/ c. https://www.reddit.com/r/asktransgender/comments/4ihwar/what_things_should_i_never_tell_my_psychologist/ d. https://www.reddit.com/r/asktransgender/comments/3gpb94/at_the_final_stage_of_questioning_need_some/#bottom-comments e. https://transgenderteensurvivalguide.tumblr.com/post/62036014416/that-was-dysphoria-8-signs-and-symptoms-of

Fig 1. Example quotes of online advice from Reddit and Tumblr.

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Participants

During the recruitment period, 256 parents completed online surveys that met the study criteria. The sample of parents included more women (91.7%) than men (8.3%) and participants were predominantly between the ages of 45 and 60 (66.1%) (Table 1). Most respondents were White (91.4%), non-Hispanic (99.2%), and lived in the United States (71.7%). Most respondents had a Bachelor's degree (37.8%) or graduate degree (33.1%). The adolescents and young adults (AYAs) described by their parents were predominantly female sex at birth (82.8%) with an average current age of 16.4 years (range, 11–27 years). See Table 2.

Procedure

A 90-question survey instrument with multiple choice, Likert-type, and open-ended questions was created by the researcher. The survey was designed for parents (respondents) to complete about their adolescent and young adult children. The survey was uploaded onto Survey Monkey (SurveyMonkey, Palo Alto, CA, USA) via an account that was HIPPA-enabled. IRB approval for the study from the Icahn School of Medicine at Mount Sinai in New York, NY was received. Recruitment information with a link to the survey was placed on three websites where parents and professionals had been observed to describe what seemed to be a sudden or rapid onset of gender dysphoria (4thwavenow, transgender trend, and youthtranscriticalprofessionals), although the specific terminology "rapid onset gender dysphoria" did not appear on these websites until the recruitment information using that term was first posted on the sites. Website moderators and potential participants were encouraged to share the recruitment information and link to the survey with any individuals or communities that they thought might include eligible participants to expand the reach of the project through snowball sampling techniques. The survey was active from June 29, 2016 to October 12, 2016 (3.5 months)

Table 1. Demographic and other baseline characteristics of parent respondents.

Characteristics of Parent-respondents		n	%
Sex		254	
	Female	233	91.7
	Male	21	8.3
Age (y)		254	
	18–29	3	1.2
	30–44	74	29.1
	45–60	168	66.1
	>60	9	3.5
Race/Ethnicity*		255	
	White	233	91.4
	Other**	22	8.6
Country of Residence		254	
	US	182	71.7
	UK	39	15.4
	Canada	17	6.7
	Other	16	6.3
Education		254	
	Bachelor's degree	96	37.8
	Graduate degree	84	33.1
	Some college or Associates degree	63	24.8
	HS grad or GED	10	3.9
	<High School	1	0.4
Parent attitude on allowing gay and lesbian couples to marry legally		256	
	Favor	220	85.9
	Oppose	19	7.4
	Don't know	17	6.6
Parent belief that transgender people deserve the same rights and protections as others		255	
	Yes	225	88.2
	No	8	3.1
	Don't know	20	7.8
	Other	2	0.8

* may select more than one answer.

** declining order includes: Other, Multiracial, Asian, Hispanic.

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and took 30–60 minutes to complete. Participants completed the survey at a time and place of their own choosing. Data were collected anonymously and stored securely with Survey Monkey.

Participation in this study was voluntary and its purpose was clearly described in the recruitment information. Electronic consent was obtained. Participants had the option to withdraw consent at any time prior to submitting responses. Inclusion criteria were (1) completion of a survey with parental response that the child had a sudden or rapid onset of gender dysphoria; and (2) parental indication that the child's gender dysphoria began during or after puberty. There was logic embedded in the survey that disqualified surveys that answered "no" (or skipped the question) about whether the child had a sudden or rapid onset of gender dysphoria and 23 surveys were disqualified prior to completion (20 "no" answers and 3 skipped

Table 2. Demographic and other baseline characteristics of AYAs.

Characteristics of AYAs		n	%
AYA sex at birth (natal sex)		256	
	Female	212	82.8
	Male	44	17.2
AYA average current age (range of ages)	16.4 (11–27)	256	
Academic diagnoses		253	
	Gifted	120	47.4
	Learning Disability	11	4.3
	Both	27	10.7
	Neither	95	37.5
Natal female expressed sexual orientation before announcement*		212	
	Asexual	18	8.5
	Bisexual or Pansexual	78	36.8
	Gay or Lesbian	58	27.4
	Straight (Heterosexual)	75	35.4
	Did not express	57	26.9
Natal male expressed sexual orientation before announcement*		44	
	Asexual	4	9.1
	Bisexual or Pansexual	5	11.4
	Gay	5	11.4
	Straight (Heterosexual)	25	56.8
	Did not express	11	25.0
Gender dysphoria began		256	
	During puberty	125	48.8
	After puberty	131	51.2
Along with a rapid onset of GD, the AYA also:		256	
	Belonged to a friend group where one or multiple friends became transgender-identified during a similar timeframe	55	21.5
	Had an increase in social media/internet use	51	19.9
	Both of the above	116	45.3
	Neither	13	5.1
	Don't know	21	8.2

* may select more than one answer.

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answers). After cleaning the data for the 274 completed surveys, 8 surveys were excluded for not having a sudden or rapid onset of gender dysphoria and 10 surveys were excluded for not having gender dysphoria that began during or after puberty, which left 256 completed surveys for inclusion. As the survey was voluntary there was no refusal or dropout rate.

Recruitment sites

There were four sites known to post recruitment information about the research study. The first three were posted due to direct communication with the moderators of the sites. The fourth site posted recruitment information secondary to the snowball sampling technique. The following descriptions provide details about these sites.

4thwavenow

4thwavenow was created in 2015. The site, as seen in digitally archived screenshots from 2015 and 2016, stated that it is a "safe place for gender-skeptical parents and their allies", offered support for parents, and expressed concern about the rush to diagnose young people as transgender and the rush to proceed to medical treatment for them [2, 48]. By June 2016, the site had expanded to include the writing of several parents, "formerly trans-identified people, and people with professional expertise and experience with young people questioning their gender identity" [9]. The perspective of this site might be described as cautious about medical and surgical transition overall—specifically with a cautious or negative view of medical and surgical interventions for children, adolescents, and young adults and an accepting view that mature adults can make their own decisions about transition [2, 9].

Transgendertrend

Transgendertrend was founded in November 2015. The digitally archived screenshots from November 2015 and July 2016 "Who Are We?" section include the following description, "We are an international group of parents based mainly in the UK, US and Canada, who are concerned about the current trend to diagnose 'gender non-conforming' children as transgender. We reject current conservative, reactionary, religious-fundamentalist views about sexuality. We come from diverse backgrounds, some with expertise in child development and psychology, some who were themselves extreme gender non-conforming children and adolescents, some whose own children have self-diagnosed as 'trans' and some who know supportive trans adults who are also questioning recent theories of 'transgenderism'" [49]. In July of 2016, there was additional text added, expressing concern about legislation regarding public bathrooms and changing rooms [50].

Youth trans critical professionals

Youth Trans Critical Professionals was created in March 2016. The digitally archived screenshot from the April 2016 "About" section stated the following: "This website is a community of professionals "thinking critically about the youth transgender movement. We are psychologists, social workers, doctors, medical ethicists, and academics. We tend to be left-leaning, open-minded, and pro-gay rights. However, we are concerned about the current trend to quickly diagnose and affirm young people as transgender, often setting them down a path toward medical transition. Our concern is with medical transition for children and youth. We feel that unnecessary surgeries and/or hormonal treatments which have not been proven safe in the long-term represent significant risks for young people" [51].

Parents of transgender children

Parents of Transgender Children is a private Facebook group with more than 8,000 members [52]. The current "About" section states that requests to join the group "will be denied if you are not the parent (or immediate caregiver or family member) of a transgender, gender-fluid, gender-questioning, agender, or other gender-nonconforming child (of any age); or if you are uncooperative during screening" and that the "group is comprised of parents and parenting figures, as well as a select group of advocates INVITED by the admin[istrative] staff to assist & help us with understanding legal and other concerns" [52]. Although the parent discussions and comments are not viewable to non-members [52], this group is perceived to be pro -gender-affirming. The Parents of Transgender Children Facebook group is considered to be a site to find parents who are supportive of their child's gender identity [53], and it is listed as a

resource in a gender affirming parenting guide [54] and by gender affirming organizations [55–56].

Measures

Basic demographic and baseline characteristics

Basic demographic and baseline characteristic questions, including parental attitudes about LGBT rights, were included. Parents were asked about their children's mental health disorders and neurodevelopmental disabilities that were diagnosed before their child's onset of gender dysphoria as well as during and after. The question, "Has your child been formally identified as academically gifted, learning disabled, both, neither?" was used as a proxy to estimate rates of academic giftedness and learning disabilities. Questions about trauma and non-suicidal self-injury were also included as were questions about social difficulties described in a previous research study about gender dysphoric adolescents [13].

DSM-5 diagnostic criteria for gender dysphoria in children

The DSM 5 criteria for gender dysphoria in children consist of eight indicators of gender dysphoria [57]. To meet criteria for diagnosis, a child must manifest at least six out of eight indicators including the one designated A1, "A strong desire to be the other gender or an insistence that one is the other gender (or some alternative gender different from one's assigned gender)." Three of the indicators (A1, A7, and A8) refer to desires or dislikes of the child. Five of the indicators (A2-A6) are readily observable behaviors and preferences such as a strong preference or strong resistance to wearing certain kinds of clothing; a strong preference or strong rejection of specific toys, games and activities; and a strong preference for playmates of the other gender [57]. The eight indicators were simplified for language and parents were asked to note which, if any, their child had exhibited prior to puberty. The requirement of six-month duration of symptoms was not included.

DSM-5 diagnostic criteria for gender dysphoria in adolescents and adults

The DSM-5 criteria for gender dysphoria in adolescents and adults consist of six indicators of gender dysphoria [57]. To meet criteria for diagnosis, an adolescent or adult must manifest at least two of the six indicators. The six indicators were simplified for language, the first indicator was adjusted for a parent to answer about their child, and parents were asked to note which, if any, their child was expressing currently. The requirement of six-month duration of symptoms was not included.

Exposure to friend groups and social media/internet content

Survey questions were developed to describe AYA friend groups, including number of friends that became transgender-identified in a similar time period as the AYA, peer group dynamics and behaviors, and exposure to specific types of social media/internet content and messages that have been observed on sites popular with teens, such as Reddit and Tumblr.

Behaviors, outcomes, clinical interactions

Survey questions were developed to specifically quantify adolescent behaviors that had been described by parents in online discussions and observed elsewhere. Participants were asked to describe outcomes such as their child's mental well-being and parent-child relationship since becoming transgender-identified. Parents were also asked about experiences with clinicians and their children's disposition regarding steps taken for transition and duration of

transgender-identification both for children who were still transgender-identified and for children who were no longer transgender-identified.

Coping with strong or negative emotions

Two questions about the AYAs' ability to cope with negative and strong emotions were included. One question was "How does your child handle strong emotions? (please select the best answer)." Offered answers were "My child is overwhelmed by strong emotions and goes to great lengths to avoid feeling them," "My child is overwhelmed by strong emotions and tries to avoid feeling them," "My child neither avoids not seeks out strong emotions," "My child tries to seek out situations in order to feel strong emotions," "My child goes to great lengths to seek out situations in order to feel strong emotions," "None of the above," "I don't know." The other question was "How would you rate your child's ability to deal with their negative emotions and channel them into something productive?" An example was given regarding dealing with a low test grade by studying harder for the next test (excellent) or by ignoring it, throwing a tantrum, blaming the teacher or distracting themselves with computer games, alcohol, drugs, etc. (extremely poor). Offered answers were: excellent, good, fair, poor, extremely poor, and I don't know.

Data analysis

Statistical analyses of quantitative data were performed using Excel and custom shell scripts (Unix). Quantitative findings are presented as frequencies, percentages, ranges, means and/or medians. ANOVAs, chi-squared, and t-tests comparisons were used where appropriate using publicly available calculators and $p<0.05$ was considered significant. Qualitative data were obtained from open text answers to questions that allowed participants to provide additional information or comments. The types of comments and descriptions were categorized, tallied, and reported numerically. A grounded theory approach was selected as the analytic strategy of choice for handling the qualitative responses because it allowed the researcher to assemble the data in accordance with the salient points the respondents were making without forcing the data into a preconceived theoretical framework of the researcher's own choosing [58]. Illustrative respondent quotes and summaries from the qualitative data are used to illustrate the quantitative results and to provide relevant examples. Two questions were targeted for full qualitative analysis of themes (one question on friend group behaviors and one on clinician interactions). For these questions, a second reviewer with expertise in qualitative methods was engaged (MM). Both the author (LL) and reviewer (MM) independently analyzed the content of the open text answers and identified major themes. Discrepancies were resolved with collaborative discussion and themes were explored and refined until agreement was reached for the final lists of themes. Representative quotes for each theme were selected by LL, reviewed by MM, and agreement was reached.

Results

Baseline characteristics

Baseline characteristics (Table 1) included that the vast majority of parents favored gay and lesbian couples' right to legally marry (85.9%) and believed that transgender individuals deserve the same rights and protections as other individuals in their country (88.2%). Along with the sudden or rapid onset of gender dysphoria, the AYAs belonged to a friend group where one or multiple friends became gender dysphoric and came out as transgender during a similar time as they did (21.5%), exhibited an increase in their social media/internet use (19.9%), both

(45.3%), neither (5.1%), and don't know (8.2%) (Table 2). For comparisons, the first three categories will be combined and called "social influence" (86.7%) and the last two combined as "no social influence" (13.3%). Nearly half (47.4%) of the AYAs had been formally diagnosed as academically gifted, 4.3% had a learning disability, 10.7% were both gifted and learning disabled, and 37.5% were neither. Sexual orientation as expressed by the AYA prior to transgender-identification is listed separately for natal females and for natal males (Table 2). Overall, 41% of the AYAs expressed a non-heterosexual sexual orientation prior to disclosing a transgender-identification.

It is important to note that none of the AYAs described in this study would have met diagnostic criteria for gender dysphoria in childhood (Table 3). In fact, the vast majority (80.4%) had zero indicators from the DSM-5 diagnostic criteria for childhood gender dysphoria with 12.2% possessing one indicator, 3.5% with two indicators, and 2.4% with three indicators. Breaking down these results, for readily observable indicators (A2-6), 83.5% of AYAs had zero indicators, 10.2% had one indicator, 3.9% had two indicators, and 1.2% had three indicators. For the desire/dislike indicators (A1, A7, A8), which a parent would have knowledge of if the child expressed them verbally, but might be unaware if a child did not, 95.7% had zero indicators and 3.5% had one indicator. Parents responded to the question about which, if any, of the indicators of the DSM criteria for adolescent and adult gender dysphoria their child was

Table 3. DSM 5 Indicators for gender dysphoria.

Characteristics		n	%
AYAs who would have met diagnostic criteria for gender dysphoria in childhood		0	0
Number of DSM 5 indicators for gender dysphoria in children exhibited prior to puberty		255	
	Zero indicators	205	80.4
	One indicator	31	12.2
	Two indicators	9	3.5
	Three indicators	6	2.4
	Four indicators	3	1.2
Desire/Dislike Indicators (A1, A7, or A8)		255	
	Zero indicators	244	95.7
	One indicators	9	3.5
	Two indicators	0	0
	Three indicators	1	0.4
Readily observable indicators (A2-A6)		254	
	Zero indicators	212	83.5
	One indicator	26	10.2
	Two indicators	10	3.9
	Three indicators	3	1.2
	Four indicators	3	1.2
Average number of DSM 5 indicators for adolescent and adult gender dysphoria that the AYA is experiencing currently (range)			
	3.5 (range 0–6)	247	
AYAs currently experiencing two or more indicators of gender dysphoria for adolescents and adults		250	
	Yes	208	83.2
	No	40	16.0
	Don't know	2	0.8

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experiencing currently. The average number of positive current indicators was 3.5 (range 0–6) and 83.2% of the AYA sample was currently experiencing two or more indicators. Thus, while the focal AYAs did not experience childhood gender dysphoria, the majority of those who were the focus of this study were indeed gender dysphoric at the time of the survey completion.

The AYAs who were the focus of this study had many comorbidities and vulnerabilities predating the onset of their gender dysphoria, including psychiatric disorders, neurodevelopmental disabilities, trauma, non-suicidal self-injury (NSSI), and difficulties coping with strong or negative emotions (Table 4). The majority (62.5%) of AYAs had one or more diagnoses of a psychiatric disorder or neurodevelopmental disability preceding the onset of gender dysphoria (range of the number of pre-existing diagnoses 0–7). Many (48.4%) had experienced a traumatic or stressful event prior to the onset of their gender dysphoria. Open text descriptions of trauma were categorized as "family" (including parental divorce, death of a parent, mental disorder in a sibling or parent), "sex or gender related" (such as rape, attempted rape, sexual harassment, abusive dating relationship, break-up), "social" (such as bullying, social isolation), "moving" (family relocation or change of schools); "psychiatric" (such as psychiatric hospitalization), and medical (such as serious illness or medical hospitalization). Almost half (45.0%) of AYAs were engaging in non-suicidal self-injury (NSSI) behavior before the onset of gender dysphoria. Coping styles for these AYAs included having a poor or extremely poor ability to handle negative emotions productively (58.0%) and being overwhelmed by strong emotions and trying to avoid (or go to great lengths to avoid) experiencing them (61.4%) (Table 4). The majority of respondents (69.4%) answered that their child had social anxiety during adolescence; 44.3% that their child had difficulty interacting with their peers, and 43.1% that their child had a history of being isolated (not associating with their peers outside of school activities).

Announcing a transgender-identification

At the time the AYA announced they were transgender-identified ("came out"), most were living at home with one or both parents (88.3%) and a small number were living at college (6.2%). The average age of announcement of a transgender-identification was 15.2 years of age (range 10–21) (Table 5). Most of the parents (80.9%) answered affirmatively that their child's announcement of being transgender came "out of the blue without significant prior evidence of gender dysphoria." Respondents were asked to pinpoint a time when their child seemed not at all gender dysphoric and to estimate the length of time between that point and their child's announcement of a transgender-identity. Almost a third of respondents (32.4%) noted that their child did not seem gender dysphoric when they made their announcement and 26.0% said the length of time from not seeming gender dysphoric to announcing a transgender identity was between less than a week to three months. The most striking examples of "not seeming at all gender dysphoric" prior to making the announcement included a daughter who loved summers and seemed to love how she looked in a bikini, another daughter who happily wore bikinis and makeup, and another daughter who previously said, "I love my body!"

The majority of respondents (69.2%) believed that their child was using language that they found online when they "came out." A total of 130 participants provided optional open text responses to this question, and responses fell into the following categories: why they thought the child was using language they found online (51); description of what the child said but didn't provide a reason that they suspected the child was using language they found online (61); something else about the conversation (8) or the child (7) and don't know (3). Of the 51 responses describing reasons why respondents thought their child was reproducing language

Table 4. AYA baseline comorbidities and vulnerabilities predating the onset of gender dysphoria.

Characteristics		n	%
Mental disorder or neurodevelopmental disability diagnosed prior to the onset of gender dysphoria*		251	
	Anxiety	117	46.6
	Depression	99	39.4
	Attention Deficit Hyperactivity Disorder (ADHD)	29	11.6
	Obsessive Compulsive Disorder (OCD)	21	8.4
	Autism Spectrum Disorder (ASD)	20	8.0
	Eating Disorder	12	4.8
	Bipolar Disorder	8	3.2
	Psychosis	6	2.4
	None of above	94	37.5
	(Other) Borderline	3	1.2
	(Other) Oppositional Defiant Disorder	2	0.8
Traumatic or stressful experience prior to the onset of gender dysphoria		252	
	Yes	122	48.4
	No	91	36.1
	Don't know	38	15.1
	Other	1	0.4
Types of trauma*		113	
	Family	50	44.2
	Sex/Gender related	34	30.1
	Social	23	20.4
	Moving	20	17.7
	Psychiatric	9	8.0
	Medical	7	6.2
Non-suicidal self-injury (NSSI) before the onset of gender dysphoria		180	
		81	45.0
Ability to handle negative emotions productively		255	
	Excellent/Good	34	13.3
	Fair	70	27.5
	Poor/Extremely Poor	148	58.0
	Don't know	3	1.2
Coping style for dealing with strong emotions		254	
	Overwhelmed by strong emotions and tries to /goes to great lengths to avoid feeling them	156	61.4
	Neither avoids nor seeks out strong emotions	29	11.4
	Tries to/goes to great lengths to seeks out strong emotions	33	13.0
	Don't know	25	9.8
	None of the above	11	4.3
Social vulnerabilities		255	
	During adolescence child had social anxiety	177	69.4
	Child had difficulty interacting with their peers	113	44.3
	History of being isolated (not interacting with peers outside of school activities)	110	43.1
	Child felt excluded by peers throughout most of grade school	93	36.5
	Child had persistent experiences of being bullied before the onset of gender dysphoria	74	29.0

*may select more than one answer.

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Table 5. Announcing a transgender-identification.

Characteristics		n	%
Age of AYA when the AYA announced a transgender-identification (range)	15.2 average (10–21)	255	
Living arrangement at announcement		256	
	Living at home with one or both parents	226	88.3
	Living at college or university	16	6.2
	Other	14	5.5
AYA's announcement came from "out of the blue, without significant prior evidence of gender dysphoria"		256	
	Yes	207	80.9
	No	33	12.9
	Other	16	6.2
If a time was pinpointed when the child seemed not at all gender dysphoric, how long between that time and the child's announcement of a transgender-identity?		250	
	Did not seem at all gender dysphoric when they announced and transgender-identity	81	32.4
	Less than a week to 3 months	65	26.0
	4–6 months	31	12.4
	7–9 months	10	4.0
	10–12 months	29	11.6
	More than 12 months	20	8.0
	Don't know	14	5.6
Parent suspects that when the child first announced a transgender-identity, that the child used language that they found online		253	
	Yes	175	69.2
	No	53	20.9
	N/A	25	9.9
Parent thinks their child is correct in their child's belief of being transgender		255	
	Yes	6	2.4
	No	195	76.5
	Don't know	38	14.9
	Other	16	6.3
How soon after the announcement did the AYA ask for transition?		255	
	At the same time	86	33.7
	Between less than one week to one month	33	12.9
	2–5 months after announcement	26	10.2
	6 or more months after announcement	19	7.5
	Other	16	6.3
	N/A	75	29.4
Intention and request for transition*		189	
	AYA told the parent that they want cross-sex hormones	127	67.2
	AYA told the parent that they want to go to a gender therapist/gender clinic	111	58.7
	AYA told the parent that they want surgery	101	53.4
	AYA brought up the issue of suicides in transgender teens as a reason that their parent should agree to treatment	59	31.2

(*Continued*)

Table 5. (Continued)

Characteristics		n	%
AYA has very high expectation that transitioning will solve their problems in social, academic, occupational, or mental health areas		256	
	Yes	143	55.9
	No	13	5.1
	Don't know	100	39.1
AYA was willing to work on basic mental health before seeking gender treatments		253	
	Yes	111	43.9
	No	71	28.1
	Don't know	30	11.9
	N/A	41	16.2

*may select more than one answer.

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they found online, the top two reasons were that it didn't sound like their child's voice (19 respondents) and that the parent later looked online and recognized the same words and phrases that their child used when they announced a transgender identity (14 respondents). The observation that it didn't sound like their child's voice was also expressed as "sounding scripted," like their child was "reading from a script," "wooden," "like a form letter," and that it didn't sound like their child's words. Parents described finding the words their child said to them "verbatim," "word for word," "practically copy and paste," and "identical" in online and other sources. The following quotes capture these top two observations. One parent said, "It seemed different from the way she usually talked—I remember thinking it was like hearing someone who had memorized a lot of definitions for a vocabulary test." Another respondent said, "The email [my child sent to me] read like all of the narratives posted online almost word for word."

The following case summaries were selected to illustrate peer, trauma, and psychiatric contexts that might indicate more complicated clinical pictures.

- A 12-year-old natal female was bullied specifically for going through early puberty and the responding parent wrote "as a result she said she felt fat and hated her breasts." She learned online that hating your breasts is a sign of being transgender. She edited her diary (by crossing out existing text and writing in new text) to make it appear that she has always felt that she is transgender.
- A 14-year-old natal female and three of her natal female friends were taking group lessons together with a very popular coach. The coach came out as transgender, and, within one year, all four students announced they were also transgender.
- A natal female was traumatized by a rape when she was 16 years of age. Before the rape, she was described as a happy girl; after the rape, she became withdrawn and fearful. Several months after the rape, she announced that she was transgender and told her parents that she needed to transition.
- A 21-year-old natal male who had been academically successful at a prestigious university seemed depressed for about six months. Since concluding that he was transgender, he went on to have a marked decline in his social functioning and has become increasingly angry and

hostile to his family. He refuses to move out or look for a job. His entire family, including several members who are very supportive of the transgender community, believe that he is "suffering from a mental disorder which has nothing to do with gender."

- A 14-year-old natal female and three of her natal female friends are part of a larger friend group that spends much of their time talking about gender and sexuality. The three natal female friends all announced they were trans boys and chose similar masculine names. After spending time with these three friends, the 14-year-old natal female announced that she was also a trans boy.

The majority (76.5%) of the surveyed parents felt that their child was incorrect in their belief of being transgender (Table 5). More than a third (33.7%) of the AYAs asked for medical and/or surgical transition at the same time that they announced they were transgender-identified. Two thirds (67.2%) of the AYAs told their parent that they wanted to take cross-sex hormones; 58.7% that they wanted to see a gender therapist/gender clinic; and 53.4% that they wanted surgery for transition. Almost a third (31.2%) of AYAs brought up the issue of suicides in transgender teens as a reason that their parent should agree to treatment. More than half of the AYAs (55.9%) had very high expectations that transitioning would solve their problems in social, academic, occupational or mental health areas. While 43.9% of AYAs were willing to work on basic mental health before seeking gender treatments, a sizable minority (28.1%) were not willing to work on their basic mental health before seeking gender treatment. At least two parents relayed that their child discontinued psychiatric care and medications for pre-existing mental health conditions once they identified as transgender. One parent, in response to the question about if their child had very high expectations that transitioning would solve their problems elaborated, "Very much so. [She] discontinued anti-depressant quickly, stopped seeing psychiatrist, began seeing gender therapist, stopped healthy eating. [She] stated 'none of it' (minding what she ate and taking her Rx) 'mattered anymore.' This was her cure, in her opinion."

Friend-group exposure

The adolescent and young adult children were, on average, 14.4 years old when their first friend became transgender-identified (Table 6). Within friendship groups, the average number of individuals who became transgender-identified was 3.5 per group. In 36.8% of the friend groups described, the majority of individuals in the group became transgender-identified. The order that the focal AYA "came out" compared to the rest of their friendship group was calculated from the 119 participants who provided the number of friends coming out both before and after their child and 74.8% of the AYAs were first, second or third of their group. Parents described intense group dynamics where friend groups praised and supported people who were transgender-identified and ridiculed and maligned non-transgender people. Where popularity status and activities were known, 60.7% of the AYAs experienced an increased popularity within their friend group when they announced a transgender-identification and 60.0% of the friend groups were known to mock people who were not transgender or LGBTIA (lesbian, gay, bisexual, transgender, intersex, or asexual).

For the question about popularity changes when the child came out as having a transgender-identification, 79 participants provided optional open text responses which were categorized as: descriptions of the responses the child received (39); descriptions of the friends (14); description that the child did not "come out" to friends (8); not sure (9); speculation on how the child felt from the response (4), other (5). Of the 39 descriptions of responses, 19 of these responses referred to positive benefits the child received after coming out including positive attention, compliments, increased status, increased popularity, increased numbers of online

Table 6. Friend group exposure.

Characteristics		n	%
The AYA has been part of a friend group where one or more friends has come out as transgender around a similar timeframe as they did		254	
	Yes	176	69.3
	No	47	18.5
	Don't know	31	12.2
Age of AYA when their first friend became transgender-identified (range)	14.4 average (11–21)	174	
Number of friends from the friendship group who became gender dysphoric average (range)	3.5 average (2–10)	138	
Where numbers known, friend groups where the MAJORITY of the friends in the friendship group became transgender-identified		125	
	Yes	46	36.8
	No	79	63.2
Order of the AYAs "coming out" compared to the others in the friendship group		119	
	First in the friendship group	4	3.4
	Second in the friendship group	52	43.7
	Third in the friendship group	33	27.7
	Fourth in the friendship group	18	15.1
	Fifth in the friendship group	5	4.2
	Sixth or Seventh in the friendship group	6	5.0
Where popularity status known, change in popularity within friend group when AYA announced their transgender-identification		178	
	Increased popularity	108	60.7
	Decreased popularity	11	6.2
	Unchanged popularity	59	33.1
Where friend group activities known, friend group known to mock people who are not transgender/LGBT		145	
	Yes	87	60.0
	No	58	40.0

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followers, and improved protection from ongoing bullying. The following are quotes from parents about the perceived benefits of transgender-identification afforded to their child. One respondent said, "Great increase in popularity among the student body at large. Being trans is a gold star in the eyes of other teens." Another respondent explained, "not so much 'popularity' increasing as 'status'. . .also she became untouchable in terms of bullying in school as teachers who ignored homophobic bullying . . .are now all at pains to be hot on the heels of any trans bullying." Seven respondents described a mixed response where the child's popularity increased with some friends and decreased with others. Seven respondents described a neutral response such as "All of the friends seemed extremely accepting." Two described a temporary increase in their child's popularity: "There was an immediate rush of support when he came out. Those same friends have dwindled to nothing as he rarely speaks to any of them now." Another described the loss of friends. And two parents described that "coming out" prevented the loss of friends explained by one respondent as "to not be trans one would not have been included in his group."

Several AYAs expressed significant concern about the potential repercussions from their friend group when they concluded that they were not transgender after all. There were two unrelated cases with similar trajectories where the AYAs spent some significant time in a different setting, away from their usual friend group, without access to the internet. Parents described that these AYAs made new friendships, became romantically involved with another person, and during their time away concluded that they were not transgender. In both cases, the adolescents, rather than face their school friends, asked to move and transfer to different high schools. One parent said that their child, ". . .couldn't face the stigma of going back to school and being branded as a fake or phony. . . . Or worse, a traitor or some kind of betrayer. . .[and] asked us if we could move." In the other case, the parent relayed that their child thought none of the original friends would understand and expressed a strong desire to ". . .get out of the culture that 'if you are cis, then you are bad or oppressive or clueless.'" Both families were able to relocate and both respondents reported that their teens have thrived in their new environments and new schools. One respondent described that their child expressed relief that medical transition was never started and felt there would have been pressure to move forward had the family not moved away from the peer group.

Qualitative analysis

The open-ended responses from the question about whether the AYAs and friends mocked, teased, or made fun of individuals who weren't transgender or LGBTIA was selected for additional qualitative analysis. Seven major themes were identified from the comments provided by participants and are described, with representative supporting quotes.

Theme: Groups targeted. The groups targeted for mocking by the friend groups are often heterosexual (straight) people and non-transgender people (called "cis" or "cisgender"). Sometimes animosity was also directed towards males, white people, gay and lesbian (non-transgender) people, aromantic and asexual people, and "terfs". One participant explained, "They are constantly putting down straight, white people for being privileged, dumb and boring." Another participant elaborated, "In general, cis-gendered people are considered evil and unsupportive, regardless of their actual views on the topic. To be heterosexual, comfortable with the gender you were assigned at birth, and non-minority places you in the 'most evil' of categories with this group of friends. Statement of opinions by the evil cis-gendered population are consider phobic and discriminatory and are generally discounted as unenlightened."

Theme: Individuals targeted. In addition to targeting specific groups of people for mocking, the AYAs and their friend groups also directed mocking towards individuals in the AYAs' lives such as parents, grandparents, siblings, peers, allies, and teachers. The following quotes describe individuals targeted. One participant said, "They call kids who are not LGBT dumb and cis. And the mocking has been aimed at my transgender-identified child's [sibling]." Another parent said, "They definitely made fun of parents and teachers who did not agree with them." And a third participant said, ". . .they were asked to leave [a school-based LGBT club] because they were not queer enough [as straight and bisexual allies]. [One of them] was [then] bullied, harassed and denounced online."

Theme: Behaviors occurred both in person and in online settings. Parents observed the behaviors both in-person and in online settings, and specifically mentioned seeing posts and conversations on Tumblr, Twitter, Facebook, and Instagram. On participant said, "They speak with derision about how cis-gendered people do not understand them and are so close-minded." Another participant said, "I hear them disparaging heterosexuality, marriage and nuclear families." Another participant said, "On my daughter's Tumblr blog, she has liked or favorited or re-posted disparaging comments about those who aren't transgender or seem to

misunderstand the transgender identity." And another parent reported, "Her real life friends don't [mock non-LGBT people] but online they are always swapping jokes and comments about cisgender and about transphobia."

Theme: Examples of behaviors. Participants gave many examples of the observed behaviors that were mocking towards non-transgender people and non-LGB people. One participant said, "My daughter called me a 'breeder' and says things in a mocking 'straight person voice'. Her friends egg her on when she does this." Another parent offered, "If they aren't mocking 'cis' people, they are playing pronoun police and mocking people who can't get the pronouns correct." Another participant said, "New vocabulary includes 'cis-stupid' and 'cis-stupidity.'" And a fourth participant described, "They assume anyone that is critical about being transgender (even just asking questions) is either ignorant or filled with hate."

Theme: Emphasizing victimhood. Participants described that their children and friend group seemed to focus on feeling as though they were victims. One participant described, "They seem to wear any problems they may have, real or perceived like badges of honor. . .I feel like they want to believe they are oppressed & have really 'been through life', when they have little life experience." Another participant said, ". . .there is a lot of feeling like a victim [and being] part of a victimized club." Another parent said "But all talk is very 'victim' centered". And finally, another said, "They passionately decry 'Straight Privilege' and 'White Male Privilege'—while emphasizing their own 'Victimhood.'"

Theme: Consequences of behaviors. A few participants describe that because of their child's behavior, there were consequences, including making it difficult for one child to return to her school and the following description from another parent, "Most relatives have blocked her on [social media] over constant jokes regarding cis and straight people."

Theme: Fueling the behaviors. In some cases, parents describe a synergistic effect of kids encouraging other kids to persist in the behavior as was described in a previous quote, "Her friends egg her on when she does this" as well as the following, "Lots of discussion revolving around how their teachers 'discriminate' or are 'mean' to them based on their declared LGBTIA identity, and they get each other riled up convincing each other of their persecution by these perceived wrongs . . . privately they mock our intolerance, and in person act upon these false beliefs by treating us as people out to get them. . ."

Internet/social media exposure

In the time period just before announcing that they were transgender, 63.5% of AYAs exhibited an increase in their internet/social media (Table 7). To assess AYA exposure to existing online content, parents were asked what kind of advice their child received from someone/people online. AYAs had received online advice including how to tell if they were transgender (54.2%); the reasons that they should transition right away (34.7%); that if their parents did not agree for them to take hormones that the parents were "abusive" and "transphobic" (34.3%); that if they waited to transition they would regret it (29.1%); what to say and what not to say to a doctor or therapist in order to convince them to provide hormones (22.3%); that if their parents were reluctant to take them for hormones that they should use the "suicide narrative" (telling the parents that there is a high rate of suicide in transgender teens) to convince them (20.7%); and that it is acceptable to lie or withhold information about one's medical or psychological history from a doctor or therapist in order to get hormones/get hormones faster (17.5%). Two respondents, in answers to other questions, described that their children later told them what they learned from online discussion lists and sites. One parent reported, "He has told us recently that he was on a bunch of discussion lists and learned tips there. Places where teens and other trans people swap info. Like to use [certain, specific] words [with] the

Table 7. Internet/Social media exposures.

		n	%
AYAs internet/social media use just prior to announcement		255	
	Increased social media/internet use	162	63.5
	Decreased social media/internet use	3	1.2
	Unchanged social media/internet use	49	19.2
	Don't know	41	16.1
AYA exposure to internet content/advice*		251	
	How to tell if they are transgender	136	54.2
	The reasons that they should transition right away	87	34.7
	That if their parents did not agree to take them for hormones, that the parents are "abusive" and "transphobic"	86	34.3
	That if they waited to transition they would regret it	73	29.1
	That if they didn't transition immediately they would never be happy	72	28.7
	How to order physical items (binders, packers, etc) without parents finding out	67	26.7
	What to say and what NOT to say to a doctor or therapist in order to convince them to provide hormones	56	22.3
	That if their parents are reluctant to take them for hormones, that they should use the "suicide narrative" to convince them (telling the parents that there is a high rate of suicide in transgender teens.)	52	20.7
	Medical advice about the risks and benefits of hormones	55	21.9
	Medical advice about the risks and benefits of surgery	47	18.7
	That it is acceptable to lie to or withhold information about one's medical or psychological history from a doctor or therapist in order to get hormones/ get hormones faster	44	17.5
	How to hide physical items from parents	40	15.9
	How to hide or make excuses for physical changes	26	10.4
	How to get money from others online in order to pay for medications, etc	25	10.0
	How to get hormones from online sources	24	9.6
	How to hide hormones from parents	21	8.4
	I don't know if my child received online advice about these topics	127	50.6

*may select more than one answer.

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therapist when describing your GD, because [they are] code for potentially suicidal and will get you a diagnosis and Rx for hormones." Another parent disclosed, "The threat of suicide was huge leverage. What do you say to that? It's hard to have a steady hand and say no to medical transition when the other option is dead kid. She learned things to say that would push our buttons and get what she wanted and she has told us now that she learned that from trans discussion sites."

Parents identified the sources they thought were most influential for their child becoming gender dysphoric. The most frequently answered influences were: YouTube transition videos (63.6%); Tumblr (61.7%); a group of friends they know in person (44.5%); a community/group of people that they met online (42.9%); a person they know in-person (not online) 41.7%. In contrast to the majority of responses, two participants commented that they didn't think the

sources influenced their child to become gender dysphoric, rather they gave their child a name for their feelings or gave the child confidence to come out. The following quotes illustrate the dominant quantitative findings. One parent wrote, "We believe the biggest influence was the online pro-transition blogs and youtube videos. We feel she was highly influenced by the 'if you are even questioning your gender-you are probably transgender' philosophy. . .In the 'real world' her friends, other trans peers, and newfound popularity were additional areas of reinforcement." Another respondent described the online influence as part of a different question, "I believe my child experienced what many kids experience on the cusp of puberty—uncomfortableness!—but there was an online world at the ready to tell her that those very normal feelings meant she's in the wrong body."

Mental well-being, mental health, and behaviors

The trajectories of the AYAs were not consistent with the narrative of discovering one's authentic self and then thriving. Specifically, parents reported that, after "coming out," their children exhibited a worsening of their mental well-being. Additionally, parents noted worsening of the parent-child relationship and observed that their children had narrowed their interests (Table 8). Although small numbers of AYAs had improvement in mental well-being (12.6%), parent-child relationship (7.4%), grades/academic performance (6.4%), and had broadened their interests and hobbies (5.1%); the most common outcomes were worsened mental well-being (47.2%); worsened parent child relationship (57.3%); unchanged or mixed grades/academic performance (59.1%); and a narrowed range of interests and hobbies

Table 8. Outcomes and behaviors.

Characteristics		n	%
AYA mental well-being since announcement		254	
	Worse	120	47.2
	Better	32	12.6
	Unchanged or mixed	101	39.8
	Don't know	1	0.4
Parent-child relationship since announcement		253	
	Worse	145	57.3
	Better	18	7.4
	Unchanged or mixed	89	35.2
	Don't know	1	0.4
Grades/academic performance		220	
	Worse	76	34.5
	Better	14	6.4
	Unchanged/mixed	130	59.1
Range of interests and hobbies		255	
	Much broader	2	0.8
	Somewhat broader	11	4.3
	Unchanged	93	36.5
	Somewhat narrower	64	25.1
	Much narrower	56	22.0
	There are very few topics outside of transgender issues that my child is interested in	28	11.0
	Don/t know	1	0.4

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(58.1%). One parent describing her child's trajectory offered, "After announcing she was transgender, my daughter's depression increased significantly. She became more withdrawn. She stopped participating in activities which she previously enjoyed, stopped participating in family activities, and significantly decreased her interaction with friends. Her symptoms became so severe that she was placed on medication by her physician." Table 9 describes cumulative rates of mental illness and neurodevelopmental disability at the time of survey.

A total of 63.8% of the parents have been called "transphobic" or "bigoted" by their children for one or more reasons, the most common being for: disagreeing with the child about the child's self-assessment of being transgender (51.2%); recommending that the child take more time to figure out if their feelings of gender dysphoria persist or go away (44.6%); expressing concerns for the child's future if they take hormones and/or have surgery (40.4%); calling their child by the pronouns they used to use (37.9%); telling the child they thought that hormones or surgery would not help them (37.5%); recommending that their child work on other mental health issues first to determine if they are the cause of the dysphoria (33.3%); calling the child by their birth name (33.3%); or recommending a comprehensive mental health evaluation before starting hormones and/or surgery (20.8%) (Table 10). There were eight cases of estrangement. Estrangement was child-initiated in six cases where the child ran away, moved out, or otherwise refused contact with parent. There were two cases where the estrangement was initiated by the parent because the AYA's outbursts were affecting younger siblings or there was a threat of violence made by the AYA to the parent.

AYAs are reported to have exhibited one or more of the following behaviors: expressed distrust of information about gender dysphoria and transgenderism coming from mainstream doctors and psychologists (51.8%); tried to isolate themselves from their family (49.4%); expressed that they only trust information about gender dysphoria and transgenderism that comes from transgender websites and/or transgender people and sources (46.6%); lost interest in activities where participants aren't predominantly transgender or LGBTIA (32.3%); stopped spending time with friends who were not transgender (25.1%); expressed distrust of people who were not transgender (22.7%) (Table 10). Many AYAs have also: withdrawn from their family (45.0%); told other people or posted on social media that their parent is "transphobic," "abusive," or "toxic" because the parent does not agree with child's self-assessment of being transgender (43.0%); refused to speak to their parent (28.5%), defended the practice of lying to or withholding information from therapists or doctors in order to obtain hormones for transition more quickly (16.5%); tried to run away (6.8%). The behaviors and outcomes listed above

Table 9. AYA Cumulative mental disorder and neurodevelopmental disability diagnoses.

Characteristics		n	%
Mental disorder or neurodevelopmental disability		243	
	Anxiety	154	63.4
	Depression	143	58.8
	Attention Deficit Hyperactivity Disorder (ADHD)	36	14.8
	Obsessive Compulsive Disorder (OCD)	30	12.3
	Autism Spectrum Disorder (ASD)	30	12.3
	Eating Disorder	17	7.0
	Bipolar Disorder	17	7.0
	Psychosis	8	3.3
	None of above	52	21.4
	(Other) Borderline	7	2.9
	(Other) Oppositional Defiant Disorder	2	0.8

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Table 10. Additional behaviors.

		n	%
Parents have been called "transphobic" or "bigoted" by their child for the following reasons*		240	
	Disagreeing with their child about the child's assessment of being transgender	123	51.2
	Recommending that their child take more time to figure out if their feelings of gender dysphoria persist or go away	107	44.6
	Expressing concerns for their child's future if the child were to take hormones and/or have surgery	97	40.4
	Referring to their child by the pronouns that they used to use before announcement	91	37.9
	Telling their child that they thought hormones/surgery would not help them	90	37.5
	Calling their child by the child's birth name	80	33.3
	Recommending that their child work on other mental health issues first to determine if they are the cause of their dysphoria	80	33.3
	Recommending therapy for basic mental health issues (not related to gender)	74	30.8
	Recommending a comprehensive evaluation before starting hormones and/or surgery	50	20.8
	None of the above	87	36.2
Distrust and isolating behaviors exhibited by AYAs*		251	
	Expressed distrust of information about gender dysphoria and transgenderism coming from mainstream doctors and psychologists	130	51.8
	Tried to isolate themselves from their family	124	49.4
	Expressed that they ONLY trust information about gender dysphoria and transgenderism that comes from transgender websites and/or transgender people and sources	117	46.6
	Lost interest in activities where participants aren't predominantly transgender or LGBTIA	81	32.3
	Lost interest in activities that were not related to transgender or LGBTIA issues	65	25.9
	Stopped spending time with friends who are not transgender	63	25.1
	Expressed distrust of people who are not transgender	57	22.7
	Expressed hostility towards people who are not transgender	46	18.3
	None of the above	44	17.5
Other behavior and outcomes for AYAs*		249	
	Withdrawn from family	112	45.0
	Told other people or posted on social media that their parent is "transphobic", "abusive", or "toxic" because the parent does not agree with the child's assessment of being transgender	107	43.0
	Refused to speak to parent	71	28.5
	Defended the practice of lying to or withholding information from therapists or doctors in order to obtain hormones for transition more quickly	41	16.5
	Tried to run away	17	6.8
	Been unable to obtain a job	25	10.0
	Been unable to hold a job	18	7.2
	Dropped out of college	12	4.8
	Dropped out of high school	12	4.8
	Needed to take a leave of absence from college	12	4.8
	Been fired from a job	9	3.6
	Needed a leave of absence from high school	1	0.4
	None of the above	86	34.5
For any of the above, is this a significant change from the child's baseline behavior?		161	
	Yes	115	71.4
	No	46	28.6

*may select more than one answer.

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were considered significant changes from the child's baseline behaviors for 71.4% of respondents checking any of the items.

There was a subset of eight cases where parents described watching their child have declining mental well-being as they became gender dysphoric and transgender-identified and then had improving mental well-being as they dropped or backed away from a transgender-identification. One parent described a marked change in her daughter when she was out of school temporarily. "[Her] routine was disrupted. She spent all day on the internet, and lost her many school friends—her only friends were on-line and members of the trans community. In three months, my daughter announced she is trans, gender dysphoric, wants binders and top surgery, testosterone shots. . .she started self-harming. Now back at school. . .she tweeted that she's so young, isn't sure if she is trans, no longer wants to be referred to by the male name she had chosen. . .Since she has started back at school and is being exposed to a wide variety of people she is WAY happier." Another parent described, "My daughter's insight has improved considerably over the last few years, and she has also outgrown the belief that she is transgender. My daughter actually seemed to be looking for a reason for her depression which is now being successfully treated. . .My daughter is MUCH happier now that she is being treated for her genuine issues. Coming out as trans made her much worse for a while."

There was a subset of 30 cases where the AYAs' transgender-identification occurred in the context of a decline in their ability to function (such as dropping out of high school or college, needing a leave of absence from high school or college, and/or being unable to obtain or hold a job), which parents reported as a significant change from their child's baseline behavior. The declines were substantial as 43.3% of these AYAs had been identified as academically gifted students (some described as top of their class in high school, earning outstanding grades at prestigious universities) before they began to fail their classes, drop out of high school or college, and became unable to hold a job. In most of these cases (76.7%), there was one or more psychiatric diagnosis made at the same time or within the year (60.0%) or within two years (16.7%) of the AYA's new transgender-identification. Of the 23 individuals who had a psychiatric diagnosis made within two years of assuming a transgender-identification, 91.3% (21/23) were diagnosed with depression; 73.9% (17/23) with anxiety; 26.0% (6/23) with bipolar disorder; 17.4% (4/23) with borderline personality disorder; 8.7% (2/23) with psychosis/psychotic episode: and 8.7% (2/23) with an eating disorder.

Clinical encounters

Parents were asked if their child had seen a gender therapist, gone to a gender clinic, or seen a physician for the purpose of beginning transition and 92 respondents (36.2%) answered in the affirmative (Table 11). Many of the respondents clarified that their child had seen a clinician regarding their gender dysphoria for evaluation only. Although participants were not asked directly what kind of provider their child saw, specialties that were mentioned in answers included: general psychologists, pediatricians, family doctors, social workers, gender therapists, and endocrinologists. For parents who knew the content of their child's evaluation, 71.6% reported that the clinician did not explore issues of mental health, previous trauma, or any alternative causes of gender dysphoria before proceeding and 70.0% report that the clinician did not request any medical records before proceeding. Despite all of the AYAs in this study sample having an atypical presentation of gender dysphoria (no gender dysphoria prior to puberty), 23.8% of the parents who knew the content of their child's visit reported that the child was offered prescriptions for puberty blockers and/or cross-sex hormones at the first visit.

One participant described, "For the most part, I was extremely frustrated with providers NOT acknowledging the mental disorder, anxiety, depression, etc before recommending

Table 11. Interactions with clinicians.

		n	%
Did the AYA see a gender therapist, go to a gender clinic or see a physician for the purpose of transition?		254	
	No	151	59.4
	Yes	92	36.2
	Don't know	11	4.3
Did the therapist/physician/clinic staff explore issues of mental health, previous trauma, or any alternative causes of gender dysphoria before proceeding?		100	
	Yes	21	21.0
	No	53	53.0
	Don't know	26	26.0
Did the therapist/physician/clinic staff request any medical records before proceeding?		99	
	Yes	21	21.2
	No	49	49.5
	Don't know	29	29.3
Of parents who knew the content of the visit, did the AYA receive an Rx for puberty blockers and/or cross-sex hormones at their first visit?		80	
	AYA received an Rx for puberty blockers and/or cross-sex hormones at their first visit	17	21.2
	AYA was offered a Rx for puberty blockers and/or cross-sex hormones at their first visit, but AYA or parent declined	2	2.5
	Total number of AYAs who received or were offered an Rx at first visit	19	23.8
	AYAs who did not receive/were not offered an Rx at their first visit	61	76.2
Did AYA misrepresent their history to the doctor or relay their history accurately?		96	
	Parent is reasonably sure or positive that their child misrepresented or omitted parts of their history	64	66.7
	Parent is reasonable sure or positive that their child relayed their history completely and accurately	12	12.5
	Don't know	20	20.8

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hormone replacement therapy." And two participants described how the clinician treating their child's gender dysphoria refused to speak with the patients' primary care physicians. One participant said, "When we phoned the clinic, the doctor was hostile to us, told us to mind our own business. Our family doctor tried to reach our son's new doctor, but the trans doctor refused to speak with her." Another respondent shared "The pediatrician/'gender specialist' did not return calls or emails from the primary care physician who requested to talk with her about my son's medical history before she saw and treated him. . .she disregarded all historical information provided by the family and primary care physician. . .did not verify any information provided by my. . .son at his first visit even after being provided with multiple other historical sources which differed significantly from his story."

When asked about whether their child relayed their history completely and accurately to clinicians or whether they misrepresented or omitted parts of their history, of those who knew the content of their child's visit, 84.2% of the parent respondents were reasonably sure or positive that their child had misrepresented or omitted parts of their history. Twenty-eight participants provided optional open text responses to this question and the responses were categorized into: describing how the parent knew that the child misrepresented their history

(5); the content of what the child misrepresented (6 misrepresenting in general, 4 misrepresenting to the clinician for a total of 10 examples); don't know/not sure (4); expressing certainty (1); and not relevant (8). For the five participants describing how they knew, the reasons included: being present when it happened, reading the report from the gender specialist, being told by their child that the child had misrepresented the truth, and being informed by the child's psychiatrist. One respondent shared, "I have read the report from the gender specialist and it omits all the relevant context painting an almost unrecognizable picture of my son." A second parent simply responded, "I was present." Another respondent relayed about their (natal male) child, "My daughter told me and her mother that the first therapist she saw asked her stereotypical questions. . .She was afraid that if she didn't describe herself as a 'typical girl' she would not be believed." And finally, one respondent wrote, "He has said now that he did [misrepresent his history] and used key words he was advised to say." Ten participants provided 13 examples of the content of misrepresentations and of these, 6 examples could have been easily verified to be false (claiming to be under the care of a psychiatrist, claiming to be on medication to treat a psychiatric condition, how one was doing academically, and claiming a childhood history of having playmates of one sex when the opposite was observed, and claiming strong childhood preferences for specific toys and clothing that is the opposite of what multiple individuals observed). Three of the content examples would have been challenging to verify as false including: how one was feeling as a child, how one was feeling when a picture was taken, and whether one was from an abusive home. And four of the content examples did not provide enough information to determine if they would be easy or challenging to verify as false, such as "My child distorts her history and our family life on a regular basis," and "He has created an entire narrative that just isn't true."

In addition to the previously mentioned case where the child literally rewrote her history by editing her diary, there were seven respondents who conveyed a process where their child was constantly rewriting their personal history to make it consistent with the idea that they always were transgender and/or had created a childhood history that was not what others had observed. It is unclear whether this process was deliberate or if the individuals were unaware of their actions. The following are quotes describing this phenomenon. One parent said, ". . .she is actively rewriting her personal history to support the idea that she was always trans." Another respondent added,". . .my daughter denies events I recollect from her childhood and puberty that contradicts her narrative of 'always knowing she was a boy.'" Another respondent offered, "He is rewriting his personal history to suit his new narrative." And a fourth respondent described, "[Our] son has completely made up his childhood to include only girl friends and dressing up in girls clothes and playing with dolls, etc. This is not the same childhood we have seen as parents."

Qualitative analysis

The open-ended comments from the question about whether the clinician explored mental health, trauma or alternative causes of gender dysphoria before proceeding were selected for qualitative analysis. Nine major themes emerged from the data. Each theme is described in the following paragraphs with supporting quotes from participants.

Theme: Failure to explore mental health, trauma or alternative causes of GD. Parents described that clinicians failed to explore their child's mental health, trauma, or any alternative causes for the child's gender dysphoria. This failure to explore mental health and trauma occurred even when patients had a history of mental health disorder or trauma, were currently being treated for a mental health disorder, or were currently experiencing symptoms. One participant said, "Nothing other than gender dysphoria was considered to explain my daughter's

desire to transition." Another participant said, "My daughter saw a child therapist and the therapist was preparing to support transgendering and did not explore the depression and anxiety or previous trauma."

Theme: Insufficient evaluation. Another theme was insufficient evaluation where parents described evaluations that were too limited or too superficial to explore mental health, trauma or alternative causes of gender dysphoria. The following are three quotes by three different parents describing insufficient evaluations. One parent said, "The exploration was egregiously insufficient, very shallow, no effort to ask questions, engage in critical thinking about coexisting anxiety, or put on the brakes or even slow down." Another participant stated, "When we tried to give our son's trans doctor a medical history of our son, she refused to accept it. She said the half hour diagnosis in her office with him was sufficient, as she considers herself an expert in the field." And a third parent wrote, "We were STUNNED by the lack of information, medical history sought by therapist and radical treatment suggestion. [One]visit. The idea is, 'if they say they were born in the wrong body, they are. To question this will only hurt her and prolong her suffering.' [Our] daughter has had trauma in [the] past. [She] never was asked about it. [The] therapist did not ask parents a single question about our daughter."

Theme: Unwillingness or disinterest in exploring mental health, trauma or alternative causes of GD. Parents described that clinicians did not seem interested or willing to explore alternative causes. One parent described. "Her current therapist seems to accept her self diagnosis of gender dysphoria and follows what she says without seeming too much interested in exploring the sexual trauma in her past." Another parent wrote, "The Asperger psychiatrist did not seem to care whether our daughter's gender dysphoria stemmed from Asperger's. If our daughter wanted to be male, then that was enough." And a third parent said. "The therapist did ask about those issues but seemed to want to accept the idea wholeheartedly that my daughter was transgender first and foremost, all other factors aside."

Theme: Mental health was explored. A few parents had the experience where the clinician either made an appropriate referral for further evaluation or the issues had been addressed previously. One parent said, "[The] previous mental health issues [were] already explored by other therapists ([my] child was in therapy and medicated before coming out as transgender)."

Theme: Failure to communicate with patients' medical providers. Several participants described clinicians who were unwilling to communicate with primary care physicians and mental health professionals even those professionals who were currently treating the patient. One participant relayed, "She did not review the extensive psychiatric records that were available in a shared EMR [electronic medical record] and she did not consult with his outpatient psychiatrist prior to or after starting cross-sex hormonal therapy." Another parent said, "My child had been seen for mental health issues for several years before presenting this new identity, but the endocrinologist did not consult the mental health professionals for their opinions before offering hormones."

Theme: Misrepresentation of information by the patient. Several participants described how their child misrepresented their history to the clinician, thus, limiting the clinician's ability to adequately explore mental health, trauma and alternative causes. One participant wrote, "At [the] first visit, [my] daughter's dialogue was well-rehearsed, fabricated stories about her life told to get [the] outcome she desired. She parroted people from the internet." Another parent reported, "My son concealed the trauma and mental health issues that he and the family had experienced." And a third parent said, "I overheard my son boasting on the phone to his older brother that 'the doc swallowed everything I said hook, line and sinker. Easiest thing I ever did.'"

Theme: Transition steps were pushed by the clinician. Some parents described clinicians who seemed to push the process of transition before the patient asked for it. One parent described that the doctor gave her daughter a prescription that she didn't ask for, "The family

doctor who gave her the Androgel Rx [prescription] did NOT ask her many questions (she was surprised by this), nor did he await her assessment by a licensed psychiatrist before giving her this Rx. Nor did she ask him for this Rx." Another parent reported that she and her child were at the endocrinologist's office only to ask questions, and described, ". . .[he] didn't listen to a word we were saying. He was too eager to get us set up with a 'gender therapist' to get the legal form he needed to start hormones, all while making sure we set up our next appointment within 6 months to start the hormones. . ."

Theme: Parent views were discounted or ignored. Parents describe that the clinicians did not take their concerns seriously. One parent described, "I have to say I don't know, but it is hard to believe that they adequately examined the history of bullying and being ostracized for being different, and the autistic traits that would lend a person like my son to risk everything for identifying with a group. I know that in the few contacts I had with the providers, my concerns were discounted." And another said, "All of our emails went unanswered and were ignored. We are left out of everything because of our constant questioning of this being right for our daughter [because of her] trauma and current depression, anxiety and self-esteem problems."

Theme: Parent had concerns about the clinicians' competence, professionalism or experience. Parents expressed doubts about the clinicians regarding their experience, competence or professionalism. One parent said, "The clinic told me they explored these issues. I asked the risk manager at [redacted] if they'd considered a personality disorder. 'Oh, no,' she laughed. 'That's only with the older patients, not the teenagers.' I'm deeply suspicious of their competence." Another parent described, "What does concern me is that the people she talked to seemed to have no sense of professional duties, but only a mission to promote a specific social ideology."

Steps towards transition and current identification status

This section reports on the duration of AYA transgender-identification (time from the AYA's announcement of a transgender identity until the time the parent completed the survey) that covers, on average, 15.0 months (range 0.1–120 months) with a median of 11 months (Table 12). The steps taken towards transition during this timeframe are listed in Table 12. At the end of the timeframe, 83.2% of the AYAs were still transgender-identified, 5.5% were not still transgender-identified (desisted), 2.7% seemed to be backing away from transgender-identification, and 8.6% of the parents did not know if their child was still identifying as transgender. Descriptions of backing away or moving from transgender-identified to not transgender-identified include the following. One parent observed, "She identified as trans for six months . . . Now back at school, she is thinking maybe she's not trans." Another parent offered, "My daughter [identified] as trans from ages 13–16. She gradually desisted as she developed more insight into who she is." One parent described that after one year of identifying as transgender, "basically, she changed her mind once she stopped spending time with that particular group of friends." The duration of transgender-identification of the AYAs who were still transgender-identified at the time of survey was compared to the duration of those who were no longer transgender-identified and those who seemed to be backing away from a transgender-identification (combined) by t-test. The difference between these groups was statistically significant ($p = .025$), with a t-value of -2.25 showing that those who were no longer transgender-identified and backing away had a longer duration of identification (mean = 24.1 months) and those who were still transgender-identified had a shorter mean duration (mean = 14.4 months).

To explore the differences between the AYAs who had exposure to social influence (friend group, internet/social media, or both) and AYAs who did not have a clear exposure to social influence (neither and don't know), a series of chi-squared calculations were performed for

Table 12. Transition steps and disposition.

		n	%
Transition Steps*		256	
	Changed hairstyle	216	84.4
	Changed style of clothing	210	82.0
	Asks to be called a new name	188	73.4
	Asks for different pronouns	175	68.4
	Taken cross-sex hormones	29	11.3
	Legally changed name on government documents	19	7.4
	Taken anti-androgens	11	4.3
	Taken puberty blockers	7	2.7
	Had surgery	5	2.0
	None of the above	14	5.5
Disposition		256	
	Still transgender-identified	213	83.2
	Not transgender-identified any more (desisted)	14	5.5
	Seems to be backing away from transgender-identification	7	2.7
	Parent doesn't know if the child is still transgender-identified	22	8.6
	De-transitioned (also counted in desisted category)	3	1.2
Duration of transgender-identification overall	Median duration 11 months, Mean duration 15.0 months (range 0.1 months-120 months), median 11 months	225	
Duration of transgender-identification if still transgender-identified	Median duration 11 months, mean duration 14.4 months, ange (0.1 months-72 months)	204	
Duration of transgender-identification if no longer transgender-identified	Median duration 12 months, mean duration 24.2 months, range (.75 months to 120 months)	13	
Duration of transgender-identification if backing away	Median duration 12 months, mean duration 15 months, range (3 months-36 months)	8	

*may select more than one answer.

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selected variables. (See Table 13.) Statistically significant differences were revealed for AYAs with exposure to social influences having worse outcomes for mental well-being and parent-child relationships, and greater numbers exhibiting distrust, isolating and anti-social behaviors including: narrowed range of interests and hobbies, expressing that they only trusted information from transgender sources, trying to isolate themselves from their family, losing interest in activities that weren't predominantly with transgender or LGBTIA participants, and telling people or posting on social media that their parent is "transphobic," "abusive," or "toxic" because the parent doesn't agree with the child's assessment of being transgender. Although the differences in additional isolating and anti-social behaviors did not reach statistical significance, these behaviors trended towards higher rates in the AYAs who were exposed to social influence and may have not reached significant levels due to small numbers. No significant difference for age of AYA (at announcement or at time of survey completion) was detected between groups by a one-way ANOVA.

Discussion

This research describes parental reports about a sample of AYAs who would not have met diagnostic criteria for gender dysphoria during their childhood but developed signs of gender dysphoria during adolescence or young adulthood. The strongest support for considering that the gender dysphoria was new in adolescence or young adulthood is the parental answers for

Table 13. chi-squared comparisons for exposure to social influence (SI) vs not exposure to social influence (NSI).

		SI n (%)	NSI n (%)	p
Sex		222	34	.123
	Female	187 (84.2)	25 (73.5)	
	Male	35 (15.8)	9 (26.5)	
Indicators of childhood GD		221	33	**.004**
	0–2 indicators	**216 (97.7)**	**29 (87.9)**	
	3–4 indicators	**5 (2.3)**	**4 (12.1)**	
Currently have two or more GD indicators		214	34	.808
	Yes	179(83.6)	29 (85.3)	
	No	35(16.4)	5(14.7)	
No mental health or NDD diagnoses before onset of GD		222	34	**.036**
	Answered "None of the above"	**87(39.9)**	**7 (20.6)**	
Mental well-being since announcement		220	33	**.001**
	Worse	**114 (51.8)**	**6 (18.2)**	
	Better	**24 (10.9)**	**8 (24.2)**	
	Unchanged/Mixed	**82 (37.3)**	**19 (57.6)**	
Parent-child relationship since announcement		219	33	**.006**
	Worse	**134 (61.2)**	**11 (33.3)**	
	Better	**13 (5.9)**	**5 (15.2)**	
	Unchanged/Mixed	**72 (32.9)**	**17 (51.5)**	
Range of interests and hobbies		**220**	**34**	**<0.001**
	Broader range of interests and hobbies	**10 (4.5)**	**3 (8.8)**	
	Narrowed range of interest and hobbies	**139 (63.2)**	**9 (26.5)**	
	Unchanged range	**71 (32.3)**	**22 (64.7)**	
Distrust and Isolating Behaviors		222	34	
	Tried to isolate themselves from family	**114(51.4)**	**10 (29.4)**	**.017**
	Expressed that they ONLY trust information about GD and transgenderism that comes from transgender sources	**107 (48.2)**	**10 (29.4)**	**.041**
	Lost interest in activities where participants aren't predominantly transgender or LGBTIA	**76 (34.2)**	**5 (14.7)**	**.023**
	Stopped spending time with non-transgender friends	59 (26.6)	4 (11.8)	.062
	Expressed distrust of people who are not transgender	52 (23.4)	5 (14.7)	.255
	Told people or posted on social media that their parent is "transphobic," "abusive," or "toxic" because the parent doesn't agree with the child's assessment of being transgender	**102 (45.9)**	**5 (14.7)**	**<0.001**
	Defended the practice of lying to or withholding information from doctors/therapists to get hormones for transition more quickly	38 (17.1)	3 (8.8)	.219
	Brought up the issue of suicide in transgender teens as a reason parents should agree to treatment	55 (24.8)	4 (11.8)	.093
Did the AYA misrepresent their history to the doctor or relay it accurately?		68	8	.075
	Parent is reasonable sure or positive that their child misrepresented or omitted parts of their history	59 (86.8)	5 (62.5)	
	Parent is reasonable sure or positive that child relayed their history completely and accurately	9 (13.2)	3 (37.5)	

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DSM 5 criteria for childhood gender dysphoria. Not only would none of the sample have met threshold criteria, the vast majority had zero indicators. Although one might argue that three of the indicators could plausibly be missed by a parent (A1, A7, and A8 if the child had not

expressed these verbally), five of the indicators (A2-6) are readily observable behaviors and preferences that would be difficult for a parent to miss. Six indicators (including A1) are required for a threshold diagnosis. The nonexistent and low numbers of readily observable indicators reported in the majority of this sample does not support a scenario in which gender dysphoria was always present but was only recently disclosed to the parents.

Parents reported that before the onset of their gender dysphoria, many of the AYAs had been diagnosed with at least one mental health disorder or neurodevelopmental disability and many had experienced a traumatic or stressful event. Experiencing a sex or gender related trauma was not uncommon, nor was experiencing a family stressor (such as parental divorce, death of a parent, or a mental health disorder in a sibling or parent). Additionally, nearly half were described as having engaged in self-harm prior to the onset of their gender dysphoria. In other words, many of the AYAs and their families had been navigating multiple challenges and stressors before gender dysphoria and transgender-identification became part of their lives. This context could possibly contribute to friction between parent and child and these complex, overlapping difficulties as well as experiences of same-sex attraction may also be influential in the development of a transgender identification for some of these AYAs. Care should be taken not to overstate or understate the context of pre-existing diagnoses or trauma in this population as they were absent in approximately one third and present in approximately two thirds of the sample.

This research sample of AYAs also differs from the general population in that it is predominantly natal female, white, and has an over-representation of individuals who are academically gifted, non-heterosexual, and are offspring of parents with high educational attainment [59–61]. The sex ratio favoring natal females is consistent with recent changes in the population of individuals seeking care for gender dysphoria. Gender clinics have reported substantial increases in referrals for adolescents with a change in the sex ratio of patients moving from predominantly natal males seeking care for gender dysphoria to predominantly natal females [26–28, 62]. Although increased visibility of transgender individuals in the media and availability of information online, with a partial reduction of stigma might explain some of the rise in the numbers of adolescents presenting for care [27], it would not directly explain why the inversion of the sex ratio has occurred for adolescents but not adults or why there is a new phenomenon of natal females experiencing late-onset and adolescent-onset gender dysphoria. The unexpectedly high rate of academically gifted AYAs may be related to the high educational attainment of the parents and may be a reflection of parents who are online, able to complete online surveys and are able to question and challenge current narratives about gender dysphoria and transition. There may be other unknown variables that render academically gifted AYAs susceptible to adolescent-onset and late-onset gender dysphoria. The higher than expected rate of non-heterosexual orientations of the AYAs (prior to announcement of a transgender-identity) may suggest that the desire to be the opposite sex could stem from experiencing homophobia as a recent study showed that being the recipient of homophobic name calling from one's peers was associated with a change in gender identity for adolescents [63]. The potential relationship of experienced homophobia and the development of a rapid onset of gender dysphoria during adolescence or young adulthood as perceived by parents deserves further study.

This sample is distinctively different than what is described in previous research about gender dysphoria because of the distribution of cases occurring in friendship groups with multiple individuals identifying as transgender, the preponderance of adolescent (natal) females, the absence of childhood gender dysphoria, and the perceived suddenness of onset. In this study, parental reports of transgender identification duration in AYAs suggest that in some cases (~8% in this study) gender dysphoria and transgender-identification may be temporary, and

that longer observation periods may be needed to assess such changes. Further research is needed to verify these results. There have been anecdotal reports of adolescents who desisted approximately 9–36 months after showing signs of a rapid onset of gender dysphoria, but longitudinal research following AYAs with gender dysphoria would be necessary to study desistance trends. Although it is still unknown whether transition in gender dysphoric individuals decreases, increases, or fails to change the rates of attempted or completed suicides [64], this study documents AYAs using a suicide narrative as part of their arguments to parents and doctors towards receiving support and transition services. Despite the possibility that the AYAs are using a suicide narrative to manipulate others, it is critical that any suicide threat, ideation or concern is taken seriously and the individual should be evaluated immediately by a mental health professional.

The majority of parents were reasonably sure or certain that their child misrepresented or omitted key parts of their history to their therapists and physicians. In some cases, the misrepresentation of one's history may simply be a deliberate act by a person who is convinced that transition is the only way that they will feel better and who may have been coached that lying is the only way to get what they think they need. For others, the misrepresentation may not be a conscious act. The creation of an alternate version of one's childhood that conforms to a story of always knowing one was transgender and that is in sharp contrast to the childhood that was observed by third parties raises the question of whether there has been the creation of false childhood memories as part of, or outside of, the therapy process. Respondent accounts of clinicians who ignored or disregarded information (such as mental health symptoms and diagnoses, medical and trauma histories) that did not support the conclusion that the patient was transgender, suggests the possibility of motivated reasoning and confirmatory biases on the part of clinicians. In the 1990s, the beliefs and practices of many mental health professionals may have contributed to their patients' creation of false childhood memories consistent with a child sexual abuse narrative and research since then has shown that false childhood memories of mundane events can be implanted in laboratory settings [65–67]. It may be worthwhile to explore if, in today's culture, there might be beliefs and practices of some mental health professionals that are contributing to their patients' creation of false childhood memories consistent with an "always knew/always were transgender" narrative.

Emerging hypotheses

Hypothesis 1: Social influences can contribute to the development of gender dysphoria

It is unlikely that friends and the internet can make people transgender. However, it is plausible that the following can be initiated, magnified, spread, and maintained via the mechanisms of social and peer contagion: (1) the *belief* that non-specific symptoms (including the symptoms associated with trauma, symptoms of psychiatric problems, and symptoms that are part of normal puberty) should be perceived as gender dysphoria and their presence as proof of being transgender; 2) the *belief* that the only path to happiness is transition; and 3) the *belief* that anyone who disagrees with the self-assessment of being transgender or the plan for transition is transphobic, abusive, and should be cut out of one's life. The spread of these beliefs could allow vulnerable AYAs to misinterpret their emotions, incorrectly believe themselves to be transgender and in need of transition, and then inappropriately reject all information that is contrary to these beliefs. In other words, "gender dysphoria" may be used as a catch-all explanation for any kind of distress, psychological pain, and discomfort that an AYA is feeling while transition is being promoted as a cure-all solution.

One of the most compelling findings supporting a potential role of social and peer contagion in the development or expression of a rapid onset of gender dysphoria is the clusters of transgender-identification occurring within friendship groups. The expected prevalence of transgender young adult individuals is 0.7% [8]. Yet, according to the parental reports, more than a third of the friendship groups described in this study had 50% or more of the AYAs in the group becoming transgender-identified in a similar time frame. This suggests a localized increase to more than 70 times the expected prevalence rate. This is an observation that demands urgent further investigation. One might argue that high rates of transgender-identified individuals within friend groups may be secondary to the process of friend selection: choosing transgender-identified friends deliberately rather than the result of group dynamics and observed coping styles contributing to multiple individuals, in a similar timeframe, starting to interpret their feelings as consistent with being transgender. More research will be needed to finely delineate the timing of friend group formation and the timing and pattern of each new declaration of transgender-identification. Although friend selection may play a role in these high percentages of transgender-identifying members in friend groups, the described pattern of multiple friends (and often the majority of the friends in the friend group) *becoming* transgender-identified in a similar timeframe suggests that there may be more than just friend selection behind these elevated percentages.

There are many insights from our understanding of peer contagion in eating disorders and anorexia that may apply to the potential role(s) of peer contagion in the development of gender dysphoria. Just as friendship cliques can set the level of preoccupation with one's body, body image, weight, and techniques for weight loss [37–39], so too may friendship cliques set a level of preoccupation with one's body, body image, gender, and the techniques to transition. The descriptions of pro-anorexia subculture group dynamics where the thinnest anorexics are admired while the anorexics who try to recover from anorexia are ridiculed and maligned as outsiders [39–41] resemble the group dynamics in friend groups that validate those who identify as transgender and mock those who do not. And the pro-eating-disorder websites and online communities providing inspiration for weight loss and sharing tricks to help individuals deceive parents and doctors [42–44] may be analogous to the inspirational YouTube transition videos and the shared online advice about manipulating parents and doctors to obtain hormones.

Hypothesis 2: Parental conflict might provide alternative explanations for selected findings

Parents reported subjective declines in their AYAs' mental health and in parent-child relationships after the children disclosed a transgender identification. Additionally, per parent report, almost half of the AYAs withdrew from family, 28.5% refused to speak to a parent, and 6.8% tried to run away. It is possible that some of these findings might be secondary to parent-child conflict. Parent-child conflict could arise from disagreement over the child's self-assessment of being transgender. It is also possible that some parents might have had difficulty coping or could have been coping poorly or maladaptively with their child's disclosure. Other potential explanations for the above findings include worsening of AYAs' pre-existing (or onset of new) psychiatric conditions or the use of maladaptive coping mechanisms. To further evaluate these possibilities, future studies should incorporate information about family dynamics, parent-child interactions, parent coping, child coping, and psychiatric trajectories. This study did not collect data about the parents' baseline coping styles, how they were coping with their child's disclosure, and whether their coping seemed to be maladaptive or adaptive. Nor did it explore parents' mental well-being. Future studies should explore these issues as well.

Although most parents reported an absence of childhood indicators for gender dysphoria, it is possible that these indicators might have existed for some of the AYAs and that some parents either failed to notice or ignored these indicators when they occurred. Because the readily observable indicators could also have been observed by other people in the child's life, future studies should include input from parents, AYAs and from third party informants such as teachers, pediatricians, mental health professionals, babysitters, and other family members to verify the presence or absence of readily observable behaviors and preferences during childhood. Parental approaches to their child's gender dysphoria might contribute to specific outcomes. This study did not specifically explore parental approaches to gender dysphoria or parental views on medical or surgical interventions. Additional studies that explore whether parents support or don't support: gender exploration; gender nonconformity; non-heterosexual sexual identities; mental health evaluation and treatment; and exploration of potential underlying causes for dysphoria would be extremely valuable. It would also be worthwhile to explore whether parents favor affirming the child as a person or affirming the child's gender identity and whether parents hold liberal, cautious, or negative views about the use of medical and surgical interventions for gender dysphoria in AYAs.

Hypothesis 3: Maladaptive coping mechanisms may underlie the development of gender dysphoria for some AYAs

For some individuals, the drive to transition may represent an ego-syntonic but maladaptive coping mechanism to avoid feeling strong or negative emotions similar to how the drive to extreme weight loss can serve as an ego-syntonic but maladaptive coping mechanism in anorexia nervosa [68–69]. A maladaptive coping mechanism is a response to a stressor that might relieve the symptoms temporarily but does not address the cause of the problem and may cause additional negative outcomes. Examples of maladaptive coping mechanisms include the use of alcohol, drugs, or self-harm to distract oneself from experiencing painful emotions. One reason that the treatment of anorexia nervosa is so challenging is that the drive for extreme weight loss and weight loss activities can become a maladaptive coping mechanism that allows the patient to avoid feeling and dealing with strong emotions [69–70]. In this context, dieting is not felt as distressing to the patient, because it is considered by the patient to be the solution to her problems, and not part of the problems. In other words, the dieting and weight loss activities are ego-syntonic to the patient. However, distress is felt by the patient when external actors (doctors, parents, hospital staff) try to interfere with her weight loss activities thus curtailing her maladaptive coping mechanism.

Findings that may support a maladaptive coping mechanism hypothesis include that the most likely description of AYA ability to use negative emotions productively was poor/extremely poor and the majority of AYAs were described as "overwhelmed by strong emotions and tries to/goes to great lengths to avoid experiencing them." Although these are not validated questions, the findings suggest, at least, that there is a history of difficulty dealing with emotions. The high frequency of parents reporting AYA expectations that transition would solve their problems coupled with the sizable minority who reported AYA unwillingness to work on basic mental health issues before seeking treatment support the concept that the drive to transition might be used to avoid dealing with mental health issues and aversive emotions. Additional support for this hypothesis is that the sample of AYAs described in this study are predominantly female, were described by parents as beginning to express symptoms during adolescence and contained an overrepresentation of academically gifted students which bears a strong resemblance to populations of individuals diagnosed with anorexia nervosa [71–75]. The risk factors, mechanisms and meanings of anorexia nervosa [69–70, 76] may ultimately

prove to be a valuable template to understand the risk factors, mechanisms, and meanings for some cases of gender dysphoria.

Transition as a drive to escape one's gender/sex, emotions, or difficult realities might also be considered when the drive to transition arises after a sex or gender-related trauma or within the context of significant psychiatric symptoms and decline in ability to function. Although trauma and psychiatric disorders are not specific for the development of gender dysphoria, these experiences may leave a person in psychological pain and in search of a coping mechanism. The first coping mechanism that a vulnerable person adopts may be the result of their environment and which narratives for pain and coping are most prevalent in that environment—in some settings a gender dysphoria/drive to transition may be the dominant paradigm, in some settings a body dysphoria/drive for extreme weight loss is dominant, and in another the use of alcohol and drugs to cope with pain may be dominant. Because maladaptive coping mechanisms do not address the root cause of distress and may cause their own negative consequences, an outcome commonly reported for this sample, AYAs experiencing a decline in their mental well-being after transgender-identification, is consistent with this hypothesis. There was a subset of AYAs for whom parents reported improvement in their mental well-being as they desisted from their transgender-identification which would not be inconsistent with moving from a maladaptive coping mechanism to an adaptive coping mechanism.

If the above hypotheses are correct, rapid onset of gender dysphoria that is socially mediated and/or used as a maladaptive coping mechanism may be harmful to AYAs in the following ways: (1) non-treatment or delayed treatment for trauma and mental health problems that might be the root of (or at least an inherent part of) the AYAs' issues; (2) alienation of the AYAs from their parents and other crucial social support systems; (3) isolation from mainstream, non-transgender society, which may curtail educational and vocational potential; and (4) the assumption of the medical and surgical risks of transition without benefit. In addition to these indirect harms, there is also the possibility that this type of gender dysphoria, with the subsequent drive to transition, may represent a form of intentional self-harm. Promoting the affirmation of a declared gender and recommending transition (social, medical, surgical) without evaluation may add to the harm for these individuals as it can reinforce the maladaptive coping mechanism, prolong the length of time before the AYA accepts treatment for trauma or mental health issues, and interfere with the development of healthy, adaptive coping mechanisms. It is especially critical to differentiate individuals who would benefit from transition from those who would be harmed by transition before proceeding with treatment.

Reflections

Clinicians need to be aware of the myriad of barriers that may stand in the way of making accurate diagnoses when an AYA presents with a desire to transition including: the developmental stage of adolescence; the presence of subcultures coaching AYAs to mislead their doctors; and the exclusion of parents from the evaluation. In this study, 22.3% of AYAs were reported as having been exposed to online advice about what to say to doctors to get hormones, and 17.5% to the advice that it is acceptable to lie to physicians; and the vast majority of parents were reasonably sure or positive that their child misrepresented their history to their doctor or therapist. Furthermore, although parents may be knowledgeable informants on matters of their own child's developmental, medical, social, behavioral, and mental health history- and quite possibly *because* they are knowledgeable- they are often excluded from the clinical discussion by the AYAs, themselves. An AYA telling their clinician that their parents are transphobic and abusive may indeed mean that the parents are transphobic and abusive. However, the findings of this research indicate that it is also possible that the AYA calls the parent

transphobic and abusive because the parent disagrees with the child's self-diagnosis, has expressed concern for the child's future, or has requested that the child be evaluated for mental health issues before proceeding with treatment.

The findings of this study suggest that clinicians need to be cautious before relying solely on self-report when AYAs seek social, medical or surgical transition. Adolescents and young adults are not trained medical professionals. When AYAs diagnose their own symptoms based on what they read on the internet and hear from their friends, it is quite possible for them to reach incorrect conclusions. It is the duty of the clinician, when seeing a new AYA patient seeking transition, to perform their own evaluation and differential diagnosis to determine if the patient is correct or incorrect in their self-assessment of their symptoms and their conviction that they would benefit from transition. This is not to say that the convictions of the patient should be dismissed or ignored, some may ultimately benefit from transition. However, careful clinical exploration should not be neglected, either. The patient's history being significantly different than their parents' account of the child's history should serve as a red flag that a more thorough evaluation is needed and that as much as possible about the patient's history should be verified by other sources. The findings that the majority of clinicians described in this study did not explore trauma or mental health disorders as possible causes of gender dysphoria or request medical records in patients with atypical presentations of gender dysphoria is alarming. The reported behavior of clinicians refusing to communicate with their patients' parents, primary care physicians, and psychiatrists betrays a resistance to triangulation of evidence which puts AYAs at considerable risk.

It is possible that some teens and young adults may have requested that their discussions with the clinicians addressing gender issues be kept confidential from their parents, as is their right (except for information that would put themselves or others at harm). However, maintaining confidentiality of the patient does not prevent the clinician from listening to the medical and social history of the patient provided by the parent. Nor does it prevent a clinician from accepting information provided by the patient's primary care physicians and psychiatrists. Because adolescents may not be reliable historians and may have limited awareness and insight about their own emotions and behaviors, the inclusion of information from multiple informants is often recommended when working with or evaluating minors. One would expect that if a patient refuses the inclusion of information from parents and physicians (prior and current), that the clinician would explore this with the patient and encourage them to reconsider. At the very least, if a patient asks that all information from parents and medical sources be disregarded, it should raise the suspicion that what the patient is presenting may be less than forthcoming and the clinician should proceed with caution.

The argument to surface from this study is not that the insider perspectives of AYAs presenting with signs of a rapid onset of gender dysphoria should be set aside by clinicians, but that the insights of parents are a pre-requisite for robust triangulation of evidence and fully informed diagnosis. All parents know their growing children are not always right, particularly in the almost universally tumultuous period of adolescence. Most parents have the awareness and humility to know that even as adults they are not always right themselves. When an AYA presents with signs of a rapid onset of gender dysphoria it is incumbent upon all professionals to fully respect the young person's insider perspective but also, in the interests of safe diagnosis and avoidance of clinical harm, to have the awareness and humility themselves to engage with parental perspectives and triangulate evidence in the interest of validity and reliability.

The strengths of this study include that it is the first empirical description of a specific phenomenon that has been observed by parents and clinicians [14] and that it explores parent observations of the psychosocial context of youth who have recently identified as transgender with a focus on vulnerabilities, co-morbidities, peer group interactions, and social media use.

Additionally, the qualitative analysis of responses about peer group dynamics provides a rich illustration of AYA intra-group and inter-group behaviors as observed and reported by parents. This research also provides a glimpse into parent perceptions of clinician interactions in the evaluation and treatment of AYAs with an adolescent-onset (or young adult-onset) of gender dysphoria symptoms.

The limitations of this study include that it is a descriptive study and thus has the known limitations inherent in all descriptive studies. This is not a prevalence study and does not attempt to evaluate the prevalence of gender dysphoria in adolescents and young adults who had not exhibited childhood symptoms. Likewise, this study's findings did not demonstrate the degree to which the onset of gender dysphoria symptoms may be socially mediated or associated with a maladaptive coping mechanism, although these hypotheses were discussed here. Gathering more data on the topics introduced is a key recommendation for further study. It is not uncommon for first, descriptive studies, especially when studying a population or phenomenon where the prevalence is unknown, to use targeted recruiting. To maximize the possibility of finding cases meeting eligibility criteria, recruitment is directed towards communities that are likely to have eligible participants. For example, in the first descriptive study about children who had been socially transitioned, the authors recruited potential subjects from gender expansive camps and gender conferences where parents who supported social transition for young children might be present and the authors did not seek out communities where parents might be less inclined to find social transition for young children appropriate [77]. In the same way, for the current study, recruitment was targeted primarily to sites where parents had described the phenomenon of a rapid onset of gender dysphoria because those might be communities where such cases could be found. The generalizability of the study must be carefully delineated based on the recruitment methods, and, like all first descriptive studies, additional studies will be needed to replicate the findings.

Three of the sites that posted recruitment information expressed cautious or negative views about medical and surgical interventions for gender dysphoric adolescents and young adults and cautious or negative views about categorizing gender dysphoric youth as transgender. One of the sites that posted recruitment information is perceived to be pro-gender-affirming. Hence, the populations viewing these websites might hold different views or beliefs from each other. And both populations may differ from a broader general population in their attitudes about transgender-identified individuals. This study did not explore specific participant views about medical and surgical interventions for gender dysphoric youth or whether participants support or don't support: exploration of gender identity, exploration of potential underlying causes for gender dysphoria, affirmation of children as valued individuals or affirmation of children's gender identity. Future studies should explore all these issues. This study cannot speak to those details about the participants.

Respondents were asked, "Do you believe that transgender people deserve the same rights and protections as others in your country?" which is a question that was adapted from a question used for a US national poll [78]. Although this question cannot elicit specific details about a persons' beliefs about medical interventions, beliefs about transgender identification, or their beliefs about their own child, it can be used to assess if the participants in this study are similar in their basic beliefs about the rights of transgender people to the participants in the US national poll. The majority (88.2%) of the study participants gave affirmative answers to the question which is consistent with the 89% affirmative response reported in a US national poll [78]. All self-reported results have the potential limitation of social desirability bias. However, comparing this self-report sample to the national self-report sample [78], the results show similar rates of support. Therefore, there is no evidence that the study sample is appreciably different in their support of the rights of transgender people than the general American population.

It is also important to note that recruitment was not limited to the websites where the information about the study was first posted. Snowball sampling was also used so that any person viewing the recruitment information was encouraged to share the information with any person or community where they thought there could be potentially eligible participants, thus substantially widening the reach of potential respondents. In follow up studies on this topic, an even wider variety of recruitment sources should be attempted.

Another limitation of this study is that it included only parental perspective. Ideally, data would be obtained from both the parent and the child and the absence of either perspective paints an incomplete account of events. Input from the youth would have yielded additional information. Further research that includes data collection from both parent and child is required to fully understand this condition. However, because this research has been produced in a climate where the input from parents is often neglected in the evaluation and treatment of gender dysphoric AYAs, this research supplies a valuable, previously missing piece to the jigsaw puzzle. If Hypothesis 3 is correct that for some AYAs gender dysphoria represents an egosyntonic maladaptive coping mechanism, data from parents are especially important because affected AYAs may be so committed to the maladaptive coping mechanism that their ability to assess their own situation may be impaired. Furthermore, parents uniquely can provide details of their child's early development and the presence or absence of readily observable childhood indicators of gender dysphoria are especially relevant to the diagnosis. There are, however, obvious limitations to relying solely on parent report. It is possible that some of the participating parents may not have noticed symptoms of gender dysphoria before their AYA's disclosure of a transgender identity; could have been experiencing shock, grief, or difficulty coping from the disclosure; or even could have chosen to deny or obscure knowledge of long term gender dysphoria. Readers should hold this possibility in mind. Overall, the 200 plus responses appear to have been prepared carefully and were rich in detail, suggesting they were written in good faith and that parents were attentive observers of their children's lives. Although this research adds the necessary component of parent observation to our understanding of gender dysphoric adolescents and young adults, future study in this area should include both parent and child input.

This research does not imply that no AYAs who become transgender-identified during their adolescent or young adult years had earlier symptoms nor does it imply that no AYAs would ultimately benefit from transition. Rather, the findings suggest that *not all* AYAs presenting at these vulnerable ages are correct in their self-assessment of the cause of their symptoms and *some* AYAs may be employing a drive to transition as a maladaptive coping mechanism. It may be difficult to distinguish if an AYA's declining mental health is occurring due to the use of a maladaptive coping mechanism, due to the worsening of a pre-existing (or onset of a new) psychiatric condition, or due to conflict with parents. Clinicians should carefully explore these options and try to clarify areas of disagreement with confirmation from outside sources such as medical records, psychiatrists, psychologists, primary care physicians, and other third party informants where possible. Further study of maladaptive coping mechanisms, psychiatric conditions and family dynamics in the context of gender dysphoria and mental health would be an especially valuable contribution to better understand how to treat youth with gender dysphoria.

More research is needed to determine the incidence, prevalence, persistence and desistence rates, and the duration of gender dysphoria for adolescent-onset gender dysphoria and to examine whether rapid-onset gender dysphoria is a distinct and/or clinically valid subcategory of gender dysphoria. Adolescent-onset gender dysphoria is sufficiently different from early-onset of gender dysphoria that persists or worsens at puberty and therefore, the research results from early-onset gender dysphoria should not be considered generalizable to

adolescent-onset gender dysphoria. It is currently unknown whether the gender dysphorias of adolescent-onset gender dysphoria and of late-onset gender dysphoria occurring in young adults are transient, temporary or likely to be long-term. Without the knowledge of whether the gender dysphoria is likely to be temporary, extreme caution should be applied before considering the use of treatments that have permanent effects such as cross-sex hormones and surgery. Research needs to be done to determine if affirming a newly declared gender identity, social transition, puberty suppression and cross-sex hormones can cause an iatrogenic persistence of gender dysphoria in individuals who would have had their gender dysphoria resolve on its own and whether these interventions prolong the duration of time that an individual feels gender dysphoric before desisting. There is also a need to discover how to diagnose these conditions, how to treat the AYAs affected, and how best to support AYAs and their families. Additionally, analyses of online content for pro-transition sites and social media should be conducted in the same way that content analysis has been performed for pro-eating disorder websites and social media content [44]. Finally, further exploration is needed for potential contributors to recent demographic changes including the substantial increase in the number of adolescent natal females with gender dysphoria and the new phenomenon of natal females experiencing late-onset or adolescent-onset gender dysphoria.

Conclusion

Collecting data from parents in this descriptive exploratory study has provided valuable, detailed information that allows for the generation of hypotheses about potential factors contributing to the onset and expression of gender dysphoria among AYAs. Emerging hypotheses include the possibility of a potential new subcategory of gender dysphoria (referred to as rapid-onset gender dysphoria) that has not yet been clinically validated and the possibility of social influences and maladaptive coping mechanisms contributing to the development of gender dysphoria. Parent-child conflict may also contribute to the course of the dysphoria. More research that includes data collection from AYAs, parents, clinicians and third party informants is needed to further explore the roles of social influence, maladaptive coping mechanisms, parental approaches, and family dynamics in the development and duration of gender dysphoria in adolescents and young adults.

Supporting information

S1 Appendix. Survey instrument.
(PDF)

S2 Appendix. COREQ checklist.
(PDF)

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ORIGINAL PAPER

Individuals Treated for Gender Dysphoria with Medical and/or Surgical Transition Who Subsequently Detransitioned: A Survey of 100 Detransitioners

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Abstract

The study's purpose was to describe a population of individuals who experienced gender dysphoria, chose to undergo medical and/or surgical transition and then detransitioned by discontinuing medications, having surgery to reverse the effects of transition, or both. Recruitment information with a link to an anonymous survey was shared on social media, professional listservs, and via snowball sampling. Sixty-nine percent of the 100 participants were natal female and 31.0% were natal male. Reasons for detransitioning were varied and included: experiencing discrimination (23.0%); becoming more comfortable identifying as their natal sex (60.0%); having concerns about potential medical complications from transitioning (49.0%); and coming to the view that their gender dysphoria was caused by something specific such as trauma, abuse, or a mental health condition (38.0%). Homophobia or difficulty accepting themselves as lesbian, gay, or bisexual was expressed by 23.0% as a reason for transition and subsequent detransition. The majority (55.0%) felt that they did not receive an adequate evaluation from a doctor or mental health professional before starting transition and only 24.0% of respondents informed their clinicians that they had detransitioned. There are many different reasons and experiences leading to detransition. More research is needed to understand this population, determine the prevalence of detransition as an outcome of transition, meet the medical and psychological needs of this population, and better inform the process of evaluation and counseling prior to transition.

Keywords Gender dysphoria · Detransition · Transgender

Introduction

Detransition is the act of stopping or reversing a gender transition. The visibility of individuals who have detransitioned is new and may be rapidly growing. As recently as 2014, it was challenging for an individual who detransitioned to find another person who similarly detransitioned (Callahan, 2018). Between 2015 and 2017, a handful of blogs written by individual detransitioners started to appear online, private support groups for detransitioners formed, and interviews with detransitioners began to appear in news articles, magazines, and blogs (Anonymous, 2017; 4thwavenow, 2016; Herzog, 2017; McCann, 2017). Although few YouTube videos about detransition existed prior to 2016, multiple detransitioners started to post videos documenting their experiences in 2016 and the numbers of these videos continues to increase.[1] In late 2017, the subreddit r/detrans (r/detrans, 2020) was revitalized and in four years has grown from 100 members to more than 21,000 members. A member poll of r/detrans conducted in 2019 estimated that approximately one-third of the members responding to the survey were desisters or detransitioners (r/detrans, 2019). The Pique Resilience Project, a group of four detransitioned or desisted young women, was founded in 2018 as a way to share the experiences of detransitioners with the public (Pique Resilience Project, 2019). In late 2019, the Detransition Advocacy Network, a nonprofit organization to "improve the well-being of detransitioned people everywhere" was launched (The

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[1] A search of the word "detransition" in YouTube can be filtered by date of upload. https://www.youtube.com/results?search_query=%22detransition%22&sp=CAI%253D22.

Detransition Advocacy Network, 2020) and the first formal, in-person conference for detransitioned people was held (Bridge, 2020). In the face of this massive change, clinicians have called for more research into the experiences of detransitioners (Butler & Hutchinson, 2020; Entwistle, 2021; Marchiano, 2020).

Although there were rare published reports about detransitioners prior to 2016, most of the published literature about detransition is recent (Callahan, 2018; D'Angelo, 2018; Djordjevic et al., 2016; Kuiper & Cohen-Kettenis, 1998; Levine, 2018; Marchiano, 2017; Pazos Guerra et al., 2020; Stella, 2016; Turban & Keuroghlian, 2018; Turban et al., 2021; Vandenbussche, 2021). The prevailing cultural narratives about detransition are that most individuals who detransition will retransition and that the reasons for detransition are discrimination, pressures from others, and nonbinary identification (Turban et al., 2021). However, case reports are shedding light on a broader and more complex range of experiences that include trauma, worsened mental health with transition, re-identification with natal sex, and difficulty separating sexual orientation from gender identity (D'Angelo, 2018; Levine, 2018; Pazos Guerra et al., 2020).[2] Detransitioners and desisters, in their own words, have provided additional depth to the discussion, describing that:

(1) Trauma (including sexual trauma) and mental health conditions contributed to their transgender identification and transition (Callahan, 2018; Herzog, 2017; twitter.com/ftmdetransed & twitter.com/radfemjourney, 2019)
(2) Their dysphoria and transition were due to homophobia and difficulty accepting themselves as homosexual (Bridge, 2020; Callahan, 2018; upperhandMARS, 2020)
(3) Peers, social media, and online communities were influential in the development of transgender identification and desire to transition (Pique Resilience Project, 2019; Tracey, 2020; upperhandMARS, 2020)
(4) Their dysphoria was rooted in misogyny (Herzog, 2017)

Two recently published convenience sample reports provide additional context about the topic of detransition. First, Turban et al. (2021) analyzed data from the United States Trans Survey (USTS) (James et al., 2016). The USTS contains data from 27,715 transgender and gender diverse adults from the U.S. who were recruited through lesbian, gay, bisexual, transgender, queer (LGBTQ), and allied organization outreach. The USTS included the question, "Have you ever detransitioned? In other words, have you ever gone back to living as your sex assigned at birth, at least for a while?" with the multiple choice options of "yes," "no," and "I have never transitioned." For the 2,242 participants who answered "yes," Turban et al. analyzed the responses to the multiple choice question, "Why did you detransition? In other words, why did you go back to living as your sex assigned at birth? (Mark all that apply)." Although most of the offered answer options were about external pressures to detransition (pressure from spouse or partner, pressure from family, pressure from friends, pressure from employer, discrimination, etc.), participants could write in additional reasons that were not listed. Turban et al.'s sample included more natal males (55.1%) than natal females (44.9%). Roughly half (50.2%) had taken cross-sex hormones and 16.5% had obtained surgery. The findings revealed that most (82.5%) of the sample expressed at least one external factor for detransitioning and 15.9% expressed at least one internal factor (factors originating from self).

The second study by Vandenbussche (2021) recruited detransitioners from online communities of detransitioners and analyzed data for the participants who answered affirmatively to the question, "Did you transition medically and/or socially and then stopped?" The sample of 237 participants was predominantly natal female (92%), and from the U.S. (51%) and Europe (32%). Most (65%) had transitioned both medically and socially. Participants selected from multiple choice options to indicate why they detransitioned with options covering a range of experiences. Respondents also had the option to write in additional reasons. Frequently endorsed reasons for detransition included realizing that their gender dysphoria was related to other issues (70%); health concerns (62%); observing that transition did not help their dysphoria (50%); and that they found alternatives to deal with their dysphoria (45%). In contrast to Turban et al. (2021), external factors such as lack of support, financial concerns, and discrimination were less common (13%, 12%, and 10%, respectively). Many in the sample described that when they detransitioned they lost support or were ostracized from lesbian, gay, bisexual, and transgender (LGBT) communities, suggesting that many of the participants in Vandenbussche (2021) would not have been reached by the recruitment efforts of the USTS (James et al., 2016).

The objective of the current study was to describe a population of individuals who experienced gender dysphoria, chose to undergo medical and/or surgical transition and then detransitioned by discontinuing medications, having surgery to reverse the effects of transition, or both. In contrast to Turban et al. (2021) and Vandenbussche (2021), this study focused only on

[2] The debate about the terminologies used to describe an individual's sex (including "assigned sex at birth," "biological sex," "natal sex," "birth sex," "sex," etc.) is far from settled. Although some professionals have argued for the use of "assigned sex at birth," others argue that this terminology is misleading and not consistent with the events that occur at birth and prior to birth (Bouman et al., 2017; Byng et al., 2018; Dahlen, 2020; Griffin et al., 2020). Supporting the unsettled nature of the discussion, I received conflicting comments from the reviewers of this manuscript about my selection of natal sex terms–one reviewer asked that I justify my preference for natal sex over the other terminologies; another reviewer expressed support for my use of natal sex. I prefer to use "natal sex" and "birth sex" because they are accurate and objective. Further, I propose that "natal sex" and "birth sex" might be seen as reasonable, polite compromise terms between "biological sex" and "assigned sex at birth."

individuals who transitioned and detransitioned medically, surgically, or both. For the purpose of this study, medical transition refers to the use of puberty blockers, cross-sex hormones, or anti-androgens and surgical transition refers to any of a variety of surgical procedures (common surgical procedures include mastectomy, genital surgery, and breast augmentation). This study does not describe the population of individuals who undergo medical or surgical transition without issue nor is it designed to assess the prevalence of detransition as an outcome of transition. Instead, the goal was to identify detransition reasons and narratives in order to inform clinical care and future research.

Method

Participants and Procedure

During the recruitment period, 101 individuals who met the study criteria completed online surveys. Inclusion criteria were (1) completion of a survey via Survey Monkey; (2) answering that they had taken or had one or more of the following for the purpose of gender transition: cross-sex hormones, anti-androgens, puberty blockers, breast surgery, genital surgery, other surgery; and (3) answering that they had done any of the following for the purpose of detransitioning: stopped taking cross-sex hormones, stopped taking anti-androgens, stopped taking puberty blockers, had any surgery to reverse transition. One survey was excluded for nonsense answers leaving 100 surveys for analysis. The sample included more natal females (69.0%) than natal males (31.0%) with respondents who were predominantly White (90.0%), non-Hispanic (98.0%), resided in the U.S. (66.0%); had no religious affiliation (63.0%), and support the rights of gay and lesbian couples to marry legally (92.9%) (see Table 1). At the time of survey completion, the mean age of respondents was 29.2 years (SD = 9.1) though natal females were significantly younger ($M = 25.8$; SD = 5.0) than natal males ($M = 36.7$; SD = 11.4), $t(98) = -6.56$, $p < .001$. Prior to transitioning, natal females were more likely to report an exclusively homosexual sexual orientation and natal males were more likely to report an exclusively heterosexual sexual orientation.

A 115-question survey instrument with multiple choice, Likert-type, and open-ended questions was created by the author and two individuals who had personally detransitioned. The author had met both detransitioners by way of introductions from colleagues. The author and both individuals who had detransitioned created questions for the survey, provided feedback, and revised the survey questions collaboratively with a focus on content, clarity, and relevance to a variety of transition and detransition experiences. The survey instrument included two questions that were adapted from an online survey of female detransitioners (Stella, 2016). Once completed, the survey was uploaded onto Survey Monkey (SurveyMonkey, Palo Alto, CA) via an account that was HIPAA-enabled.

Recruitment information with a link to the survey was posted on blogs that covered detransition topics and shared in a private online detransition forum, in a closed detransition Facebook group, and on Tumblr, Twitter, and Reddit. Recruitment information was also shared on the professional listservs for the World Professional Association for Transgender Health, the American Psychological Association Section 44, and the SEXNET listserv (which is a listserv of sex researchers and clinicians) and the professionals on the listservs were asked to share recruitment information with anyone they knew who might be eligible. Efforts were made to reach out to communities with varied views about the use of medical and surgical transition and recruitment information stated that participation was sought from individuals regardless of whether their transition experiences were positive, negative or neutral. Potential participants were invited to share recruitment information with any potentially eligible person or community with potentially eligible people. The survey was active from December 15, 2016 to April 30, 2017 (4.5 months). The median time to complete a survey was 49 min; 50% of the surveys were completed between 32 and 71 min. There were no incentives offered for participating. Data were collected anonymously, without IP addresses, and stored securely with Survey Monkey.

Participation in this study was voluntary. Electronic consent was obtained from all participants in the following manner. The first page of the online survey informed respondents about the research purpose, potential risks and benefits, that participation was voluntary, and provided contact information for the researcher. Survey questions were only displayed if the participant clicked "agree" which indicated that they read the information, voluntarily agreed to participate and were at least 18 years of age.

Measures

Demographic and Baseline Characteristics

Information was collected about participant age, natal sex, race/ethnicity, country of residence, educational attainment, socioeconomic status, religion, attitudes about legal marriage for gay and lesbian couples, and where they first heard about the study. The term sexual orientation in this article is intended to refer to the natal sex of the participant and the natal sex of the individuals with whom they are sexually attracted. Participants were asked to select one or more labels for how they identified their sexual orientation prior to transition with options inclusive of participant sex (e.g., asexual female, bisexual female, heterosexual female, etc.). These responses were coded to be consistent with participant natal sex and were categorized into homosexual, heterosexual, bisexual, pansexual, asexual, and multiple. The multiple category included respondents who

Table 1 Demographic and baseline characteristics

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Race/ethnicity**		
White	62 (89.9%)	28 (90.3%)
Multiracial	6 (8.7%)	3 (9.7%)
Other	4 (5.8%)	0 (0%)
Asian	1 (1.4%)	1 (3.2%)
Hispanic	1 (1.4%)	1 (3.2%)
Black	0 (0%)	0 (0%)
Country of residence		
USA	46 (66.7%)	20 (64.5%)
UK	8 (11.6%)	1 (3.2%)
Canada	5 (7.2%)	4 (12.9%)
Australia	2 (2.9%)	2 (6.5%)
Other	8 (11.6%)	4 (12.9%)
Education		
Bachelor's or graduate degree	29 (42.0%)	18 (58.1%)
Associates degree	3 (4.3%)	1 (3.2%)
Some college but no degree	28 (40.6%)	9 (29.0%)
High school graduate or GED	8 (11.6%)	2 (6.5%)
< High school	1 (1.4%)	0 (0%)
Other	0 (0%)	1 (3.2%)
Socioeconomic status compared to others in country of residence		
Above average (somewhat or very much)	19 (27.5%)	12 (38.7%)
About average	20 (29.0%)	7 (22.6%)
Below average (somewhat or very much)	27 (39.1%)	12 (38.7%)
Prefer not to say	3 (4.3%)	0 (0%)
Categorized sexual orientation (by natal sex) prior to transition[a]		
Homosexual	18 (26.1%)	2 (6.5%)
Heterosexual	6 (8.7%)	12 (38.7%)
Bisexual	15 (21.7%)	8 (25.8%)
Pansexual	4 (5.8%)	1 (3.2%)
Multiple	20 (29.0%)	5 (16.1%)
Asexual	6 (8.7%)	3 (9.7%)
Religious affiliation		
No religious affiliation	41 (59.4%)	22 (73.3%)
Liberal Christian	5 (7.2%)	3 (10.0%)
Liberal Jewish	5 (7.2%)	0 (0%)
Conservative Christian	1 (1.4%)	2 (6.7%)
Liberal Muslim	1 (1.4%)	0 (0%)
Conservative Jewish	0 (0%)	0 (0%)
Conservative Muslim	0 (0%)	0 (0%)
Other	16 (23.2%)	3 (10.0%)
Legal marriage for gay and lesbian couples		
Favor	65 (97.0%)	26 (83.9%)
Oppose	1 (1.5%)	5 (16.1%)
Don't know	1 (1.5%)	0 (0%)
Source where participant first heard about study		
Detransition blogs	26 (37.7%)	15 (48.4%)
Other social media	37 (53.6%)	11 (35.5%)
A person they know	3 (4.3%)	3 (9.7%)
Other	3 (4.3%)	2 (6.5%)

*May select more than one answer

[a]Natal females were more likely to express an exclusively homosexual sexual orientation prior to transition ($\chi^2 = 5.15$. The *p*-value is .023). Natal males were more likely to express an exclusively heterosexual sexual

Table 1 (continued)

orientation prior to transition ($\chi^2 = 13.05$. The p value is $< .001$). Natal sex differences were not significant for individuals expressing pre-transition sexual orientations of bisexual, pansexual, multiple, and asexual. For bisexual sexual orientation, $\chi^2 = 0.20$. For pansexual sexual orientation, $\chi^2 = 0.29$. For multiple sexual orientations reported, $\chi^2 = 1.88$. For asexual sexual orientation, $\chi^2 = 0.02$

selected more than one response where responses indicated more than one pattern of sexual attraction (e.g., lesbian female and heterosexual female). Other questions about baseline characteristics included questions about diagnosed psychiatric disorders and neurodevelopmental disabilities, trauma, and non-suicidal self-injury (NSSI) before the onset of gender dysphoria.

Gender Dysphoria Onset and Typologies

Participants were asked how old they were when they first experienced gender dysphoria and whether this was during childhood, at the onset of puberty, during puberty, or later. Respondents were categorized as having early-onset gender dysphoria if they indicated that their gender dysphoria began "during childhood" and late-onset gender dysphoria if their gender dysphoria began "at the onset of puberty" or later. To evaluate typologies, participants were characterized by Blanchard's (1985, 1989) typology as homosexual (if the sexual orientations listed prior to transition were exclusively homosexual) or non-homosexual which includes heterosexual, asexual, bisexual, pansexual, and multiple responses.

Transition

Participants were asked for their age and the year that they first sought care to transition, sources that encouraged them to believe that transition would be helpful to them, and whether they felt pressured to transition. The friendship group dynamics that were identified in previous work were assessed by asking respondents whether their friendship group mocked people who were not transgender, whether people in their pre-existing friend group transitioned before the participant decided to transition, and how participant popularity changed after announcing that they would transition (Littman, 2018). Questions were asked about participant experiences with clinicians, the social, medical, and surgical steps they took to transition, and the duration of time spent taking each medication.

Detransition

Participants were asked for their age and the year that they decided to detransition, how long they were transitioned before deciding to detransition, their reasons for wanting to detransition, what sources encouraged them to believe that detransition would be helpful to them, and whether they felt pressured to detransition. Participants were also asked which social, medical, and surgical steps they took to detransition and whether they contacted the doctor or clinic that they used for their transition to tell them that they detransitioned.

Transition and Detransition Narratives

In this article, "narratives" denote participant interpretations of their experiences and rationales surrounding their decisions to transition and detransition. To associate each participant survey with a set of relevant narratives, the data were reviewed with horizontal (beginning to end) passes and vertical passes for selected questions (these questions are listed in the supplemental materials). Surveys were coded as belonging to zero or more of the following narrative categories: discrimination, nonbinary, retransition, trauma and mental health, internalized homophobia, social influence, and misogyny. Each narrative and the responses that were associated with them are detailed below. Example quotes were selected with care taken to avoid quoting a participant more than once per narrative. Narratives are ordered and reported with the more commonly accepted narratives first and the newer narratives next.

The *discrimination* narrative was defined as when someone detransitioned due to experiencing discrimination or external social pressures. The *nonbinary* narrative consisted of answering that their current identification was "nonbinary/genderqueer" or providing open-text responses that described aspects of discovering or maintaining a nonbinary identification. Although there were no questions in the survey specifically asking about retransition, the *retransition* narrative was identified if participants expressed that they had retransitioned or resumed transition in any of the open-text responses in the survey. The *gender dysphoria was caused by trauma or a mental health condition* narrative was identified by selection for the answers, "what I thought were feelings of being transgender were actually the result of trauma," "what I thought were feelings of being transgender were actually the result of a mental health condition," "I discovered that my gender dysphoria was caused by something specific (ex. trauma, abuse, mental health condition)" or open-text responses consistent with these reasons. The *internalized homophobia/difficulty accepting oneself as a lesbian female, gay male, or bisexual person* narrative consisted of descriptions that the respondents' discomfort and distress about being lesbian, gay, or bisexual was related to their gender dysphoria, transition, or detransition, or that they assumed they were transgender because they did not yet understand themselves to be lesbian, gay or bisexual. The *social pressure to transition* narrative was identified with an affirmative

answer to whether they felt pressured to transition with an open-text response indicating that the pressure came from a person or group of people. The *misogyny* narrative was identified for natal female respondents with open-text responses using the word "misogyny" or expressing a hatred of femaleness.

Gender Identification at Start of Transition and at Survey Completion

Participants were asked how they identified their gender when they started their transition and at the time of survey completion. They were given options of female, male, nonbinary/genderqueer, trans man/FTM, trans woman/MTF, none of the above, and other. Responses were coded by natal sex and categorized as transgender, birth sex, nonbinary, and other. Answers that were combinations of the above categories were reported as combinations such as "birth sex and nonbinary."

Self-Appraisal of Transition and Detransition

One question asked if participants believe they were helped and another if they were harmed by their transition with options of "very much," "a little," or "not at all." These results were categorized into exclusively helped, exclusively harmed, and both helped and harmed. Participants were asked which of the following reflected their feelings about their transition: "I am glad that I transitioned," "I wish I had never transitioned," "Transitioning distracted me from what I should have been doing," "Transition was a necessary part of my journey." Participants were asked to rate their regret about their transition ("no regrets," "mild regrets," "strong regrets," and "very strong regrets") and were asked to indicate their satisfaction with their decisions to transition and detransition ("extremely satisfied," "very satisfied," "somewhat satisfied," "somewhat dissatisfied," "very dissatisfied," and "extremely dissatisfied"). Satisfaction options were collapsed into "satisfied" and "dissatisfied." In addition, participants were asked if they knew then what they know now, would they have chosen to transition.

Data Analysis

After data were cleaned, statistical analyses were performed using google sheets. Results are presented as frequencies, percentages, medians, means and standard deviations. *t* tests and chi-square tests were performed for selected variables and were considered significant for $p < .05$. Qualitative data were obtained from the open-text answers to questions that allowed participants to provide additional information. Selected open-text responses were categorized, tallied, and reported numerically. Salient respondent quotes and summaries from the qualitative data were selected to illustrate the quantitative results and to provide relevant examples.

Results

Before Transition

Mental health diagnoses and traumatic experiences before the onset of gender dysphoria. Table 2 shows data about psychiatric disorders, neurodevelopmental disabilities, NSSI, and trauma that were reported as occurring prior to the onset of gender dysphoria. Because these conditions and events occurred before participants began to feel gender dysphoric, they cannot be considered to be secondary to gender incongruence or transphobia.

Gender dysphoria onset and typology. Most participants (82.0%) were living with one or both parents when they first experienced gender dysphoria at a mean age of 11.2 years (SD = 5.6). The mean age of gender dysphoria onset was not statistically different between natal females ($M = 11.3$; SD = 5.4) and natal males ($M = 11.0$; SD = 5.9), $t(96) = 0.25$. By Blanchard typologies, 26.1% of natal females were exclusively homosexual and 73.9% non-homosexual while 6.5% of natal males were exclusively homosexual and 93.5% non-homosexual (Blanchard, 1985, 1989). Slightly more than half of the respondents (56.0%) experienced early-onset gender dysphoria and slightly less than half (44.0%) experienced late-onset gender dysphoria. Although late-onset gender dysphoria in natal females was largely absent from the scientific literature prior to 2012 (Steensma et al., 2013; Zucker & Bradley, 1995; Zucker et al., 2012a), 55.1% of the natal female participants reported that their gender dysphoria began with puberty or later. Because the information about the timing of gender dysphoria onset was obtained from participants reporting on their own experiences, it can be assumed that these cases were indeed late-onset rather than early-onset gender dysphoria that was concealed from parents and other people.

Transition reasons. Table 3 shows data about the reasons that individuals wanted to transition and the most frequently endorsed were: wanting to be perceived as the target gender (77.0%); believing that transitioning was their only option to feel better (71.0%); the sensation that their body felt wrong the way it was (71.0%), and not wanting to be associated with their natal sex (70.0%). Most participants believed that transitioning would eliminate (65.0%) or decrease (63.0%) their gender dysphoria and that with transitioning they would become their true selves (64.0%).

Sources of transition encouragement and friend group dynamics. Participants identified sources that encouraged them to believe transitioning would help them. Social media and online communities were the most frequently reported, including YouTube transition videos (48.0%), blogs (46.0%), Tumblr (45.0%), and online communities (43.0%) (see supplemental materials). Also common were people who the respondents knew offline such as therapists (37.0%); someone (28.0%) or a group of friends (27.0%) that they knew in-person. A subset of

Table 2 Mental health diagnoses and traumatic experiences prior to the onset of gender dysphoria

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Diagnosed with a mental illness or neurodevelopmental disability**[a]		
Depression	27 (39.1%)	5 (16.1%)
Anxiety	22 (31.9%)	5 (16.1%)
Attention deficit hyperactivity disorder (ADHD)	10 (14.5%)	2 (6.5%)
Post-traumatic stress disorder (PTSD)	10 (14.5%)	1 (3.2%)
Eating disorders	10 (14.5%)	0 (0%)
Autism spectrum disorders	9 (13.0%)	1 (3.2%)
Bipolar disorder	9 (13.0%)	0 (0%)
Obsessive compulsive disorder	6 (8.7%)	3 (9.7%)
Borderline personality disorder	5 (7.2%)	0 (0%)
Schizophrenia or other psychotic disorders	1 (1.4%)	0 (0%)
None of the above	28 (40.6%)	17 (54.8%)
Other	7 (10.1%)	2 (6.5%)
Non-suicidal self-injury (NSSI)[b]		
Engaged in NSSI before the onset of gender dysphoria	19 (27.5%)	5 (16.1%)
Trauma[c]		
Experienced a trauma less than one year before the start of gender dysphoria	33 (47.8%)	4 (12.9%)

*May select more than one answer

[a]Natal sex difference for one or more pre-existing diagnoses (100-none of the above) was not significant [$\chi^2(1, 100) = 1.76$]

[b]Natal sex differences for NSSI before the onset of gender dysphoria was not significant ($\chi^2 = 1.52$)

[c]Experiencing a trauma less than one year before the start of gender dysphoria was statistically different [$\chi^2(1, 100) = 11.19$, $p < .001$] with natal females > natal males

Table 3 Transition reasons

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Reasons for transition**		
I wanted others to perceive me as the target gender	53 (76.8%)	24 (77.4%)
I thought transitioning was my only option to feel better	50 (72.5%)	21 (67.7%)
My body felt wrong to me the way it was	50 (72.5%)	21 (67.7%)
I didn't want to be associated with my natal sex/natal gender	51 (73.9%)	19 (61.3%)
It made me uncomfortable to be perceived romantically/sexually as a member of my natal sex/natal gender	49 (71.0%)	18 (58.1%)
I thought transitioning would eliminate my gender dysphoria	43 (62.3%)	22 (71.0%)
I felt I would become my true self	42 (60.9%)	22 (71.0%)
I identified with the target gender	40 (58.0%)	24 (77.4%)
I thought transitioning would lessen my gender dysphoria	45 (65.2%)	18 (58.1%)
I felt I would fit in better with the target gender	36 (56.5%)	20 (64.5%)
I felt I would be more socially acceptable as a member of the target gender	38 (55.1%)	11 (35.5%)
I felt I would be treated better if I was perceived as the target gender	35 (50.7%)	14 (45.2%)
I saw myself as a member of the target gender	31 (44.9%)	18 (58.1%)
I thought transitioning would reduce gender-related harassment or trauma I was experiencing	35 (50.7%)	5 (16.1%)
I had erotic reasons for wanting to transition	9 (13.0)	12 (38.7%)
Other	9 (13.0%)	3 (9.7%)

*May select more than one answer

participants experienced the friendship group dynamics identified in previous work, including belonging to a friendship group that mocked people who were not transgender (22.2%), having one or more friend from the pre-existing friend group transition before the participant decided to transition (36.4%), and experiencing an increase in popularity after announcing plans to transition (19.6%) (Littman, 2018). Most did not have this experience (68.7%, 61.6%, and 62.9%, respectively).

Pressure to transition. More than a third of the participants (37.4%) felt pressured to transition. Natal sex differences in feeling pressured to transition were significant by chi-square test with natal females > natal males $\chi^2(1, 99) = 4.22$, $p = .04$. Twenty-eight participants provided open-text responses of which 24 described sources of pressure (17 described social pressures and 7 described sources that were not associated with other people). Clinicians, partners, friends, and society were named as sources that applied pressure to transition, as seen in the following quotes: "My gender therapist acted like it [transition] was a panacea for everything;" "[My] [d]octor pushed drugs and surgery at every visit;" "I was dating a trans woman and she framed our relationship in a way that was contingent on my being trans;" "A couple of later trans friends kept insisting that I needed to stop delaying things;" "[My] best friend told me repeatedly that it [transition] was best for me;" "The forums and communities and internet friends;" "By the whole of society telling me I was wrong as a lesbian;" and "Everyone says that if you feel like a different gender…then you just are that gender and you should transition." Participants also felt pressure to transition that did not involve other people as illustrated by the following: "I felt pressured by my inability to function with dysphoria" and "Not by people. By my life circumstances."

Experiences with clinicians. When participants first sought care for their gender dysphoria or desire to transition, more than half of the participants (53.0%) saw a psychiatrist or psychologist; about a third saw a primary care doctor (34.0%) or a counselor (including licensed clinician social worker, licensed professional counselor, or marriage and family therapist) (32.0%); and 17.0% saw an endocrinologist. For transition, 45.0% of participants went to a gender clinic (44.4% of those attending a gender clinic specified that the gender clinic used the informed consent model of care); 28.0% went to a private doctor's office; 26.0% went to a group practice; and 13.0% went to a mental health clinic (see supplemental materials).

The majority (56.7%) of participants felt that the evaluation they received by a doctor or mental health professional prior to transition was not adequate and 65.3% reported that their clinicians did not evaluate whether their desire to transition was secondary to trauma or a mental health condition. Although 27.0% believed that the counseling and information they received prior to transition was accurate about benefits and risks, nearly half reported that the counseling was overly positive about the benefits of transition (46.0%) and not negative enough about the risks (26.0%). In contrast, only a small minority found the counseling not positive enough about benefits (5.0%) or too negative about risks (6.0%) suggesting a bias toward encouraging transition.

Transition

Participants were on average 21.9 years old (SD = 6.1) when they sought medical care to transition with natal females seeking care at younger ages ($M = 20.0$; SD = 4.2) than natal males ($M = 26.0$; SD = 7.5), $t(97) = -5.07$, $p < .001$. Given that the majority of natal males were categorized as Blanchard typology non-homosexual, the finding that natal males sought medical care to transition at older ages than natal females is concordant with previous research (Blanchard et al., 1987). The average year for seeking care was more recent for natal females ($M = 2011$; SD = 3.8) than natal males ($M = 2007$; SD = 6.9), $t(96) = 2.78$, $p = .007$, and thus, there may have been differences in the care they received due to differences in the culture surrounding transition and the prevailing medical approaches to gender dysphoria for the time.

At the start of transitioning, nearly all (98.0%) of the participants identified as either transgender (80.0%), nonbinary (15.0%), or both transgender and nonbinary (3.0%). Participants identified which social, medical, and surgical steps they had taken to transition. Table 4 shows these steps, separated by natal sex where appropriate. Most respondents adopted new pronouns (91.0%) and names (88.0%), and the vast majority (97.1%) of natal females wore a binder. Most participants took cross-sex hormones (96.0%) and most natal males took anti-androgens (87.1%). The most frequent transition surgery was breast or chest surgery for natal females (33.3%). Genital surgery was less common (1.4% of natal females and 16.1% of natal males). Natal females took testosterone for a mean duration of 2.0 years (SD = 1.6). Natal males took estrogen for a mean duration of 5.1 years (SD = 5.9) and anti-androgens for 2.8 years (SD = 2.6). The minority of patients who took puberty blockers took them for a mean duration of less than a year ($M = 0.9$ years; SD = 0.6).

Detransition

Before deciding to detransition, participants remained transitioned for a mean duration of 3.9 years (SD = 4.1) with natal females remaining transitioned for a shorter period of time ($M = 3.2$ years; SD = 2.7) than natal males ($M = 5.4$ years; SD = 6.1), $t(96) = -2.40$, $p = .018$. When participants decided to detransition they were a mean age of 26.4 years old (SD = 7.4) though natal females were significantly younger ($M = 23.6$; SD = 4.5) than natal males ($M = 32.7$; SD = 8.8), $t(97) = -6.75$, $p < .001$. The mean calendar year when participants decided to detransition was 2014 ($M = 2014$; SD = 3.3), but the difference

Table 4 Steps taken for social, medical, and surgical transition

	N (%)
*Social transition**	
Pronouns	91 (91.0%)
Different name	88 (88.0%)
Clothes/hair/makeup	90 (90.0%)
Legal name change	49 (49.0%)
Gender/sex changed on government documents	36 (36.0%)
Voice training	20 (20.0%)
Natal female	
Wore a binder	67 (97.1%)
*Medical transition**	
Cross-sex hormones	96 (96.0%)
Puberty blockers	7 (7.0%)
Natal male	
Anti-androgens	27 (87.1%)
*Surgical transition**	
Face/neck surgery	5 (5.0%)
Natal female	
Breast/chest surgery	23 (33.3%)
Genital surgery (to create a penis)	1 (1.4%)
Natal male	
Breast implants	5 (16.1%)
Genital surgery (to create a vagina)	5 (16.1%)

*May select more than one answer

between natal females and natal males was not significant ($M = 2014$, SD = 3.3; $M = 2014$, SD = 3.5), $t(95) = 0.52$.

Respondents detransitioned for a variety of reasons and most (87.0%) selected more than one reason. The most frequently endorsed reason for detransitioning was that the respondent's personal definition of male and female changed and they became comfortable identifying with their natal sex (60.0%) (see Table 5). Other commonly endorsed reasons were concerns about potential medical complications (49.0%); transition did not improve their mental health (42.0%); dissatisfaction with the physical results of transition (40.0%); and discovering that something specific like trauma or a mental health condition caused their gender dysphoria (38.0%). External pressures to detransition such as experiencing discrimination (23.0%) or worrying about paying for treatments (17.0%) were less common.

Encouragement and pressure to detransition. Participants were asked to select sources that encouraged them to believe that detransitioning would help them. These included blogs (37.0%), Tumblr (35.0%), and YouTube detransition videos (23.0%) (see supplemental materials). At some point in their process, 23.2% felt pressured to detransition. There was no significant difference between natal females and natal males for feeling pressured to detransition, $\chi^2(1, 99) = 1.11$. Of the 21 open-text responses provided, 14 respondents expressed social pressure to detransition; three expressed internal pressure to detransition and four provided responses that were neither

Table 5 Reasons for detransitioning

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Reasons for detransitioning**		
My personal definition of female or male changed and I became more comfortable identifying as my natal sex	45 (65.2%)	15 (48.4%)
I was concerned about potential medical complications from transitioning	40 (58.0%)	9 (29.0%)
My mental health did not improve while transitioning	31 (44.9%)	11 (35.5%)
I was dissatisfied by the physical results of the transition/felt the change was too much	35 (50.7%)	5 (16.1%)
I discovered that my gender dysphoria was caused by something specific (ex, trauma, abuse, mental health condition)	28 (40.6%)	10 (32.3%)
My mental health was worse while transitioning	27 (39.1%)	9 (29.0%)
I was dissatisfied by the physical results of the transition/felt the change was not enough	22 (31.9%)	11 (35.5%)
I found more effective ways to help my gender dysphoria	25 (36.2%)	7 (22.6%)
My physical health was worse while transitioning	21 (30.4%)	11 (35.5%)
I felt discriminated against	12 (17.4%)	11 (35.5%)
I had medical complications from transitioning	12 (17.4%)	7 (22.6%)
Financial concerns about paying for transition care	11 (15.9%)	6 (19.4%)
My gender dysphoria resolved	10 (14.5%)	5 (16.1%)
My physical health did not improve while transitioning	9 (13.0%)	2 (6.5%)
I resolved the specific issue that was the cause of my gender dysphoria	6 (8.7%)	4 (12.9%)
I realized that my desire to transition was erotically motivated	1 (1.4%)	5(16.1%)
Other	19 (27.5%)	6 (19.4%)

*May select more than one answer

or unclear. Regarding social pressure to detransition, seven participants expressed that the pressure came from partners, parents, or other family members as shown in the following example quotes: "I was threatened that if I did not immediately detransition I would NEVER see my […] children again," "My father very much wanted me to desist," and "Parents constantly encouraging me to detransition." Five participants expressed societal pressure to detransition as expressed in the following quotes: "I did not pass, I was mocked in public, I could not get a job. It was not ok to be trans" and "Well, I mean basically the entire world was against me transitioning, so yeah." One participant felt pressured by doctors and another one from a blog.

Detransition steps. Table 6 shows data about the social, medical, and surgical steps participants took to detransition. Nearly all participants medically detransitioned by ceasing cross-sex hormones (95.0%). Social detransition steps were also common and included returning to the use of previously used pronouns (63.0%) and birth names (33.0%) and changing one's clothes and hair presentations (48.0%). Surgical detransition steps were less common (9.0%).

Finding better ways of coping with gender dysphoria**.** Participants were asked to select responses that that they considered to have been better ways for them to cope with their gender dysphoria. Responses included community (44.0%), mindfulness/meditation (41.0%), exercise (39.0%), therapy (24.0%), trauma work (24.0%), medication to treat a mental health condition (18.0%), and yoga (14.0%).

Table 6 Social, medical, and surgical detransition steps

	N (%)
*Social detransition**	
Previous pronouns	63 (63.0%)
Clothes/hair/makeup	48 (48.0%)
Birth name	33 (33.0%)
New name (not birth name)	24 (24.0%)
None of the above	2 (2.0%)
*Medical detransition**	
Stopped cross-sex hormones	95 (95.0%)
Stopped puberty blockers	4 (4.0%)
Started hormones consistent with natal sex	14 (14.0%)
Natal male	
Stopped anti-androgens	17 (54.8%)
*Surgical detransition**	
Surgery to reverse changes from transition	9 (9.0%)

*May select more than one answer

Transition and Detransition Narratives

Several transition and detransition narratives emerged from the data. A sizable minority of participants (41.0%) expressed more than one narrative in their responses.

The *discrimination and external pressures to detransition* narrative was described by 29.0% of participants. Examples include: "I had to detransition in order to get a job"; "I was afraid of being homeless and unable to support myself"; "I felt much happier with myself but I couldn't go anywhere without being afraid. I passed okay but not perfectly. I was stared down and sneered at in the women's clothes section, I wouldn't dare use a public toilet because I'd find either violent men or women who wished an encounter with a violent man on me."

A *nonbinary* narrative was expressed by 16.0% of participants. Some described that they discovered their nonbinary gender identity during their transition, as in the following quotes: "I still was uncomfortable with my body and figured I should stop and make sure I really wanted to keep going. I didn't and I decided I must be nonbinary, not FTM"; "Transitioning didn't do what I thought I wanted it to. I had transitioned to the wrong gender. I still felt wrong. Then, I realized I was not male, but genderqueer. I detransitioned to suit my true identity." And others described a consistent nonbinary identification, as in the following quote, "I identified the same way that I did before. I had gotten what I wanted out of HRT and was ready to stop taking it." (Cross-sex hormones are sometimes referred to as "hormone replacement therapy" and abbreviated as HRT).

Three participants (3.0%) expressed the *retransition* narrative in open-text answers indicating that they had retransitioned, including the following quotes: "I am now transitioning for a second time"; I retransitioned after 5 years of detransitioning"; and "Anyway, I retransitioned over 10 years after detransitioning."

Most participants (58.0%) expressed the *gender dysphoria was caused by trauma or a mental health condition* narrative which included endorsing the response options indicating that their gender dysphoria was caused by something specific, such as a trauma or a mental health condition. More than half of the participants (51.2%) responded that they believe that the process of transitioning delayed or prevented them from dealing with or being treated for trauma or a mental health condition. The following are example quotes that were in response to why participants chose to detransition: "I slowly began addressing the mental health conditions and traumatic experiences that caused such a severe disconnect between myself and my body…"; "I was starting to become critical of transition because I felt that many people were doing it out of self-hatred and started to realize that applied to me as well"; "I was deeply uncomfortable with my secondary sex characteristics, which I now understand was a result of childhood trauma and associating my secondary sex characteristics with those events."

Despite the absence of any questions about this topic in the survey, nearly a quarter (23.0%) of the participants expressed the *internalized homophobia and difficulty accepting oneself as lesbian, gay, or bisexual* narrative by spontaneously describing that these experiences were instrumental to their gender dysphoria, their desire to transition, and their detransition. All

of the participants in this category indicated that they were either same-sex attracted exclusively or were same-sex attracted in combination with opposite-sex attraction (such as bisexual, pansexual, etc.). The following responses were written in as "other" for the question about why participants transitioned: "Transitioning to male would mean my attraction to girls would be 'normal'"; "being a 'gay trans man' (female dating other females) felt better than being a lesbian, less shameful"; "I felt being the opposite gender would make my repressed same-sex attraction less scary"; "I didn't want to be a gay man." Some participants described that it took time for them to gain an understanding of themselves as lesbian, gay, or bisexual as seen in the following: "At the time I was trying to figure out my identity and felt very male and thought I was transgender. I later discovered that I was a lesbian…"; and "Well, after deep discovery, I realized I was a gay man and realized that a sexual trauma after puberty might [have] confused my thought. I wanted to live as a gay man again." Several natal female respondents expressed that seeing other butch lesbians would have been helpful to them as shown by the following: "What would have helped me is being able to access women's community, specifically lesbian community. I needed access to diverse female role-models and mentors, especially other butch women."

The *social influence* narrative was identified where participants added information to the question about if they had felt pressured to transition and the response described pressure from a person or people. One-fifth (20.0%) of participants expressed that they felt pressured by a person or people to transition. Example quotes for social influence were described in a previous section.

Of the natal females, 7.2% expressed the *misogyny* narrative. Example quotes include: "…I realized how much of it [dysphoria] may have been caused by internalized misogyny and homophobia"; "Finally realizing there's nothing wrong or disgusting or weak about being female"; and "My transition was a desperate attempt to distance myself from womanhood and femaleness due to internalized lesbophobia and misogyny combined with a history of sexual trauma."

After Detransition

Disposition. At the time of survey completion, most participants had returned to identifying solely as their birth sex (61.0%) with an additional 10.0% identifying as their birth sex plus another identification. Fourteen percent of the participants identified solely as nonbinary with an additional 11.0% identifying as nonbinary plus a second identification. Eight percent of the participants identified solely as transgender with an additional 5.0% identifying as transgender plus another identification. Four percent of the responses did not fit into the above categories and were coded as "other." Figure 1 illustrates the distribution of participants' current gender identification (post-detransition). Only 24.0% of participants had informed

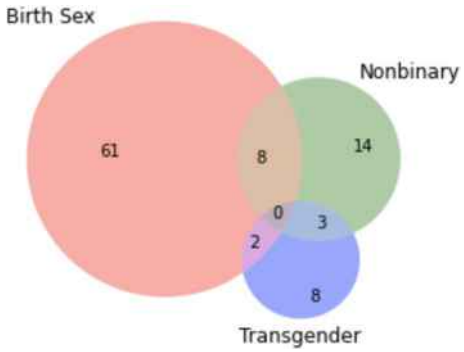

Fig. 1 Distribution of participants' current gender identification (after detransition) (n = 100). *Notes*: The sum of the numbers appearing in the "Birth Sex" circle indicates the number of participants who returned to identifying with their birth sex (71)—either as birth sex alone (61) or birth sex in addition to a second identification (10) represented in the overlap between two circles. For example, eight participants identify as their birth sex and as nonbinary. The sum of the numbers appearing in the "Nonbinary" circle indicates the number of participants who identify as nonbinary (25)—either as nonbinary alone (14) or nonbinary in addition to a second identification (11). The sum of the numbers appearing in the "Transgender" circle indicates the number of participants who identify as transgender (13)—either as transgender alone (8) or transgender in addition to a second identification (5). Four participants had responses that did not fit the categories above and were coded as "other"

the doctor or clinic that facilitated their transitions that they had detransitioned.

Self-appraisal of past transgender identification. Table 7 presents the data for responses endorsed by participants to reflect how they feel currently about having identified as transgender in the past. The statements most frequently selected included: "I thought gender dysphoria was the best explanation for what I was feeling" (57.0%), "My gender dysphoria was similar to the gender dysphoria of those who remain transitioned" (42.0%), "What I thought were feelings of being transgender actually were the result of trauma" (36.0%), "What I thought were feelings of being transgender actually were the result of a mental health condition" (36.0%).

Self-appraisal of transition and detransition. When asked to select which statement best reflects their feelings about their transition, nearly a third (30.0%) indicated that they wish they had never transitioned while 11.0% indicated they were glad they transitioned. Some (34.0%) selected the statement that transition "was a necessary part of [their] journey" but others (21.0%) indicated that the process of transitioning distracted them from what they should have been doing. Responses about whether transition helped or harmed them were also complicated. While 50.5% selected answers consistent with being both helped and harmed, 32.3% indicated that they were only harmed and 17.2% indicated that they were only helped. The majority of respondents were dissatisfied with their decision to transition (69.7%) and satisfied with their decision to detransition (84.7%). At least some amount of transition regret was

Table 7 Self-appraisal of past transgender identification

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Self-appraisal about identifying as transgender in the past**		
I thought gender dysphoria was the best explanation for what I was feeling	39 (56.5%)	18 (58.1%)
My gender dysphoria was similar to the gender dysphoria of those who remain transitioned	32 (46.4%)	10 (32.3%)
What I thought were feelings of being transgender actually were the result of trauma	31 (44.9%)	5 (16.1%)
What I thought were feelings of being transgender actually were the result of a mental health condition	28 (40.6%)	8 (25.8%)
Someone else told me that the feelings I was having meant that I was transgender and I believed them	25 (36.2%)	10 (32.3%)
I still identify as transgender	20 (29.0%)	10 (32.3%)
I believed I was transgender then, but I was mistaken	16 (23.2%)	6 (19.4%)
I was transgender then but I am not transgender now	15 (21.7%)	7 (22.6%)
I formerly identified as transgender and now identify as genderqueer/nonbinary	12 (17.4%)	5 (16.1)
My gender dysphoria was different from the gender dysphoria of those who remain transitioned	11 (15.9%)	4 (12.9%)
I was never transgender	8 (11.6%)	3 (9.7%)
I thought I had gender dysphoria but I was mistaken	4 (5.8%)	4 (12.9%)
I never had gender dysphoria	1 (1.4)	2 (6.5%)
N/A as I did not identify as transgender in the past	0 (0%)	1 (3.2%)
Other	18 (26.1%)	5 (16.1%)

*May select more than one answer

common (79.8%) and nearly half (49.5%) reported strong or very strong regret. Most respondents (64.6%) indicated that if they knew then what they know now, they would not have chosen to transition.

Discussion

This study was designed to explore the experiences of individuals who obtained medical and surgical treatment for gender dysphoria and then detransitioned by discontinuing the medications or having surgery to reverse the changes from transition. The findings of this study, however, should not be assumed to be representative of all individuals who detransition. Although this study further documents that detransitioners exist, the prevalence of detransition as an outcome of transition is unknown. Only a small percentage of detransitioners (24.0%) informed the clinicians and clinics that facilitated their transitions that they had detransitioned. Therefore, clinic rates of detransition are likely to be underestimated and gender transition specialists may be unaware of how many of their own patients have detransitioned, particularly for patients who are no longer under their care.

This research demonstrates that the experiences of individuals who detransition are varied and the reasons for detransition are complex. Nearly all participants identified as transgender or nonbinary at the start of their transition and most sought transition because they did not want to be associated with their natal sex, their bodies felt wrong the way they were, and they believed that transition was the only option to relieve their distress. Some were helped by transition and only detransitioned because they were pressured to do so by people in their lives, society, or because they had medical complications. Some were harmed by transition and detransitioned because they concluded that their gender dysphoria was caused by trauma, a mental health condition, internalized homophobia, or misogyny—conditions that are not likely to be resolved with transition. These findings highlight the complexity of gender dysphoria and suggest that, in some cases, failure to explore co-morbidities and the context in which the gender dysphoria emerged can lead to misdiagnosis, missed diagnoses, and inappropriate gender transition. Some individuals detransitioned because their gender dysphoria resolved, because they found better ways to address their symptoms, or because their personal definitions of male and female changed and they became comfortable identifying as their natal sex.

The study sample was predominantly young natal females, many of whom experienced late-onset gender dysphoria which mirrors the recent, striking changes in the demographics of gender dysphoric youth seeking care as well as the youth described by their parents in Littman (2018) (see also Aitken et al., 2015; de Graaf et al., 2018; Zucker, 2019). Concerns have been raised that this new cohort of gender dysphoric individuals is unlike previous cohorts. Professionals have started to call for caution before treating this cohort with interventions with permanent effects because the etiologies, desistance and persistence rates,

expected duration of symptoms, and whether this new population is helped or harmed by gender transition is still unknown (D'Angelo et al., 2021; Kaltiala-Heino et al., 2018). The natal females and natal males in this sample differed on several dimensions, including that natal females were younger than natal males when they sought transition, when they decided to detransition, and at the time of survey completion. Natal females were more likely than natal males to have experienced a trauma less than one year before the onset of their gender dysphoria and were more likely to have felt pressured to transition. Compared to natal males, natal females remained transitioned for a shorter duration of time before deciding to detransition. Additionally, natal females transitioned more recently than natal males, so their experiences may vary due to changing trends in the clinical management of gender dysphoria and the cultural settings in which they became gender dysphoric.

The study findings covered a wide range of detransition experiences that are consistent with the diversity of experiences described in previously published clinical case reports and case series. Overlap of findings include: transition regret; absence of transition regret; re-identification with birth sex; continued identification as transgender; improvement or worsening of well-being with transition; retransitioning; detransitioning due to external social pressures; nonbinary identification; and recognizing and accepting oneself as homosexual or bisexual (D'Angelo, 2018; Djordjevic et al., 2016; Levine, 2018; Pazos Guerra et al., 2020; Turban & Keuroghlian, 2018; Turban et al., 2021; Vandenbussche, 2021). The population in this study is similar to the population in Vandenbussche in that both were predominantly natal females in their mid-20s. Because the current study recruited in 2016–2017 and Vandenbussche recruited in 2019, the similar mean age of participants may reflect the age of individuals who can be reached in online detransitioner communities. Several findings in this study were consistent with Vandenbussche's findings, including similar reasons for detransition (realizing that their gender dysphoria was related to other issues, finding alternatives to address gender dysphoria, gender dysphoria resolved, etc.). Although these two studies were recruited in different years, had different eligibility criteria, and included participants from several countries, it is possible that there may be some overlap of study populations.

The current study findings provide additional insight into the complex relationships between internalized homophobia, gender dysphoria, and desire to transition. Contrary to arguments against the potential role of homophobia in gender transitions (Ashley, 2020), participants reported that their own gender dysphoria and desire to transition stemmed from the discomfort they felt about being same-sex attracted, their desire to not be gay, and the difficulties that they had accepting themselves as lesbian, gay or bisexual. For these individuals, exploring their distress and discomfort around sexual orientation issues may have been more helpful to them than medical and surgical transition or at least an important part of exploration before making the decision to transition. This research adds to the existing evidence that gender dysphoria can be temporary (Ristori & Steensma, 2016; Singh et al., 2021; Zucker, 2018). It has been established that the most likely outcome for prepubertal youth with gender dysphoria is to develop into lesbian, gay, bisexual (LGB) (non-transgender) adults (Ristori & Steensma, 2016; Singh et al., 2021; Wallien & Cohen-Kettenis, 2008; Zucker, 2018). And, temporary gender dysphoria may be a common part of LGB identity development (Korte et al., 2008; Patterson, 2018). Therefore, intervening too soon to medicalize gender dysphoric youth risks iatrogenically derailing the development of youth who would otherwise grow up to be LGB non-transgender adults. Participants who detransitioned because they became comfortable identifying as their natal sex and because their gender dysphoria resolved further support that gender dysphoria is not always permanent.

The data in this study strengthen, with first-hand accounts, the rapid-onset gender dysphoria (ROGD) hypotheses which, briefly stated, are that psychosocial factors (such as trauma, mental health conditions, maladaptive coping mechanisms, internalized homophobia, and social influence) can cause or contribute to the development of gender dysphoria in some individuals (Littman, 2018). Littman also postulated that certain beliefs could be spread by peer contagion, including the belief that a wide range of symptoms should be interpreted as gender dysphoria (and proof of being transgender) and the belief that transition is the only solution to relieve distress. The current study supports the potential role of psychosocial factors in the development of gender dysphoria and further suggests, by participant responses that transitioning prevented or delayed them from addressing their underlying conditions, that maladaptive coping mechanisms may be relevant for some individuals. The potential role of social influence is demonstrated as well. First, when respondents were asked to describe how they currently feel about having identified as transgender in the past, more than a third endorsed the option, "Someone told me that the feelings I was having meant that I was transgender, and I believed them." Second, a subset of participants experienced the unique friendship group dynamics reported in Littman where peer groups mocked people who were not transgender and popularity within the friend group increased when respondents announced their plan to transition. Additionally, respondents identified several social sources that encouraged them to believe that transitioning would help them including: YouTube transition videos, blogs, Tumblr, and online communities. And finally, 20.0% of participants felt pressured to transition by social sources that included friends, partners, and society. More research is needed to further explore these hypotheses.

The current study and the Turban et al. (2021) analysis of the USTS data share some similarities and differences. Similarities include the use of convenience samples, targeted recruitment, and anonymous data collection. The findings of Turban et al. (including external pressures to detransition and transgender

identification after detransition) are a subset of the array of experiences described in the current study. The current study differed from James et al. (2016) and Turban et al. in that it enrolled participants based on the criterion of detransition after medical or surgical transition regardless of how they currently identified, recruited from communities with diverse perspectives about transition and detransition, used a precise definition for detransition that specifies the use of medication or surgery, and included answer options that were relevant to many different types of detransition experiences. In contrast, the USTS only enrolled transgender-identifying individuals regardless of whether they medically or surgically transitioned, recruited from communities likely to have similar perspectives about transition and detransition, and provided multiple choice answer options that were relevant to a narrower range of detransition experiences (James et al., 2016). Further, the definition used by the USTS for "detransitioned" (having "gone back to living as [their] sex assigned as birth, at least for a while") is quite vague. Although Turban et al. provide valuable information about the subset of transgender-identifying people who may have detransitioned, the current study provides a more comprehensive view of individuals who detransition after medical or surgical transition.

Over the past 15 years, there have been substantial changes in the clinical approach to gender dysphoric patients notable for a shift from approaches that employ thorough evaluations and judicious use of medical and surgical transition (the watchful waiting or Dutch approach, the developmentally informed approach, and the medical model of care) to approaches with minimized or eliminated evaluation and liberal use of transition interventions (the affirmative approach and the informed consent model of care) (Cavanaugh et al., 2016; de Vries & Cohen-Kettenis, 2012; Meyer et al., 2002; Rafferty et al., 2018; Schulz, 2018; Zucker et al., 2012b). This trend is prominent in the U.S. where the American Academy of Pediatrics endorsed the affirmative approach in 2018 and Planned Parenthood currently uses the informed consent model to provide medical transition in more than 200 clinics in 35 states (Planned Parenthood, 2021; Rafferty et al., 2018). It is plausible that an unintended consequence of these clinical shifts may be an increase in people who detransition. Many participants in this study believe that they did not receive an adequate evaluation by a clinician before transition. The definition of "adequate evaluation" was not provided in the survey and may be open to respondent interpretation. But given the complexities of the gender dysphoria described in the current study, one might consider a low bar of "adequate" to be the exploration of factors that could be misinterpreted as non-temporary gender dysphoria as well as factors that could be underlying causes for gender dysphoria. The most recently emerging approach to gender dysphoria is called the "exploratory approach" which is a neutral psychotherapeutic approach to help individuals gain a deeper understanding of their gender distress and the factors contributing to their dysphoria (Churcher Clarke & Spiliadis, 2019; Spiliadis, 2019). The study's findings suggest that an exploratory type of approach may have been beneficial to some of the respondents. Future research is needed to determine which patients are best treated by which approaches long term.

Patients considering medical and surgical interventions deserve accurate information about the risks, benefits, and alternatives to that treatment. In this sample, nearly half of the participants reported that the counseling they received about transition was overly positive about the benefits of transition and more than a quarter reported that the counseling was not negative enough about the risks. Several participants felt pressured to transition by their doctors and therapists. If these types of clinical interactions are verified, exploration is needed to determine the extent to which this situation occurs and what measures might be taken to ensure that clinicians provide patients with their options accurately and dispassionately.

There are several obstacles to obtaining accurate rates of detransition and desistance, including stigma and the low numbers of detransitioners who inform their clinicians that they detransitioned. One approach to bypass some of these barriers would be to incorporate non-judgmental questions about detransition and desistance into nationally representative surveys that collect health data. For example, the Behavioral Risk Factor Surveillance System contains an optional module about sexual orientation and gender identity that includes two questions to explore gender issues (Downing & Przedworski, 2018). By changing one existing question, "Do you consider yourself to be transgender?" into two questions, "Have you ever, at any point in your life, considered yourself to be transgender?" and "Do you currently consider yourself to be transgender?" and by adding a follow-up question if answers indicate past but not current transgender identification, "Did you ever take puberty blockers, cross-sex hormones, anti-androgens, or have any surgery as part of your transition?", valuable information about desistance, detransition, and current transgender identification could be obtained. These types of questions may also be of use in clinical practice and electronic medical records. The information gained about rates of detransition and desistance would enhance transgender healthcare by aiding informed consent processes at the start of any medical or surgical transition.

One of the strengths of this study is that it is one of the largest samples of detransitioners to date. Other strengths include the use of a precise definition for detransition, enrollment of detransitioners regardless of their post-detransition gender identification, recruitment from communities with likely divergent views about transition and detransition, and collaboration with two individuals who had detransitioned which helped to create a survey instrument with questions relevant to a variety of detransition experiences and enhanced the recruitment efforts.

There are several limitations to this study that should be considered when interpreting the findings. Like Vandenbussche (2021), James et al. (2016), and Turban et al. (2021), this study

used a cross-sectional design, anonymous surveying, and a convenience sample and therefore shares the same limitations that are inherent to these methodologies. These limitations include that conclusions about causation cannot be determined, identities of participants cannot be verified, and the findings of this study may not be generalizable to the entire population of people who detransition or to people outside of the countries where participants were from. Although this study reached out to communities with differing perspectives about transition and detransition, targeted recruitment and convenience samples always introduce the limitations associated with selection biases which should be addressed in future research. Finally, many of the participants in this study had less than ideal outcomes to their medical and surgical transitions, and it is possible that these experiences may have colored some of the responses.

Additional research is needed to determine the prevalence of detransition as an outcome of transition and to identify and meet the psychological and medical needs of the emerging detransitioned population. Because many individuals who detransition re-identify with their birth sex, are no longer connected to LGBT communities, and don't return to gender clinics, future research about detransition needs to expand recruitment efforts beyond gender clinics and transgender communities. The development and testing of non-medical interventions for gender dysphoria could provide valuable options to be used as alternatives or in conjunction with medical and surgical treatments. Because of the potential for some to experience trauma, mental health conditions, internalized homophobia, and misogyny as gender dysphoria, research needs to be conducted on the evaluation process before transition to find approaches that respectfully and collaboratively explore factors that might contribute to gender-related distress. There continues to be an absence of long-term outcomes evidence for youth treated with medical and surgical transition and a lack of information about the trajectories of youth experiencing late-onset gender dysphoria–research is needed to address these gaps. Continued work is needed to reduce rigid gender roles, increase representation of gender stereotype nonconformity, and to address discrimination and social pressures exerted against people who are transgender, lesbian, gay, bisexual, and gender stereotype non-conforming.

Conclusion

This study described individuals who, after transitioning with medications or surgery, have detransitioned. The prevalence of detransitioning after transition is unknown but is likely underestimated because most of the participants did not inform the doctors who facilitated their transitions that they had detransitioned. There is no single narrative to explain the experiences of all individuals who detransition and we should take care to avoid painting this population with a broad brush. Some detransitioners return to identifying with their birth sex, some assume (or maintain) a nonbinary identification, and some continue to identify as transgender. Some detransitioners regret transitioning and some do not. Some of the detransitioners reported experiences that support the ROGD hypotheses, including that their gender dysphoria began during or after puberty and that mental health issues, trauma, peers, social media, online communities, and difficulty accepting themselves as lesbian, gay, or bisexual were related to their gender dysphoria and desire to transition. Natal female and natal male detransitioners appear to have differences in their baseline characteristics and experiences and these differences should be further delineated. Future research about gender dysphoria and the outcomes of transition should consider the diversity of experiences and trajectories. More research is needed to determine how best to provide support and treatment for the long-term medical and psychological well-being of individuals who detransition. Findings about detransition should be used to improve our understanding of gender dysphoria and to better inform the processes of evaluation, counseling, and informed consent for individuals who are contemplating transition.

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Declarations

Conflict of interest The author has no relevant financial or non-financial conflicts of interest to disclose.

Consent to Participate Electronic consent was obtained from all participants included in the study. On the first page of the online survey, participants were informed of the research purpose and potential risks and benefits of participating, that their participation was voluntary, and were presented with a way to contact the researcher. The research survey questions were displayed only if the participant clicked "agree" which indicated that the participant read the information, voluntarily agreed to participate, and were at least 18 years of age.

Ethical Approval The research was determined to be Exempt Human Research by the Program for the Protection of Human Subjects of the Icahn School of Medicine at Mount Sinai in New York, NY. All procedures were performed in accordance with the ethical standards of the Program for the Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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Detransition-Related Needs and Support: A Cross-Sectional Online Survey

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ABSTRACT

The aim of this study is to analyze the specific needs of detransitioners from online detrans communities and discover to what extent they are being met. For this purpose, a cross-sectional online survey was conducted and gathered a sample of 237 male and female detransitioners. The results showed important psychological needs in relation to gender dysphoria, comorbid conditions, feelings of regret and internalized homophobic and sexist prejudices. It was also found that many detransitioners need medical support notably in relation to stopping/changing hormone therapy, surgery/treatment complications and reversal interventions. Additionally, the results indicated the need for hearing about other detransitioners' experiences and meeting each other. A major lack of support was reported by the respondents overall, with a lot of negative experiences coming from medical and mental health systems and from the LGBT+ community. The study highlights the importance of increasing awareness and support given to detransitioners.

KEYWORDS

Detransition; gender dysphoria; gender identity; cross-sex hormones; detransitioners; transgender; transition; support

Introduction

In recent years, there has been an increasing interest in the phenomenon of detransition. Many testimonies have been shared by self-identified detransitioners online and detrans communities have formed on social media. This phenomenon started to attract the attention of scholars, who have emphasized the need for research into the specific needs of this group (e.g., Butler & Hutchinson, 2020; Entwistle, 2020; Hildebrand-Chupp, 2020). A few case studies have been conducted in order to explore individual experiences of detransition (Pazos-Guerra et al., 2020; Turban & Keuroghlian, 2018). The latter studies highlighted the complexity of detransition experiences but did not provide sufficient data to assess the general needs and characteristics of detransitioners. The current study aims to explore this issue in more depth and to serve as a basis for future research on the phenomenon of detransition.

To date there has been little agreement on a definition of the word "detransition." As explained by Expósito-Campos (2021), this term has been used interchangeably to refer to what he perceives to be two distinctive situations: in

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the first, the detransitioning individual stops identifying as transgender; in the second, they do not. It is therefore necessary here to clarify exactly what is meant when writing about detransition.

In this paper, I will be using the following concepts: "medical detransition," "social detransition" and (male or female) "detransitioner." Medical detransition refers to the process of ceasing/reversing the medical aspects of one's medical transition. This might include stopping or changing hormone therapy and undergoing reversal surgeries, among others. Likewise, social detransition refers to the process of changing/undoing the social aspects of one's social transition. For example, it might include presenting oneself as one's birth sex again, changing one's post-transition name or going back to using the pronouns associated with one's birth sex.

The term "detransitioner" will be used here to refer to someone who possibly underwent some of these medical and/or social detransition steps and, more importantly, who identifies as a detransitioner. It is important to add this dimension, because the act of medical/social detransition can be performed by individuals who did not cease to identify as transgender and who do not identify as detransitioners or as members of the detrans community. Furthermore, some individuals might identify as detransitioners after having ceased to identify as trans, while not being in a position to medically or socially detransition due to medical or social concerns. As Hildebrand-Chupp (2020) puts it: "[B]ecoming a detransitioner involves a fundamental shift in one's subjective understanding of oneself, an understanding that is constructed within these communities." (p.802). More qualitative research should be conducted in order to better understand how members of the detrans community define themselves and make sense of their own detransition process. However, this goes beyond the scope of this study.

The creation of support and advocacy groups for detransitioners in recent years (e.g., DetransCanada, n.d., Detrans Voices, n.d., The Detransition Advocacy Network, n.d., Post Trans, n.d.) testifies to the formation of a detrans community whose members have specific needs. Scholars and clinicians have recently started raising concerns around the topic (e.g., Butler & Hutchinson, 2020; Entwistle, 2020; Hildebrand-Chupp, 2020; Marchiano, 2020). However, little research has been done specifically into the characteristics of this seemingly growing community.

Two informal surveys conducted by detransitioners (Hailey, 2017; Stella, 2016) have explored the demographics and (de)transition experiences of members of online female detrans communities. These will constitute interesting points of comparison in the discussion section of the current research.

The purpose of this exploratory study is to offer an overview of the current needs of detransitioners from online detrans communities, which will hopefully serve as a useful basis for further experimental studies around the topic of detransition. The current research primarily seeks to address the following

questions: What are the current needs of detransitioners? What support is given to detransitioners in order to fulfil these needs?

Methods

Procedure

A cross-sectional survey was conducted, using online social media to recruit detransitioners. Access to the questionnaire was open from the 16th of November until the 22nd of December 2019. Any detransitioner of any age or nationality was invited to take part in the study. The survey was shared by Post Trans (www.post-trans.com)—a platform for female detransitioners—via public posts on Facebook, Instagram and Twitter. Participants were also recruited through private Facebook groups and a Reddit forum for detransitioners (r/detrans). Some of the latter platforms were addressed exclusively to female detransitioners. The purpose of the study was presented as gaining a better understanding of detransitioners' current needs. Potential participants were asked to fill out the form and share it to fellow detransitioners. All participants have been fully anonymized.

Everyone who answered "yes" to the question "Did you transition medically and/or socially and then stopped?" was selected in the study. The individual questionnaires of the 9 respondents who answered "no" to this question were looked at closely, in order to assess whether they should be included in the study. Eight of them were added to the final sample, as their other answers indicated that their experiences lead them to identify as detransitioners.

This research was approved by the Ethics Committee for Noninvasive Research on Humans in the Faculty of Society and Economics of the Rhine-Waal University of Applied Sciences

Questionnaire design

The questionnaire consisted of 24 questions (see Appendix). The first series of questions was aimed at defining the profile of the respondent (age, sex, country, etc.), the second was asking about relevant aspects of transition and detransition experiences (transition type, gender dysphoria, therapy, medical interventions, reasons for detransitioning etc.), and the third focused on the needs encountered as well as the support (or lack of) received during the process of detransition (medical, psychological, legal and social needs and support).

Most of the items were multiple-choice questions. The conception of the multiple choices was based on observations drawn from several detransition online resources and forums. An open "other" category was available when relevant for the respondents to write in possibly lacking options. The survey

was designed to leave a lot of free space to add answers, since the detransition population is still very much under-researched and there is a lot to learn from each of its members. This is why a more qualitative approach was taken for the last question notably, leaving an open field for adding comments about the support—or lack of—received while detransitioning. This qualitative data was analyzed through the identification of recurrent themes, which will be presented in the results section.

Participants

A total of 237 participants were included in the final sample. The large majority was female; 217 female (92%) for 20 male respondents (8%). This was determined based on the answers to the question: "What sex were you assigned at birth?" The average age was 25.02 years (SD = 7.72), ranging from 13 to 64. The mean age of female detransitioners (M = 24.38; SD = 6.86) was lower than that of male detransitioners (M = 31.95; SD = 12.26).

Around half of the sample (51%) reported coming from the United States and close to a third from Europe (32%). Fifteen respondents are from Canada (6%), twelve from Australia (5%), and one from each of the following countries: Brazil, Kazakhstan, Mexico, Russia and South Africa.

Close to two thirds (65%) transitioned both socially and medically; 31% only socially. A few respondents rightly criticized the fact that the option of medically transitioning only was not available in the questionnaire. The absence of this option needs to be kept in mind when looking at the results.

Around half (51%) of the respondents started socially transitioning before the age of 18, and a quarter (25%) started medically transitioning before that age as well. The average age of social transition was 17.96 years (17.42 for females; 23,63 for males) (SD = 5.03) and that of medical transition was 20.70 years (20.09 for females; 26.19 for males) (SD = 5.36). Fourteen percent of the participants detransitioned before turning 18. The average age of detransition was 22.88 years (22.22 for females; 30.00 for males) (SD = 6.46). The average duration of transition of the respondents (including both social and medical transition) was 4.71 years (4.55 for females; 6.37 for males) (SD = 3.55).

Eighty percent of the male detransitioners underwent hormone therapy, compared to 62% for female detransitioners. Out of the respondents who medically transitioned, 46% underwent gender affirming surgeries.

Results

For sake of clarity, the results will be presented based on the three categories mentioned above in the methods section: profile of the respondents, relevant aspects of transition and detransition and, finally, detransition-related needs and support. The qualitative results will be displayed at the end of this section.

Profile of the respondents

Most of the information related to the profile of the respondents can be found in the methods section. The sample showed a high prevalence of comorbidities, considering that over half of the participants (54%) reported having had at least 3 diagnosed comorbid conditions (out of the 11 conditions listed in the survey—see Table 1). The most prevalent diagnosed comorbid conditions are depressive disorders (69%) and anxiety disorders (63%), including PTSD (33%) (see Table 1).

Relevant aspects of transition and detransition

A great majority of the sample (84%) reported having experienced both social and body dysphoria. (Social dysphoria being defined as a strong desire to be seen and treated as being of a different gender, and body dysphoria as a strong desire to have sex characteristics of the opposite sex/rejection of your own sex). Eight percent reported having experienced only body dysphoria, 6% only social dysphoria and 2% neither of them.

Forty-five percent of the whole sample reported not feeling properly informed about the health implications of the accessed treatments and interventions before undergoing them. A third (33%) answered that they felt partly informed, 18% reported feeling properly informed and 5% were not sure.

The most common reported reason for detransitioning was realized that my gender dysphoria was related to other issues (70%). The second one was health concerns (62%), followed by transition did not help my dysphoria (50%), found alternatives to deal with my dysphoria (45%), unhappy with the social changes (44%), and change in political views (43%). At the very bottom of the list are: lack of support from social surroundings (13%), financial concerns (12%) and discrimination (10%) (see Figure 1).

34 participants (14%) added a variety of other reasons such as absence or desistance of gender dysphoria, fear of surgery, mental health concerns related

Table 1. Number of participants with comorbid conditions.

Comorbid condition	Diagnosed	Suspected
Depressive disorder	163 (70%)	32 (14%)
Anxiety disorder	149 (63%)	43 (18%)
Post-traumatic stress disorder	79 (33%)	63 (27%)
Attention deficit disorder	57 (24%)	50 (21%)
Autism spectrum condition	47 (20%)	61 (26%)
Eating disorder	46 (19%)	58 (25%)
Personality disorder	40 (17%)	26 (11%)
Obsessive compulsive disorder	35 (15%)	44 (19%)
Polycystic ovary syndrome (only females)	22 (10%)	13 (6%)
Dissociative identity disorder	14 (6%)	23 (10%)
Schizo-spectrum disorder	5 (2%)	9 (4%)

"Diagnosed" and "Suspected" were mutually exclusive categories.

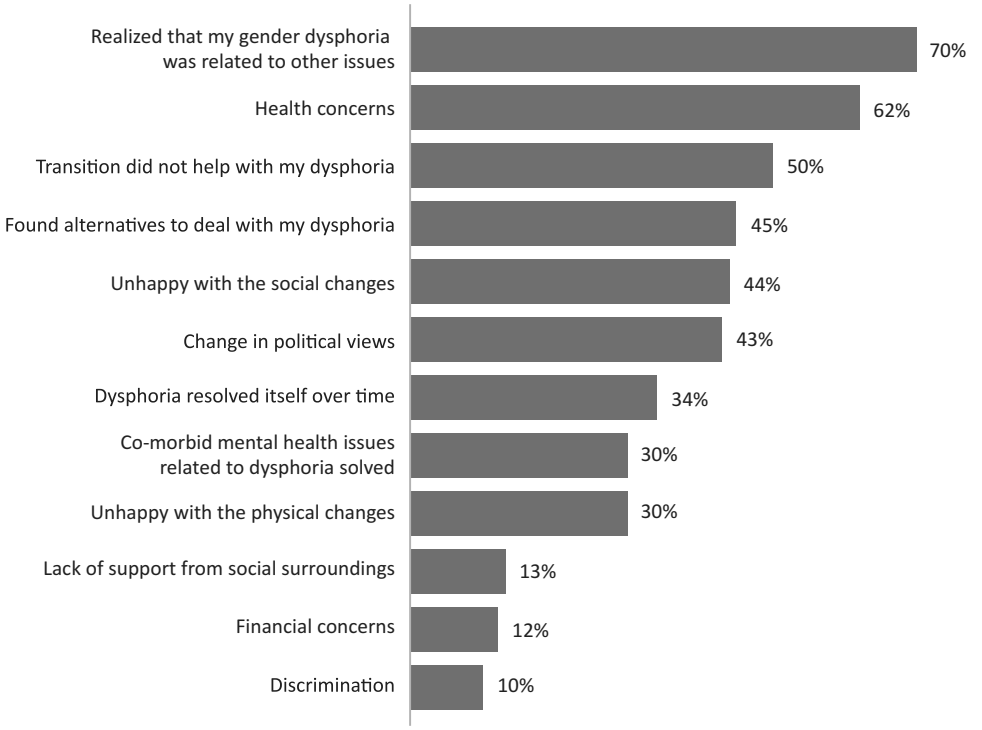

Figure 1. Reasons for detransitioning.

to treatment, shift in gender identity, lack of medical support, dangerosity of being trans, acceptance of homosexuality and gender non-conformity, realization of being pressured to transition by social surroundings, fear of surgery complications, worsening of gender dysphoria, discovery of radical feminism, changes in religious beliefs, need to reassess one's decision to transition, and realization of the impossibility of changing sex.

Detransition-related needs and support

The different types of needs were divided into four categories in the questionnaire: medical, psychological, legal and social needs.

Medical needs

The most commonly chosen answer was the need for receiving accurate information on stopping/changing hormonal treatment (49%), followed by receiving help for complications related to surgeries or hormonal treatment (24%) and receiving information and access to reversal surgeries/procedures (15%). Forty-six percent of the participants reported not having any detransition-related medical need. Sixteen respondents (7%) added another non-listed answer, such as tests to determine current reproductive health, information

about long-term effects of hormone therapy, about the health consequences of having had a full hysterectomy and about pain related to chest binding.

Psychological needs

Psychological needs appeared to be the most prevalent of all, with only 4% of the respondents reporting not having any. The answers working on comorbid mental issues related to gender dysphoria and learning to cope with gender dysphoria; finding alternatives to medical transition are at the top of the list, both with 65%. Below that, learning to cope with feelings of regret (60%), followed by learning to cope with the new physical and/or social changes related to detransitioning (53%) and learning to cope with internalized homophobia (52%). Thirty-four respondents (14%) added another non-listed answer, such as trauma therapy, learning how to deal with shame and internalized misogyny, how to cope with rejection from the LGBT and trans communities and how to deal with the aftermath of leaving a manipulative group. Other answers disclosed the need for help recovering from addictive sexual behavior related to gender dysphoria, psychosexual counseling and peer support.

Legal needs

More than half of the sample (55%) reported not having any detransition-related legal need. The main legal need expressed was changing back legal gender/sex marker and/or name (40%), followed by legal advice and support to take legal action over medical malpractice (13%). Five respondents (2%) added another non-listed answer, such as employment legal aid and support to take legal action for having been forced to go through a sterilization.

Social needs

The big majority of the respondents reported a need for hearing about other detransition stories (87%). The second most common answer was getting in contact with other detransitioners (76%), followed by receiving support to come out and deal with negative reactions (57%). Thirty-three respondents (14%) added another non-listed answer such as being accepted as female while looking male, help navigating social changes at the workplace, building a new social network, more representation of butch lesbians, real life support and finding a community.

When looking at from whom the respondents received support while transitioning and detransitioning, it appears that the biggest source of help comes from online groups/forums/social media for both transition and detransition (65%). The support received from friends, partner(s) and family is a little higher for detransition (64%) than for transition (56%).

Only 8% of the respondents reported having received help from an LGBT+ organization while detransitioning, compared to 35% while transitioning.

Similarly, 5% reported having received help from a trans-specific organization while detransitioning, compared to 17% while transitioning.

A total of 29% reported having received support for their detransition from the medical professionals that helped them during their transition. In contrast, 38% sought support from a new therapist/doctor. A part of the sample reported not receiving help from anybody for transitioning (8%) and for detransitioning (11%) (see Figure 2).

Around half of the respondents (51%) reported having the feeling of not having been supported enough throughout their detransition, 31% said they did not know and 18% answered that they had received enough support.

Qualitative results

Two open-ended questions allowed participants to write more extensively about their needs and support in the questionnaire. The first one enabled the respondents to write about any additional need that they encountered while detransitioning, while the second asked about the support—or lack of—that they had received.

Additional comments about needs

Thirty-seven participants (16%) left various comments about specific needs that they experienced during their transition and detransition.

Several respondents expressed the need for different types of therapy and counseling for dealing with issues of dissociation, childhood sexual trauma, anorexia, relationship issues and body issues caused by irreversible gender affirming surgeries. A participant also mentioned the importance of help revolving around suicide prevention for those who need it.

Additionally, someone emphasized the need for therapists to validate the feelings of being harmed by transition that some detransitioners experience, rather than dismissing or opposing them. Similarly, another respondent expressed the need for non-judgmental medical practitioners. Someone else described the need for as much medical autonomy as possible and a total freedom from psychology and psychiatry. A participant also explained that she would have needed to know the health risks of chest binding before experiencing them.

Furthermore, two respondents highlighted the need to look into individual experiences and needs without forcing them into a rigid model of transition. Others wrote about the need for more information about detransition and a better general understanding of this phenomenon.

Lastly, a few female detransitioners expressed the need for being valued as a woman, for learning about feminist theories and for more gender-nonconforming role models.

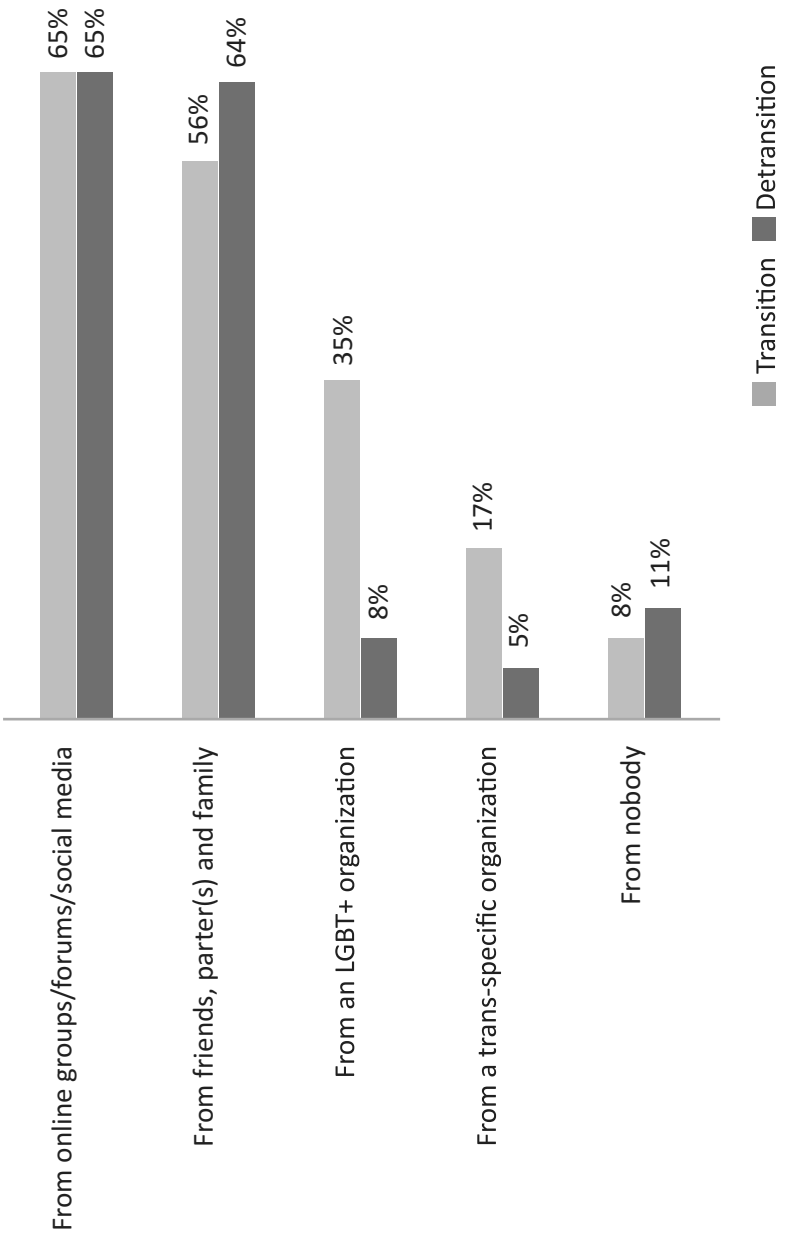

Figure 2. Comparison between transition and detransition support.

Additional comments about support

At the end of the questionnaire, a second open-ended question invited the participants to give further comments about the support—or lack of—that they had received during their detransition process.

A third of the participants (34%) answered this question, often with long and detailed accounts of their personal experiences with regard to this aspect. The most common themes identified were: loss of support from the LGBT community and friends (see Table 2), negative experiences with medical professionals (see Table 3), difficulty to find a detrans-friendly therapist and lack of offered alternatives to transitioning (see Table 4), as well as isolation and lack of overall support. Some gave more positive accounts of the support that they had received from their family, partners and friends and emphasized their important role.

A recurrent theme in the answers was a sense amongst respondents that it was very difficult to talk about detransition within LGBT+ spaces and with trans friends. Many expressed a feeling of rejection and loss of support in relation to their decision to detransition, which lead them to step away from LGBT+ groups and communities (see Table 2).

Whilst a minority reported positive experiences with medical professionals during their detransition, most participants expressed strong difficulties finding the help that they needed during their detransition process. Participants' own descriptions of the nature of these difficulties can be found in Table 3.

Another reported issue was the difficulty of finding a therapist willing and able to look at the factors behind gender dysphoria and to offer alternatives to transitioning. Some respondents highlighted the fact that they were

Table 2. Extracts about experiences of exclusion from LGBT+ communities.

"The LGBT+ community doesn't support detransitioners and I lost all LGBT+ friends I had because they deemed me transphobic/terfy, only non-LGBT+ friends supported me."
"Where I live detransitioners are seen bad for most of the LGBT community, so it's hard to talk about it with freedom."
"It is unacceptable that, at least in my experience, detransition is not something allowed to be talked about in LGBT spaces."
"Only lesbians and feminists helped me. The trans and queer community demonized me and ostracized me for my reidentification."
"I lost a lot of support and attracted a lot of hostility from trans people when I detransitioned socially. I also deal with a lot of people assuming that my dysphoria is gone entirely/cured because I have detransitioned socially, and decided not to go through with medical transition."
"Lgbt organizations don't want to talk about detransition. I did not feel welcome at lgbt events after I detransitioned."
"Telling my trans friends that I'm desisting is nearly impossible. The community is too toxic to allow any kind of discussion about alternatives to transition, sources of dysphoria beyond 'that's just who you are', or stories about detransitioners."
"I've been shunned by most of my trans identifying friends. I had to leave my old doctor, therapist and LGBT group out of shame and embarrassment."
"I have several de-trans friends whom had permanent body alterations they regretted that led to more dysphoria and eventually their suicides. Biggest factors were a lack of medical support and outright rejection from LGBT organisations/communities."
"I still have transgender friends who don't want me to talk about detransition. They're okay with me being detransitioned, but they don't want me to criticize transition or discuss the negative side effects of HRT."

Table 3. Extracts about negative medical experiences during detransition.

"I needed gender and transition experienced providers to assist with my medical detransition, but none of them seemed to understand or provide the type of care I needed, despite my self-advocacy. I got better care from providers outside of the LGBT and transgender specialty clinics."
"I still struggle to find a doctor who has knowledge of detransition and the effects HRT had on me/my best course of action since stopping."
"When I first brought up wanting to stop T to my doctor, they were very dismissive and condescending about it."
"My experience with transition left me with greatly diminished faith in medicine and zero faith in the mental health profession. I now avoid all doctors most of the time (unless I am convinced they are the only way to access a strongly evidence-based treatment or diagnostic tool for a condition which causes more suffering than doctors themselves- many do not) and totally avoid any contact with mental health professionals, and am much better off for it."
"As soon as I 'detransed' I was discharged from all gender services, despite asking for help in dealing with sex dysphoria should it arise again."
"I had no medical help from the doctor who prescribed me T, she wanted nothing to do with me."
"The team that transitioned you is not willing to help you detransition. You need new doctors."
"The medical team that helped me transition is helpful, but they are also causing a lot of hassle, which is very frustrating for me. Like for example they keep me stuck with my male sex marker for I don't know how long, and they don't believe I'm sure enough that I want to detransition, because they think I should have consistent 'reverse dysphoria' and mine kinda isn't so consistent."
"My hormone blocker implant is several years old and is only barely still functioning but they will not remove it. It's in my arm and I have no contact with the doctor because he shut down his business apparently."

Table 4. Extracts about the difficulty of finding a detrans-friendly therapist.

"It is very hard to find a therapist who won't tell you it's 'internalized transphobia' or that dealing with dysphoria in other ways is 'conversion therapy'."
"The only thing that comes to mind is one of the therapists I had, who pushed me not to detransition."
"Therapists are unprepared to handle the detrans narrative and some that I have seen since detransitioning have pushed the trans narrative. Some therapists couldn't tell the difference between being transgender and having internalized misogyny and homophobia."
"I could have benefitted from counseling but don't trust psychologists ideological bias."
"I struggled to find a therapist who supported questioning my trans identity and considering alternatives to transitioning; most only knew how to encourage transitioning and reinforced the harmful ideas that led to my wrongly identifying as FtM in the first place."
"I was doubtful that transition would help my dysphoria before beginning and was assured by multiple professionals that transition was The Solution and proven to work for everyone with dysphoria. A 'gender specialist' therapist flat-out told me that transitioning was the only method of reducing dysphoria that worked when I expressed my desperation for an alternate solution."
"The gender clinic I went to basically told me that the only way to deal with gender dysphoria was transitioning even when I told them I wanted to detransition."
"I struggled to find a therapist who supported questioning my trans identity and considering alternatives to transitioning; most only knew how to encourage transitioning and reinforced the harmful ideas that led to my wrongly identifying as FtM in the first place."
"The biggest issue for me was that when I did try to get support from a therapist or psychologist on entangling the actual reasons behind my dysphoria and how to deal with it, and deal with detransitioning, nobody had any clue or any experience, so they couldn't help me. Which made me even feel more lonely, and made detransitioning so much harder mentally than transitioning was."

cautious regarding the possible ideological bias or lack of knowledge of therapists.

Overall, most respondents explained that their detransition was a very isolating experience, during which they did not receive enough support. However, some participants emphasized the fact that the support that they received from their family, partners and friends, as well as online detrans groups and lesbian and feminist communities was extremely important and valuable to them.

Discussion

The present study was designed to better understand the needs of detransitioners, as well as the support—or lack of—that they are currently receiving. In order to do so, members of online detrans communities were recruited to answer a survey, in which questions were asked about their demographics, their transition and detransition experiences and the needs that they faced as well as the support that they received while detransitioning. In this section, I will discuss the results in relation to the main research question of the current study: What are the needs of detransitioners?

The sample surveyed appeared to be mostly female, young, from Western countries, with an experience of both social and medical transition and a high prevalence of certain comorbid conditions. The current study found that most detransitioners stopped transitioning before their mid-twenties, after an average of 4 years of transition. This observation is consistent with that made by Stella (2016) in her informal study on female detransitioners. The average transition age of the 203 respondents of her survey was 17.09 years, compared to 17.42 years in female detransitioners of the current study. The average detransition age of her sample was 21.09 years, compared to 22.22 years here.

Another finding of the current study was that a majority of the sample underwent hormone therapy (62% for females; 80% for males) and 45% of those who medically transitioned underwent gender affirming surgeries. This is likely to have implications in terms of the medical needs faced by this population. Close to half of the sample (49%) reported a need for receiving accurate information on stopping or changing hormone therapy, and almost a quarter (24%) reported the need for receiving help for complications related to surgeries or hormone therapy. The latter finding is concerning when looking at the negative medical experiences described by respondents in Table 3. Participants recounted situations in which their doctors either did not believe them, did not listen to them, refused them services, or simply did not have the required knowledge to help them during their detransition process. These experiences had a negative impact on some of the participants' trust in healthcare providers.

Similarly, the current study suggested that detransitioners have important psychological needs. This was made visible on the one hand through the fact that a majority of respondents (65%) reported the need for help in working on comorbid mental conditions related to gender dysphoria and in finding alternatives to medical transition. Other needs were reported by a majority of participants, such as learning to cope with feelings of regret (60%), learning to cope with the new physical and/or social changes related to detransitioning (53%) and learning to cope with internalized homophobia (52%). On the other hand, the high prevalence of comorbid conditions described in Table 1 might also be an indicator of important psychological needs. These results are similar

to that found by Hailey (2017) in her informal survey of comorbid mental health in detransitioned females. In her study, 77% reported a diagnosis of a depressive disorder (compared to 70% here), 74% of the sample reported a diagnosis of an anxiety disorder (compared to 63% here), 32% reported a diagnosis of PTSD (compared to 33% here) and 22% reported a diagnosis of an eating disorder (compared to 19% here). This is also very concerning information considering the descriptions made by detransitioners about the difficulty of finding a therapist willing or able to help them, and of finding alternative ways to deal with gender dysphoria after detransitioning (see Table 4).

The majority (84%) of the respondents reported having experienced both body and social gender dysphoria. Half of the sample (50%) later reported having decided to detransition due to the fact that their transition did not alleviate their gender dysphoria. Others (45%) reported having found alternative ways to deal with their gender dysphoria (see Figure 1). These results highlight the necessity to start looking into alternative solutions for treating gender dysphoria, in order to help those who did not find medical and/or social transition fulfilling.

In addition to that, 70% of the sample reported having realized that their gender dysphoria was related to other issues. Further research should be conducted in order to identify the ways in which other issues such as comorbid mental health conditions, trauma or internalized misogyny and homophobia possibly interact with gender dysphoria, and what can be done to alleviate them.

Furthermore, the high prevalence of autism spectrum condition (ASC) (20%) found in detransitioners in the current study, which is supported by Hailey (2017) findings (15%), also constitutes an interesting avenue for future research. Previous studies have provided evidence suggesting a co-occurrence of gender dysphoria and ASC (e.g., De Vries, Noens, Cohen-Kettenis, Van Berckelaer- Onnes, & Doreleijers, 2010; Glidden, Bouman, Jones, & Arcelus, 2016; VanderLaan et al., 2014; Van Der Miesen, Hurley, & De Vries, 2016; Zucker et al., 2017), which might explain the high number of detransitioners with an ASC diagnosis found in the current study.

In general, support given to detransitioners seems to be very poor at the moment, considering the fact that only 18% of the participants in the current study reported having received enough support during their detransition.

Based on the results of the current study, it appears that detransitioning is often accompanied by a break with LGBT+ communities. Only 13% of the participants reported having received support from an LGBT+ or trans-specific organization while detransitioning, compared to 51% while transitioning (see Figure 2). In addition to that, many respondents described experiences of outright rejection from LGBT+ spaces due to their decision to detransition (see Table 2). Looking at studies showing the positive role

of peer support and trans community connectedness on the mental health of its members (Johnson & Rogers, 2019; Pflum, Testa, Balsam, Goldblum, & Bongar, 2015; Sherman, Clark, Robinson, Noorani, & Poteat, 2020), it seems reasonable to suspect that this loss of support experienced by detransitioners must have serious implications on their psychological well-being.

Fortunately, the current study shows that detransitioners have access to other sources of support, online (groups, forums, social media) and in their social surroundings (family, partners and friends) (see Figure 2). Online groups and websites for detransitioners seem to be particularly important in light of the social needs expressed by the respondents of the current study. An overwhelming majority of respondents reported the need for hearing about other detransition stories (87%) and for getting in contact with other detransitioners (76%). Detransitioners need platforms and spaces where they can connect with each other and build a community. This point is best illustrated by the following account of one participant: "I found the peer support I received through other detransitioned women to be totally adequate and feel I benefited substantially from learning how to exist without institutional validation."

Conclusion

The aim of the present research was to examine detransitioners' needs and support. The four categories of needs (psychological, medical, legal and social) that were created for sake of clarity in the survey were a simplification of the real complexity of the experiences made by detransitioners and they have their limitations. Nonetheless, these categories enabled the current study to uncover the fact that most detransitioners could benefit from some form of counseling and in particular when it comes to psychological support on matters such as gender dysphoria, comorbid conditions, feelings of regret, social/physical changes and internalized homophobic or sexist prejudices. Medical support was also found to be needed by many, in order to address concerns related to stopping/changing hormone therapy, surgery/treatment complications and access to reversal interventions. Furthermore, the current study has shown that detransitioners need spaces to hear about other detransition stories and to exchange with each other.

Unfortunately, the support that detransitioners are receiving in order to fulfill these needs appears to be very poor at the moment. Participants described strong difficulties with medical and mental health systems, as well as experiences of outright rejection from the LGBT+ community. Many respondents have expressed the wish to find alternative treatments to deal with their gender dysphoria but reported that it was impossible to talk about it within LGBT+ spaces and in the medical sphere.

These accounts are concerning and they show the urgency to increase awareness and reduce hostility around the topic of detransition among healthcare providers and members of the LGBT+ community in order to address the specific needs of detransitioners.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Appendix.

Full Questionnaire

(1) How old are you?
(2) What country are you living in?
(3) What sex were you assigned at birth?
- Female
- Male
- Other:

(4) How do you see yourself now? (Tick all that apply)
- Woman
- Man
- Trans man
- Trans woman
- Female detransitioner
- Male detransitioner
- Non binary
- Other:

(5) Did you transition socially and/or medically and then stopped?
- Yes, both
- Only socially
- No

(6) Did you experience body dysphoria and/or social dysphoria? (Body dysphoria = strong desire to have sex characteristics of the opposite sex/rejection of your own sex; Social dysphoria = strong desire to be seen and treated as being of a different gender)
- Yes, both
- Only body dysphoria
- Only social dysphoria
- No

(7) Who helped you starting your social/medical transition? (Tick all that apply)
- A medical team specialized in transition
- An LGBT+ organization
- A trans-specific organization
- A therapist/doctor
- Online groups/forums/social media
- Friends, partner(s) and family
- Nobody
- Other:

(8) If you transitioned medically, how long were you in therapy before getting any hormones or surgeries? (in months; write 0 if none)

(9) During your transition, did you undergo some of the following interventions/treatments? (Tick all that apply)
- Hormone blockers
- Feminizing hormone treatment
- Masculinizing hormone treatment
- Gender affirming surgery(ies)
- No

(10) Do you feel like you were properly informed about the health implications of these treatments/interventions before undergoing them?
- Yes
- Partly
- No
- I am not sure

(11) What were the reasons that made you stop transitioning/detransition? (Tick all that apply)
- Health concerns
- Change in political views
- Transition did not help with my dysphoria
- Lack of support from social surroundings
- Discrimination
- Financial concerns
- Dysphoria resolved itself over time
- Unhappy with the physical changes
- Unhappy with the social changes
- Comorbid mental health issues related to dysphoria solved
- Realized that my gender dysphoria was related to other issues
- Found alternatives to deal with dysphoria
- Other:

(12) Were you diagnosed with or do you suspect having any of the following conditions?

	Diagnosed	Suspected	No
Attention Deficit (Hyperactive) Disorder			
Autism Spectrum Condition			
Anxiety Disorders			
Depressive Disorders			
Dissociative Identity Disorder			
Eating Disorders			
Obsessive Compulsive Disorder			
Polycystic Ovary Syndrome			
Post Traumatic Stress Disorder			
Personality Disorders			
Schyzo-spectrum Disorder			

(13) If you transitioned socially, at what age did you start?
(14) If you transitioned medically, at what age did you start?
(15) At what age did you start detransitioning/stop transitioning?
(16) What are the medical needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Receiving accurate information on stopping/changing hormonal treatment
- Receiving information and access to reversal surgeries/procedures
- Receiving help for complications related to surgeries or hormonal treatment
- None
- Other:

(17) What are the psychological needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Learning to cope with gender dysphoria; finding alternatives to medical transition
- Learning to cope with the new physical and/or social changes related to detransitioning
- Learning to cope with feelings of regret
- Learning to cope with internalized homophobia
- Working on comorbid mental issues related to gender dysphoria
- None
- Other:

(18) What are the legal needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Changing back legal gender/sex marker and/or name
- Legal advice and support to take legal action over medical malpractice
- None
- Other:

(19) What are the social needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Getting in contact with other detransitioners
- Receiving support to come out and deal with negative reactions
- Hearing about other detransition stories
- None
- Other:

(20) Is there any other need that you would like to mention?

(21) Which of these needs did you get support for?

	Full support	Partly	Not at all	Not needed
Medical needs				
Psychological needs				
Legal needs				
Social needs				

(22) From whom? (Tick all that apply)
- The medical team that helped me transition
- An LGBT+ organization
- A trans specific organization
- The therapist/doctor who supported me through my transition
- A new therapist/doctor
- Online groups/forums/social media
- Friends, partner(s) and family
- Nobody
- Other:

(23) Do you feel like you have received enough support throughout your detransition process overall?
- Yes
- No
- I don't know

(24) If you have any comment concerning the support/lack of support you received during your detransition, you can write it here.

DEFENDANT'S EXHIBIT 23

Young Adult Psychological Outcome After Puberty Suppression and Gender Reassignment

WHAT'S KNOWN ON THIS SUBJECT: Puberty suppression has rapidly become part of the standard clinical management protocols for transgender adolescents. To date, there is only limited evidence for the long-term effectiveness of this approach after gender reassignment (cross-sex hormones and surgery).

WHAT THIS STUDY ADDS: In young adulthood, gender dysphoria had resolved, psychological functioning had steadily improved, and well-being was comparable to same-age peers. The clinical protocol including puberty suppression had provided these formerly gender-dysphoric youth the opportunity to develop into well-functioning young adults.

abstract

BACKGROUND: In recent years, puberty suppression by means of gonadotropin-releasing hormone analogs has become accepted in clinical management of adolescents who have gender dysphoria (GD). The current study is the first longer-term longitudinal evaluation of the effectiveness of this approach.

METHODS: A total of 55 young transgender adults (22 transwomen and 33 transmen) who had received puberty suppression during adolescence were assessed 3 times: before the start of puberty suppression (mean age, 13.6 years), when cross-sex hormones were introduced (mean age, 16.7 years), and at least 1 year after gender reassignment surgery (mean age, 20.7 years). Psychological functioning (GD, body image, global functioning, depression, anxiety, emotional and behavioral problems) and objective (social and educational/professional functioning) and subjective (quality of life, satisfaction with life and happiness) well-being were investigated.

RESULTS: After gender reassignment, in young adulthood, the GD was alleviated and psychological functioning had steadily improved. Well-being was similar to or better than same-age young adults from the general population. Improvements in psychological functioning were positively correlated with postsurgical subjective well-being.

CONCLUSIONS: A clinical protocol of a multidisciplinary team with mental health professionals, physicians, and surgeons, including puberty suppression, followed by cross-sex hormones and gender reassignment surgery, provides gender dysphoric youth who seek gender reassignment from early puberty on, the opportunity to develop into well-functioning young adults. *Pediatrics* 2014;134:696–704

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KEY WORDS

gender dysphoria, transgenderism, adolescents, psychological functioning, puberty suppression, longitudinal outcomes

ABBREVIATIONS

ABCL—Adult Behavior Checklist
ASR—Adult Self-Report
BDI—Beck Depression Inventory
BIS—Body Image Scale
CBCL—Child Behavior Checklist
CGAS—Children's Global Assessment Scale
CSH—cross-sex hormones
GD—gender dysphoria
GnRHa—gonadotropin-releasing hormone analogs
GRS—gender reassignment surgery
SHS—Subjective Happiness Scale
STAI—Spielberger's Trait Anxiety Scale
SWLS—Satisfaction With Life Scale
TPI—Spielberger's Trait Anger Scale
UGDS—Utrecht Gender Dysphoria Scale
YSR—Youth Self-Report

Dr de Vries conceptualized the study, clinically assessed the participants, drafted the initial manuscript, and reviewed and revised the manuscript; Dr McGuire conceptualized the study, planned and carried out the analyses, assisted in drafting the initial manuscript, and reviewed and revised the manuscript; Dr Steensma conceptualized the study, coordinated and supervised data collection, and reviewed and revised the manuscript; Dr Wagenaar coordinated and invited participants for assessments and reviewed and revised the manuscript; Drs Doreleijers and Cohen-Kettenis conceptualized the study and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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(Continued on last page)

Transgender adolescents experience an incongruence between their assigned gender and their experienced gender and may meet the Diagnostic and Statistical Manual of Mental Disorders 5 criteria for gender dysphoria (GD).[1] Fifteen years ago, pubertal delay was introduced as an aid in the treatment of a gender dysphoric adolescent.[2] Although not without debate, blocking pubertal development has rapidly become more widely available[3–7] and is now part of the clinical management guidelines for GD.[8–12]

Gonadotropin-releasing hormone analogs (GnRHa) are a putatively fully reversible[13] medical intervention intended to relieve distress that gender dysphoric adolescents experience when their secondary sex characteristics develop. A protocol designed by Cohen-Kettenis and Delemarre-van de Waal[14] (sometimes referred to as "the Dutch model")[4,7] considers adolescents, after a comprehensive psychological evaluation with many sessions over a longer period of time, eligible for puberty suppression, cross-sex hormones (CSH), and gender reassignment surgery (GRS) at the respective ages of 12, 16, and 18 years when there is a history of GD; no psychosocial problems interfering with assessment or treatment, for example, treatment might be postponed because of continuous moving from 1 institution to another or repeated psychiatric crises; adequate family or other support; and good comprehension of the impact of medical interventions.[12] Puberty suppression is only started after the adolescent actually enters the first stages of puberty (Tanner stages 2–3), because although in most prepubertal children GD will desist, onset of puberty serves as a critical diagnostic stage, because the likelihood that GD will persist into adulthood is much higher in adolescence than in the case of childhood GD.[15,16]

Despite the apparent usefulness of puberty suppression, there is only limited evidence available about the effectiveness of this approach. In the first cohort of adolescents who received GnRHa, we demonstrated an improvement in several domains of psychological functioning after, on average, 2 years of puberty suppression while GD remained unchanged.[16] The current study is a longer-term evaluation of the same cohort, on average, 6 years after their initial presentation at the gender identity clinic. This time, we were not only interested in psychological functioning and GD, but added as important outcome measures objective and subjective well-being (often referred to as "quality of life"), that is, the individuals' social life circumstances and their perceptions of satisfaction with life and happiness.[17–19] After all, treatment cannot be considered a success if GD resolves without young adults reporting they are healthy, content with their lives, and in a position to make a good start with their adult professional and personal lives.[20] Because various studies show that transgender youth may present with psychosocial problems,[21,22] a clinical approach that includes both medical (puberty suppression) and mental health support (regular sessions, treatment when necessary, see Cohen-Kettenis et al[12]) aims to improve long-term well-being in all respects.

In the present longitudinal study, 3 primary research questions are addressed. Do gender dysphoric youth improve over time with medical intervention consisting of GnRHa, CSH, and GRS? After gender reassignment, how satisfied are young adults with their treatment and how do they evaluate their objective and subjective well-being? Finally, do young people who report relatively greater gains in psychological functioning also report a higher subjective well-being after gender reassignment?

METHODS

Participants and Procedure

Participants included 55 young adults (22 transwomen [natal males who have a female gender identity] and 33 transmen [natal females who have a male gender identity]) of the first cohort of 70 adolescents who had GD who were prescribed puberty suppression at the Center of Expertise on Gender Dysphoria of the VU University Medical Center and continued with GRS between 2004 and 2011. These adolescents belonged to a group of 196 consecutively referred adolescents between 2000 and 2008, of whom 140 had been considered eligible for medical intervention and 111 were prescribed puberty suppression (see de Vries et al[16]). The young adults were invited between 2008 and 2012, when they were at least 1 year past their GRS (vaginoplasty for transwomen, mastectomy and hysterectomy with ovariectomy for transmen; many transmen chose not to undergo a phalloplasty or were on a long waiting list). Nonparticipation (n = 15, 11 transwomen and 4 transmen) was attributable to not being 1 year postsurgical yet (n = 6), refusal (n = 2), failure to return questionnaires (n = 2), being medically not eligible (eg, uncontrolled diabetes, morbid obesity) for surgery (n = 3), dropping out of care (n = 1), and 1 transfemale died after her vaginoplasty owing to a postsurgical necrotizing fasciitis. Between the 55 participants and the 15 nonparticipating individuals, Student's t tests revealed no significant differences on any of the pretreatment variables. A similar lack of differences was found between the 40 participants who had complete data and the 15 who were missing some data.

Participants were assessed 3 times: pre-treatment (T0, at intake), during treatment (T1, at initiation of CSH), and post-treatment (T2, 1 year after GRS). See Table 1 for age at the different time points. The VU University Medical Center medical ethics committee approved the study, and all participants gave informed consent.

TABLE 1 Age at Different Treatment Milestones and Intelligence by Gender

Variable	All Participants[a] ($N = 55$)		Transwomen (Natal Males) ($N = 22$)	Transmen (Natal Females) ($N = 33$)
Age, y	Mean (SD)	Range	Mean (SD)	Mean (SD)
At assessment PreT	13.6 (1.9)	11.1–17.0	13.6 (1.8)	13.7 (2.0)
At start of GnRHa	14.8 (1.8)	11.5–18.5	14.8 (2.0)	14.9 (1.9)
At start of CSH	16.7 (1.1)	13.9–19.0	16.5 (1.3)	16.8 (1.0)
At GRS	19.2 (0.9)	18.0–21.3	19.6 (0.9)	19.0 (0.8)
At assessment PostT	20.7 (1.0)	19.5–22.8	21.0 (1.1)	20.5 (0.8)
Full-scale intelligence[b]	99.0 (14.3)	70–128	97.8 (14.2)	100.4 (14.3)

PostT, post-treatment; PreT, pre-treatment.

[a] Comparisons between those who had complete data ($n = 40$) and those who had missing data on the CBCL/ABCL ($n = 15$) reveal no significant differences between the groups in age at any point in the study or in natal sex.

[b] WISC-R, the WISC-III, or the WAIS-III at first assessment, depending on age and time.[45–47]

Measures

Time was the predominate independent variable. Other demographic characteristics were incorporated in some models, including, age, natal sex, Full Scale Intelligence, and parent marital status; where significantly different they are reported.

Gender Dysphoria/Body Image

There was 1 indicator measuring GD (Utrecht Gender Dysphoria Scale [UGDS]) and 3 indicators measuring body image (Body Image Scale [BIS] with primary, secondary, and neutral subscales). Higher UGDS (12 items, 1–5 range, total score ranging from 12–60) total scores indicate higher levels of GD, for example, "I feel a continuous desire to be treated as a man/woman."[23] There are separate versions of the UGDS for males and females with mostly different items, permitting no gender difference analyses. BIS (30 items, 1–5 range) higher scores indicate more dissatisfaction with primary sex characteristics (important gender-defining body characteristics, eg, genitals, breasts), secondary sex characteristics (less obvious gender-defining features, eg, hips, body hair), and neutral (hormonally unresponsive) body characteristics (eg, face, height).[24] The male and the female BIS are identical except for the sexual body parts. The UGDS and the BIS of the natal gender were administered at T0 and T1. At T1, we chose the UGDS of the assigned gender, because no physical changes had occurred yet and some were still treated as their assigned gender. This way, however, decreased GD caused by social transitioning was not measured. At T2 young adults filled out the versions of their affirmed gender.

Psychological Functioning

There were 10 indicators assessing psychological functioning. To assess global functioning, the Children's Global Assessment Scale (CGAS) was used.[25] The Beck Depression Inventory (BDI; 21 items, 0–3 range) indicates presence and severity of depressive symptoms.[26] Spielberger's Trait Anger (TPI) and Spielberger's Trait Anxiety (STAI; 10 and 20 items, respectively, 1–4 range) scales of the State-Trait Personality Inventory were administered to assess the tendency to respond with anxiety or anger, respectively, to a threatening or annoying situation.[27,28]

Behavioral and emotional problems were assessed by the total, internalizing, and externalizing T scores as well as clinical range scores for these 3 indices (T score >63) of the Child/Adult Behavior Checklist (CBCL at T0 and T1, ABCL at T2), the Youth/Adult Self-Report (YSR at T0 and T1, ASR at T2).[29–31] Items referring to GD in the CBCL/YSR and ABCL/ASR were scored as 0 (for more explanation, see Cohen-Kettenis et al[32]).

Objective and Subjective Well-Being (T2 Only)

A self-constructed questionnaire was used to ask the young adults about their current life circumstances, such as living conditions, school and employment, and social support (objective well-being), and satisfaction with treatment (subjective well-being). Three instruments further assessed subjective well-being. To measure quality of life, the WHOQOL-BREF (quality of life measure developed by the World Health Organization) was administered (24 items, 4 domains: Physical Health, Psychological Health, Social Relationships, and Environment, 1–5 range with higher scores indicating better quality of life).[17] The Satisfaction With Life Scale (SWLS, 5 items, 5–35 range, 20 being neutral) was used to assess life satisfaction.[18] Higher scores on the Subjective Happiness Scale (SHS, 4 items, 7-point Likert scale, average score 1–7) reflect greater happiness.[19]

Data Analyses

General Linear Models examined the repeated measures with an analysis of variance-based model, incorporating continuous and categorical predictors, and correcting for the unbalanced cell sizes. Linear and quadratic effects of the 14 indicators across 3 time points, with time as the within-subjects factor, and sex as a between-subjects factor in a second set of analyses are reported in Tables 2 and 3 and Fig 1. A linear effect signifies an overall change across T0 to T2. A quadratic effect signifies that the change was not continuous, such as when an indicator does not improve from T0 to T1 but improves from T1 to T2. It is possible to have both a significant linear and quadratic effect on the same

TABLE 2 Gender Dysphoria and Body Image of Adolescents at Intake (T0), While on Puberty Suppression (T1), and After Gender Reassignment (T2)

	N[a]	T0	T1	T2	T0–T2	Time	Time × Sex
					t test	Linear Effect Quadratic Effect	Linear Effect Quadratic Effect
		Mean (SD)	Mean (SD)	Mean (SD)	*P*	*P*	*P*
UGDS	33	53.51 (8.29)	54.39 (7.70)	15.81 (2.78)	<.001		
MtF	11	47.07 (11.05)	48.95 (10.80)	17.27 (2.57)	<.001	<.001 <.001	n/a
FtM	22	56.74 (3.74)	57.11 (3.40)	15.08 (2.64)	<.001	<.001 <.001	n/a
Body Image (BIS)							
Primary sex characteristics	45	4.13 (0.59)	4.05 (0.60)	2.59 (0.82)	<.001	<.001 <.001	.01 .45
MtF	17	4.03 (0.68)	3.82 (0.56)	2.07 (0.74)	<.001		
FtM	28	4.18 (0.53)	4.13 (0.60)	2.89 (0.71)	<.001		
Secondary sex characteristics	45	2.73 (0.72)	2.86 (0.67)	2.27 (0.56)	<.001	<.001 <.001	.10 <.001
MtF	17	2.63 (0.60)	2.34 (0.68)	1.93 (0.63)	<.001		
FtM	28	2.80 (0.72)	3.18 (0.43)	2.48 (0.40)	.05		
Neutral body characteristics	45	2.35 (0.68)	2.49 (0.53)	2.23 (0.49)	.29	.29 .01	.007 .01
MtF	17	2.57 (0.70)	2.29 (0.50)	2.09 (0.56)	.014		
FtM	28	2.21 (0.64)	2.61 (0.52)	2.32 (0.44)	.40		

FtM, female to male transgender; MtF, male to female transgender; n/a, not applicable.

[a] Participants who had complete data at all 3 waves were included. Some assessments were added to the study later, yielding fewer total participants for those scales.

indicator. Other potential between-subjects factors (age, total IQ, parental marital status) were examined but excluded owing to a lack of relationship with the 14 indicators at T0. The 1 exception, age predicting secondary sex characteristics, is described below in the findings. We compared T2 sample means to population norms for subjective well-being using 1-sample *t* tests from previously published validation studies. Finally, we examined T2 subjective well-being correlations with residual change scores from T0 to T2 on the 14 indicators (an indicator of who improved relatively more or less over time).

All measures used were self-reported, except the CGAS (attending clinician) and the CBCL/ASR (parents). Each participant was given all measures at each of 3 assessments. Numbers varied across indicators owing to the later inclusion of the YSR, CGAS, BDI, TPI, and STAI, yielding 8 persons who had missing data at T0 and a clinician error yielding missing data at T1 for 10 participants on the UGDS. Dutch versions were used (see de Vries et al[16]).

RESULTS

Gender Dysphoria and Body Satisfaction

Figure 1 and Table 2 show that GD and body image difficulties persisted through puberty suppression (at T0 and T1) and remitted after the administration of CSH and GRS (at T2) (significant linear effects in 3 of 4 indicators, and significant quadratic effects in all indicators). Time by sex interactions revealed that transwomen reported more satisfaction over time with primary sex characteristics than transmen and a continuous improvement in satisfaction with secondary and neutral sex characteristics. Transmen reported more dissatisfaction with secondary and neutral sex characteristics at T1 than T0, but improvement in both from T1 to T2. Age was a significant covariate with secondary sex characteristics (the only significant demographic covariate with any outcome indicator in the study), indicating that older individuals were more dissatisfied at T0, but the age gap in body satisfaction narrowed over time ($F(1, 42) = 8.18$; $P < .01$).

Psychological Functioning

As presented in Table 3, significant linear effects showed improvement over time in global functioning (CGAS), CBCL/ABCL total, internalizing and externalizing *T* scores, and YSR/ASR total and internalizing *T* scores. Quadratic effects revealed decreases from T0 to T1 followed by increases from T1 to T2 in depression and YSR/ASR internalizing *T* scores. Quadratic trends revealed decreases from T0 to T1, followed by increases from T1 to T2 in depression and YSR/ASR internalizing *T* scores. For all CBCL/ABCL and YSR/ASR indicators except YSR/ASR externalizing, the percentage in the clinical range dropped significantly (McNemar's test, *P* value <0.05) from T0 to T1, from T0 to T2, or from T1 to T2.

Over time, transmen showed reduced anger, anxiety, and CBCL/ABCL externalizing *T* scores, whereas transwomen showed stable or slightly more symptomatology on these measures. Transwomen improved in CBCL/ABCL total *T* scores in a quadratic fashion (all the improvement between T1 and T2),

TABLE 3 Psychological Functioning of Adolescents at Intake (T0), While on Puberty Suppression (T1), and After Gender Reassignment (T2)

	N[a]	T0	T1	T2	T0–T2	Time	Time × Sex
					t test	Linear Effect Quadratic Effect	Linear Effect Quadratic Effect
		Mean (SD)	Mean (SD)	Mean (SD)	*P*	*P*	*P*
Global functioning (CGAS)	32	71.13 (10.46)	74.81 (9.86)	79.94 (11.56)	<.001	<.001	.89
						.61	.68
MtF	15	74.33 (7.53)	78.20 (9.56)	82.40 (8.28)	<.001		
FtM	17	67.65 (11.87)	70.65 (9.89)	76.29 (14.48)	.02		
Depression (BDI)	32	7.89 (7.52)	4.10 (6.17)	5.44 (8.40)	.21	.23	.66
						.04	.49
MtF	12	4.73 (4.20)	2.25 (3.54)	3.38 (4.40)	.12		
FtM	20	10.09 (8.34)	5.05 (7.08)	6.95 (9.83)	.32		
Anger (TPI)	32	17.55 (5.72)	17.22 (5.61)	16.01 (5.28)	.20	.15	.04
						.52	.12
MtF	12	14.17 (3.01)	14.00 (3.36)	5.58 (3.92)	.18		
FtM	20	19.55 (5.96)	19.25 (5.69)	16.56 (6.06)	.05		
Anxiety (STAI)	32	39.57 (10.53)	37.52 (9.87)	37.61 (10.39)	.45	.42	.05
						.47	.52
MtF	12	31.87 (7.42)	31.71 (8.36)	35.83 (10.22)	.14		
FtM	20	44.41 (9.06)	41.59 (9.03)	39.20 (10.53)	.12		
CBCL–ABCL							
Total *T* score	40	60.20 (12.66)	54.70 (11.58)	48.10 (9.30)	<.001	<.001	.25
% Clinical		38_x	20_y	5_y		.68	.03
MtF	15	57.40 (12.76)	49.67 (12.29)	48.13 (12.58)	.002		
FtM	25	61.88 (12.56)	57.72 (10.23)	48.08 (6.95)	<.001		
Int *T* score	40	60.83 (12.36)	54.42 (10.58)	50.45 (10.04)	<.001	<.001	.91
% Clinical		30_x	12.5_y	10_y		.42	.33
MtF	15	59.40 (10.03)	50.93 (11.15)	48.73 (12.61)	<.001		
FtM	25	61.68 (13.70)	56.52 (9.86)	51.48 (8.25)	<.001		
Ext *T* score	40	57.85 (13.73)	53.85 (12.77)	47.85 (8.59)	<.001	<.001	.19
% Clinical		40_x	25_x	2.5_y		.43	.12
MtF	15	52.53 (14.11)	47.87 (12.07)	46.33 (10.95)	.10		
FtM	25	61.04 (12.71)	57.44 (12.01)	48.76 (6.89)	<.001		
YSR-ASR							
Total *T* score	43	54.72 (12.08)	49.16 (11.16)	48.53 (9.46)	.005	.005	.28
% Clinical		30_x	14_{xy}	7_y		.07	.75
MtF	17	50.65 (12.19)	45.94 (12.24)	47.24 (12.28)	.28		
FtM	26	57.38 (11.47)	51.27 (10.08)	49.38 (7.21)	.01		
Int *T* score	43	55.47 (13.08)	48.65 (12.33)	50.07 (11.15)	.03	.03	.87
% Clinical		30_x	9.3_y	11.6_{xy}		.008	.73
MtF	17	54.00 (12.31)	47.59 (14.26)	48.12 (12.54)	.04		
FtM	26	56.42 (13.86)	49.35 (11.13)	51.35 (10.19)	.17		
Ext *T* score	43	52.77 (12.47)	49.44 (9.59)	49.44 (9.37)	.14	.14	.005
% Clinical		21_x	11.6_x	7_x		.09	.14
MtF	17	46.00 (11.58)	44.71 (9.53)	50.24 (11.18)	.17		
FtM	26	57.16 (11.14)	52.54 (8.43)	48.92 (8.18)	.006		

FtM, female to male transgender; MtF, male to female transgender.

$_{xy}$ Percent clinical range, shared subscripts indicate no significant difference in values. In no case was an increase in percent in the clinical range significant from 1 time point to any other time point, indicating an overall decline or stability of clinical symptoms over time.

[a] Participants who had complete data at all 3 waves were included. Some assessments were added to the study later, yielding fewer total participants for those scales.

whereas transmen improved steadily across the 3 time points (linear effect only).

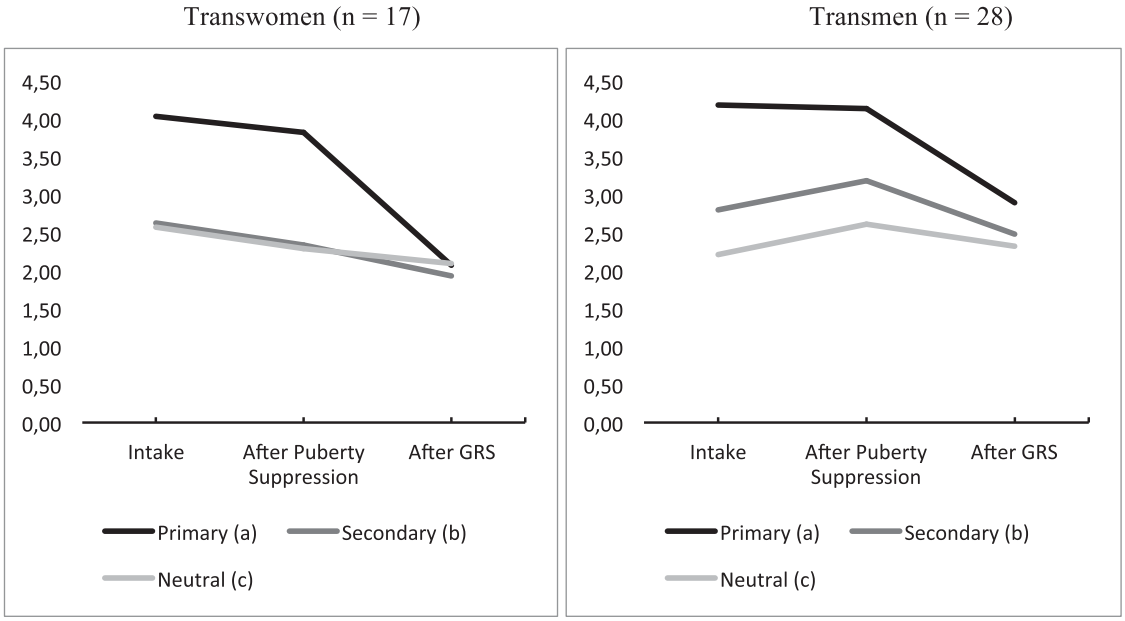
Objective Well-Being

At T2, the participants were vocationally similar to the Dutch population except they were slightly more likely to live with parents (67% vs 63%), and more likely, when studying, to be pursuing higher education (58% vs 31%).[33]

Families were supportive of the transitioning process: 95% of mothers, 80% of fathers, and 87% of siblings. Most (79%) young adults reported having 3 or more friends, were satisfied with their male (82%) and female peers (88%), and almost all (95%) had received support from friends regarding their gender reassignment. After their GRS, many participants (89%) reported having been never or seldom called names or harassed. The majority (71%) had experienced social transitioning as easy.

Subjective Well-Being

None of the participants reported regret during puberty suppression, CSH



Eta Squared for Linear and Quadratic Effects

(a) Primary sex characteristics
Time: .79 ($P < .001$), .66 ($P < .001$),
Time × sex: .14 ($P = .01$), .01 ($P = .45$),

(b) Secondary sex characteristics
Time: .31($P < .001$), .30 ($P < .001$),
Time × sex: .06 ($P = .10$), .22 ($P < .001$)

(c) Neutral body characteristics
Time: .07($P < .001$), .09 ($P = .29$)
Time × sex: .16 ($P = .007$), .15 ($P = .01$)

FIGURE 1
BIS[23] for transwomen and transmen at T0 (pretreatment, at intake), T1 (during treatment, at initiation of cross-gender hormones), and T2 (post-treatment, 1 year after GRS).

treatment, or after GRS. Satisfaction with appearance in the new gender was high, and at T2 no one reported being treated by others as someone of their assigned gender. All young adults reported they were very or fairly satisfied with their surgeries.

Mean scores on WHOQOL-BREF, the SWLS, and the SHS are presented in Table 4, together with scores from large validation and reliability studies of these measures,[17,19,34] revealing similar scores in all areas except WHOQOL-Environment subdomain, which was higher for the participants than the norm. There were some differences across gender; transwomen scored higher than transmen on the SWLS (mean = 27.7; SD = 5.0 vs mean = 23.2; SD = 6.0; t (52) = 2.82; $P < .01$) and on the psychological subdomain of the WHOQOL (mean = 15.77; SD = 2.0 vs mean = 13.92; SD = 2.5; t (53) = 2.95; $P < .01$).

Correlations With Residual Change Scores

The residual change scores of secondary sex characteristics, global functioning, depression, anger, anxiety, and YSR total, internalizing and externalizing from T0 to T2, were significantly correlated with the 6 T2 quality of life indicators. Most correlation coefficients were within the moderate to large magnitude (eg, 0.30–0.60), except depression, which was highly correlated (0.60–0.80) (see Table 5).

DISCUSSION

Results of this first long-term evaluation of puberty suppression among transgender adolescents after CSH treatment and GRS indicate that not only was GD resolved, but well-being was in many respects comparable to peers.

The effectiveness of CSH and GRS for the treatment of GD in adolescents is in line with findings in adult transsexuals.[35,36] Whereas some studies show that poor surgical results are a determinant of postoperative psychopathology and of dissatisfaction and regret,[37,38] all young adults in this study were generally satisfied with their physical appearance and none regretted treatment. Puberty suppression had caused their bodies to

TABLE 4 Subjective Well-Being: Quality of Life, Satisfaction With Life, and Subjective Happiness Mean Scores With Scores From Validation Studies

	N	Mean (SD)	Range	Validation Studies Scores Mean (SD)	Comparison *P*
WHOQOL[a] Physical	55	15.22 (2.49)	8.6–20.0	15.0 (2.9)[b]	.56
WHOQOL Psychological	55	14.66 (2.44)	6.67–20.0	14.3 (2.8)[b]	.24
WHOQOL Social Relations	55	14.91 (2.35)	9.3–20.00	14.5 (3.4)[b]	.18
WHOQOL Environment	55	15.47 (2.06)	10.5–20.00	13.7 (2.6)[b]	<.001
SWLS	54	24.98 (6.0)	9.0–35.0	26.18 (5.7)[c]	.16
SHS	54	4.73 (0.77)	2.75–6.0	4.89 (1.1)[d]	.17

[a] WHOQOL, Bref, Skevington et al.[16]
[b] International field trial, ages 21 to 30 years, Skevington et al.[16]
[c] Dutch young adults, Arindell et al.[33]
[d] US Public College Students, Lyubomirsky.[18]

not (further) develop contrary to their experienced gender.

Psychological functioning improved steadily over time, resulting in rates of clinical problems that are indistinguishable from general population samples (eg, percent in the clinical range dropped from 30% to 7% on the YSR/ASR[30]) and quality of life, satisfaction with life, and subjective happiness comparable to same-age peers.[17,19,34] Apparently the clinical protocol of a multidisciplinary team with mental health professionals, physicians, and surgeons gave these formerly gender dysphoric youth the opportunity to develop into well-functioning young adults. These individuals, of whom an even higher percentage than the general population were pursuing higher education, seem different from the transgender youth in community samples with high rates of mental health disorders, suicidality and self-harming behavior, and poor access to health services.[21,22,39,40]

In this study, young adults who experienced relatively greater improvements in psychological functioning were more likely to also report higher levels of subjective postsurgical well-being. This finding suggests value to the protocol that involves monitoring the adolescents' functioning, physically and psychologically, over many years, and providing more support whenever necessary.

This clinic-referred sample perceived the Environmental subdomain (with items like "access to health and social care" and "physical safety and security") of the WHOQOL-BREF as even better than the Dutch standardization sample.[17] Whereas in some other contexts transgender youth may experience gender-related abuse and victimization,[22,41,42] the positive results may also be attributable to supportive parents, open-minded peers, and the social and financial support (treatment is covered by health insurance) that gender dysphoric individuals can receive in the Netherlands.

Both genders benefitted from the clinical approach, although transwomen showed more improvement in body image satisfaction (secondary sex characteristics) and in psychological functioning (anger and anxiety). None of the transmen in this study had yet had a phalloplasty because of waiting lists or

TABLE 5 Correlations Between Residual Change in Psychological Functioning Over Time and Young Adult Subjective Well-Being

	WHOQOL BREF					
	Physical	Psychological	Social	Environment	SWLS	SHS
Gender dysphoria (UGDS)	0.01 (.97)	0.05 (.75)	−0.09 (.57)	−0.02 (.89)	0.06 (.71)	0.30 (.04)
Body image subscales (BIS)						
Primary sex characteristics	−0.22 (.14)	−0.25 (.09)	−0.35 (.02)	−0.04 (.78)	−0.22 (.14)	−0.21 (.17)
Secondary sex characteristics	−0.39 (.006)	−0.45 (<.001)	−0.47 (<.001)	−0.34 (.02)	−0.35 (.02)	−0.26 (.08)
Neutral body characteristics	−0.21 (.16)	−0.27 (.07)	−0.15 (.32)	−0.28 (.06)	−0.26 (.08)	−0.16 (.28)
Psychological functioning						
Global functioning (CGAS)	0.60 (<.001)	0.52 (.002)	0.52 (.002)	0.27 (.14)	0.58 (<.001)	0.50 (.004)
Depression (BDI)	−0.76 (<.001)	−0.72 (<.001)	−0.51 (.002)	−0.49 (.003)	−0.61 (<.001)	−0.77 (<.001)
Trait anger (TPI)	−0.37 (.03)	−0.18 (.31)	−0.22 (.20)	−0.29 (.09)	−0.33 (.07)	−0.35 (.05)
Trait anxiety (STAI)	−0.58 (<.001)	−0.64 (<.001)	−0.38 (.03)	−0.44 (.01)	−0.49 (.004)	−0.57 (<.001)
CBCL–ABCL						
Total *T* score	−0.20 (.20)	−0.12 (.45)	−0.07 (.65)	−0.14 (.35)	−0.32 (.03)	−0.16 (.29)
Internalizing *T* score	−0.29 (.06)	−0.29 (.06)	−0.23 (.14)	−0.12 (.44)	−0.48 (<.001)	−0.36 (.02)
Externalizing *T* score	−0.13 (.40)	−0.05 (.75)	0.16 (.29)	−0.20 (.19)	−0.15 (.36)	0.00 (.99)
Youth Self Report (YSR–ASR)						
Total *T* score	−0.53 (<.001)	−0.45 (.002)	−0.33 (.03)	−0.42 (.005)	−0.52 (<.001)	−0.55 (<.001)
Internalizing *T* score	−0.62 (<.001)	−0.61 (<.001)	−0.47 (<.001)	−0.40 (.007)	−0.66 (<.001)	−0.60 (<.001)
Externalizing *T* score	−0.23 (.13)	−0.10 (.53)	−0.07 (.67)	−0.37 (.02)	−0.22 (.15)	−0.35 (.02)

P values are in parentheses.

a desire for improved surgery techniques. This finding warrants further study of the specific concerns of young transmen.

Despite promising findings, there were various limitations. First, the study sample was small and came from only 1 clinic. Second, this study did not focus on physical side effects of treatment. Publications on physical parameters of the same cohort of adolescents are submitted or in preparation. A concurring finding exists in the 22-year follow-up of the well-functioning first case now at age 35 years who has no clinical signs of a negative impact of earlier puberty suppression on brain development, metabolic and endocrine parameters, or bone mineral density.[43] Third, despite the absence of pretreatment differences on measured indicators, a selection bias could exist between adolescents of the original cohort that participated in this study compared with nonparticipants.

Age criteria for puberty suppression and CSH are under debate, although they worked well for adolescents in the current study. Especially in natal females, puberty will often start before the age of 12 years. Despite the fact that developing evidence suggests that cognitive and affective cross-gender identification, social role transition, and age at assessment are related to persistence of childhood GD into adolescence, predicting individual persistence at a young age will always remain difficult.[44] The age criterion of 16 years for the start of CSH may be problematic especially for transwomen, as growth in height continues as long as cross-sex steroids are not provided (causing the growth plates to close). Therefore, psychological maturity and the capacity to give full informed consent may surface as the required criteria for puberty suppression and CSH[45] in cases that meet other eligibility criteria.

CONCLUSIONS

Results of this study provide first evidence that, after CSH and GRS, a treatment protocol including puberty suppression leads to improved psychological functioning of transgender adolescents. While enabling them to make important age-appropriate developmental transitions, it contributes to a satisfactory objective and subjective well-being in young adulthood. Clinicians should realize that it is not only early medical intervention that determines this success, but also a comprehensive multidisciplinary approach that attends to the adolescents' GD as well as their further well-being and a supportive environment.

ACKNOWLEDGMENTS

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Young Adult Psychological Outcome After Puberty Suppression and Gender Reassignment

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DEFENDANT'S EXHIBIT 24

POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents

Jason Rafferty, MD, MPH, EdM, FAAP, COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, COMMITTEE ON ADOLESCENCE, SECTION ON LESBIAN, GAY, BISEXUAL, AND TRANSGENDER HEALTH AND WELLNESS

As a traditionally underserved population that faces numerous health disparities, youth who identify as transgender and gender diverse (TGD) and their families are increasingly presenting to pediatric providers for education, care, and referrals. The need for more formal training, standardized treatment, and research on safety and medical outcomes often leaves providers feeling ill equipped to support and care for patients that identify as TGD and families. In this policy statement, we review relevant concepts and challenges and provide suggestions for pediatric providers that are focused on promoting the health and positive development of youth that identify as TGD while eliminating discrimination and stigma.

INTRODUCTION

In its dedication to the health of all children, the American Academy of Pediatrics (AAP) strives to improve health care access and eliminate disparities for children and teenagers who identify as lesbian, gay, bisexual, transgender, or questioning (LGBTQ) of their sexual or gender identity.[1,2] Despite some advances in public awareness and legal protections, youth who identify as LGBTQ continue to face disparities that stem from multiple sources, including inequitable laws and policies, societal discrimination, and a lack of access to quality health care, including mental health care. Such challenges are often more intense for youth who do not conform to social expectations and norms regarding gender. Pediatric providers are increasingly encountering such youth and their families, who seek medical advice and interventions, yet they may lack the formal training to care for youth that identify as transgender and gender diverse (TGD) and their families.[3]

This policy statement is focused specifically on children and youth that identify as TGD rather than the larger LGBTQ population, providing brief, relevant background on the basis of current available research

abstract

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Dr Rafferty conceptualized the statement, drafted the initial manuscript, reviewed and revised the manuscript, approved the final manuscript as submitted, and agrees to be accountable for all aspects of the work.

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TABLE 1 Relevant Terms and Definitions Related to Gender Care

Term	Definition
Sex	An assignment that is made at birth, usually male or female, typically on the basis of external genital anatomy but sometimes on the basis of internal gonads, chromosomes, or hormone levels
Gender identity	A person's deep internal sense of being female, male, a combination of both, somewhere in between, or neither, resulting from a multifaceted interaction of biological traits, environmental factors, self-understanding, and cultural expectations
Gender expression	The external way a person expresses their gender, such as with clothing, hair, mannerisms, activities, or social roles
Gender perception	The way others interpret a person's gender expression
Gender diverse	A term that is used to describe people with gender behaviors, appearances, or identities that are incongruent with those culturally assigned to their birth sex; gender-diverse individuals may refer to themselves with many different terms, such as transgender, nonbinary, genderqueer,[7] gender fluid, gender creative, gender independent, or noncisgender. "Gender diverse" is used to acknowledge and include the vast diversity of gender identities that exists. It replaces the former term, "gender nonconforming," which has a negative and exclusionary connotation.
Transgender	A subset of gender-diverse youth whose gender identity does not match their assigned sex and generally remains persistent, consistent, and insistent over time; the term "transgender" also encompasses many other labels individuals may use to refer to themselves.
Cisgender	A term that is used to describe a person who identifies and expresses a gender that is consistent with the culturally defined norms of the sex they were assigned at birth
Agender	A term that is used to describe a person who does not identify as having a particular gender
Affirmed gender	When a person's true gender identity, or concern about their gender identity, is communicated to and validated from others as authentic
MTF; affirmed female; trans female	Terms that are used to describe individuals who were assigned male sex at birth but who have a gender identity and/or expression that is asserted to be more feminine
FTM; affirmed male; trans male	Terms that are used to describe individuals who were assigned female sex at birth but who have a gender identity and/or expression that is asserted to be more masculine
Gender dysphoria	A clinical symptom that is characterized by a sense of alienation to some or all of the physical characteristics or social roles of one's assigned gender; also, gender dysphoria is the psychiatric diagnosis in the *DSM-5*, which has focus on the distress that stems from the incongruence between one's expressed or experienced (affirmed) gender and the gender assigned at birth.
Gender identity disorder	A psychiatric diagnosis defined previously in the *DSM-IV* (changed to "gender dysphoria" in the *DSM-5*); the primary criteria include a strong, persistent cross-sex identification and significant distress and social impairment. This diagnosis is no longer appropriate for use and may lead to stigma, but the term may be found in older research.
Sexual orientation	A person's sexual identity in relation to the gender(s) to which they are attracted; sexual orientation and gender identity develop separately.

This list is not intended to be all inclusive. The pronouns "they" and "their" are used intentionally to be inclusive rather than the binary pronouns "he" and "she" and "his" and "her." Adapted from Bonifacio HJ, Rosenthal SM. Gender variance and dysphoria in children and adolescents. *Pediatr Clin North Am*. 2015;62(4):1001–1016. Adapted from Vance SR Jr, Ehrensaft D, Rosenthal SM. Psychological and medical care of gender nonconforming youth. *Pediatrics*. 2014;134(6):1184–1192. DSM-5, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*; FTM, female to male; MTF, male to female.

and expert opinion from clinical and research leaders, which will serve as the basis for recommendations. It is not a comprehensive review of clinical approaches and nuances to pediatric care for children and youth that identify as TGD. Professional understanding of youth that identify as TGD is a rapidly evolving clinical field in which research on appropriate clinical management is limited by insufficient funding.[3,4]

DEFINITIONS

To clarify recommendations and discussions in this policy statement, some definitions are provided. However, brief descriptions of human behavior or identities may not capture nuance in this evolving field. "Sex," or "natal gender," is a label, generally "male" or "female," that is typically assigned at birth on the basis of genetic and anatomic characteristics, such as genital anatomy, chromosomes, and sex hormone levels. Meanwhile, "gender identity" is one's internal sense of who one is, which results from a multifaceted interaction of biological traits, developmental influences, and environmental conditions. It may be male, female, somewhere in between, a combination of both, or neither (ie, not conforming to a binary conceptualization of gender). Self-recognition of gender identity develops over time, much the same way as a child's physical body does. For some people, gender identity can be fluid, shifting in different contexts. "Gender expression" refers to the wide array of ways people display their gender through clothing, hair styles, mannerisms, or social roles. Exploring different ways of expressing gender is common for children and may challenge social expectations. The way others interpret this expression is referred to as "gender perception" (Table 1).[5,6]

These labels may or may not be congruent. The term "cisgender" is used if someone identifies and expresses a gender that is consistent with the culturally defined norms of the sex that was assigned at birth. "Gender diverse" is an umbrella term to describe an ever-evolving array of labels that people may apply when their gender identity, expression, or even perception does not conform

to the norms and stereotypes others expect of their assigned sex. "Transgender" is usually reserved for a subset of such youth whose gender identity does not match their assigned sex and generally remains persistent, consistent, and insistent over time. These terms are not diagnoses; rather, they are personal and often dynamic ways of describing one's own gender experience.

Gender identity is not synonymous with "sexual orientation," which refers to a person's identity in relation to the gender(s) to which they are sexually and romantically attracted. Gender identity and sexual orientation are distinct but interrelated constructs.[8] Therefore, being transgender does not imply a sexual orientation, and people who identify as transgender still identify as straight, gay, bisexual, etc, on the basis of their attractions. (For more information, *The Gender Book*, found at www.thegenderbook.com, is a resource with illustrations that are used to highlight these core terms and concepts.)

EPIDEMIOLOGY

In population-based surveys, questions related to gender identity are rarely asked, which makes it difficult to assess the size and characteristics of the population that is TGD. In the 2014 Behavioral Risk Factor Surveillance System of the Centers for Disease Control and Prevention, only 19 states elected to include optional questions on gender identity. Extrapolation from these data suggests that the US prevalence of adults who identify as transgender or "gender nonconforming" is 0.6% (1.4 million), ranging from 0.3% in North Dakota to 0.8% in Hawaii.[9] On the basis of these data, it has been estimated that 0.7% of youth ages 13 to 17 years (~150 000) identify as transgender.[10] This number is much higher than previous estimates, which were extrapolated from individual states or specialty clinics, and is likely an underestimate given the stigma regarding those who openly identify as transgender and the difficulty in defining "transgender" in a way that is inclusive of all gender-diverse identities.[11]

There have been no large-scale prevalence studies among children and adolescents, and there is no evidence that adult statistics reflect young children or adolescents. In the 2014 Behavioral Risk Factor Surveillance System, those 18 to 24 years of age were more likely than older age groups to identify as transgender (0.7%).[9] Children report being aware of gender incongruence at young ages. Children who later identify as TGD report first having recognized their gender as "different" at an average age of 8.5 years; however, they did not disclose such feelings until an average of 10 years later.[12]

MENTAL HEALTH IMPLICATIONS

Adolescents and adults who identify as transgender have high rates of depression, anxiety, eating disorders, self-harm, and suicide.[13–20] Evidence suggests that an identity of TGD has an increased prevalence among individuals with autism spectrum disorder, but this association is not yet well understood.[21,22] In 1 retrospective cohort study, 56% of youth who identified as transgender reported previous suicidal ideation, and 31% reported a previous suicide attempt, compared with 20% and 11% among matched youth who identified as cisgender, respectively.[13] Some youth who identify as TGD also experience gender dysphoria, which is a specific diagnosis given to those who experience impairment in peer and/or family relationships, school performance, or other aspects of their life as a consequence of the incongruence between their assigned sex and their gender identity.[23]

There is no evidence that risk for mental illness is inherently attributable to one's identity of TGD. Rather, it is believed to be multifactorial, stemming from an internal conflict between one's appearance and identity, limited availability of mental health services, low access to health care providers with expertise in caring for youth who identify as TGD, discrimination, stigma, and social rejection.[24] This was affirmed by the American Psychological Association in 2008[25] (with practice guidelines released in 2015[8]) and the American Psychiatric Association, which made the following statement in 2012:

> *Being transgender or gender variant implies no impairment in judgment, stability, reliability, or general social or vocational capabilities; however, these individuals often experience discrimination due to a lack of civil rights protections for their gender identity or expression.… [Such] discrimination and lack of equal civil rights is damaging to the mental health of transgender and gender variant individuals.*[26]

Youth who identify as TGD often confront stigma and discrimination, which contribute to feelings of rejection and isolation that can adversely affect physical and emotional well-being. For example, many youth believe that they must hide their gender identity and expression to avoid bullying, harassment, or victimization. Youth who identify as TGD experience disproportionately high rates of homelessness, physical violence (at home and in the community), substance abuse, and high-risk sexual behaviors.[5,6,12,27–31] Among the 3 million HIV testing events that were reported in 2015, the highest percentages of new infections were among women who identified as transgender[32] and were also at particular risk for not knowing their HIV status.[30]

GENDER-AFFIRMATIVE CARE

In a gender-affirmative care model (GACM), pediatric providers offer developmentally appropriate care that is oriented toward understanding and appreciating the youth's gender experience. A strong, nonjudgmental partnership with youth and their families can facilitate exploration of complicated emotions and gender-diverse expressions while allowing questions and concerns to be raised in a supportive environment.[5] In a GACM, the following messages are conveyed:

- transgender identities and diverse gender expressions do not constitute a mental disorder;
- variations in gender identity and expression are normal aspects of human diversity, and binary definitions of gender do not always reflect emerging gender identities;
- gender identity evolves as an interplay of biology, development, socialization, and culture; and
- if a mental health issue exists, it most often stems from stigma and negative experiences rather than being intrinsic to the child.[27,33]

The GACM is best facilitated through the integration of medical, mental health, and social services, including specific resources and supports for parents and families.[24] Providers work together to destigmatize gender variance, promote the child's self-worth, facilitate access to care, educate families, and advocate for safer community spaces where children are free to develop and explore their gender.[5] A specialized gender-affirmative therapist, when available, may be an asset in helping children and their families build skills for dealing with gender-based stigma, address symptoms of anxiety or depression, and reinforce the child's overall resiliency.[34,35] There is a limited but growing body of evidence that suggests that using an integrated affirmative model results in young people having fewer mental health concerns whether they ultimately identify as transgender.[24,36,37]

In contrast, "conversion" or "reparative" treatment models are used to prevent children and adolescents from identifying as transgender or to dissuade them from exhibiting gender-diverse expressions. The Substance Abuse and Mental Health Services Administration has concluded that any therapeutic intervention with the goal of changing a youth's gender expression or identity is inappropriate.[33] Reparative approaches have been proven to be not only unsuccessful[38] but also deleterious and are considered outside the mainstream of traditional medical practice.[29,39–42] The AAP described reparative approaches as "unfair and deceptive."[43] At the time of this writing,* conversion therapy was banned by executive regulation in New York and by legislative statutes in 9 other states as well as the District of Columbia.[44]

Pediatric providers have an essential role in assessing gender concerns and providing evidence-based information to assist youth and families in medical decision-making. Not doing so can prolong or exacerbate gender dysphoria and contribute to abuse and stigmatization.[35] If a pediatric provider does not feel prepared to address gender concerns when they occur, then referral to a pediatric or mental health provider with more expertise is appropriate. There is little research on communication and efficacy with transfers in care for youth who identify as TGD, particularly from pediatric to adult providers.

DEVELOPMENTAL CONSIDERATIONS

Acknowledging that the capacity for emerging abstract thinking in childhood is important to conceptualize and reflect on identity, gender-affirmation guidelines are being focused on individually tailored interventions on the basis of the physical and cognitive development of youth who identify as TGD.[45] Accordingly, research substantiates that children who are prepubertal and assert an identity of TGD know their gender as clearly and as consistently as their developmentally equivalent peers who identify as cisgender and benefit from the same level of social acceptance.[46] This developmental approach to gender affirmation is in contrast to the outdated approach in which a child's gender-diverse assertions are held as "possibly true" until an arbitrary age (often after pubertal onset) when they can be considered valid, an approach that authors of the literature have termed "watchful waiting." This outdated approach does not serve the child because critical support is withheld. Watchful waiting is based on binary notions of gender in which gender diversity and fluidity is pathologized; in watchful waiting, it is also assumed that notions of gender identity become fixed at a certain age. The approach is also influenced by a group of early studies with validity concerns, methodologic flaws, and limited follow-up on children who identified as TGD and, by adolescence, did not seek further treatment ("desisters").[45,47] More robust and current research suggests that, rather than focusing on who a child will become, valuing them for who they are, even at a young age, fosters secure attachment and resilience, not only for the child but also for the whole family.[5,45,48,49]

* For more information regarding state-specific laws, please contact the AAP Division of State Government Affairs at stgov@ aap.org.

MEDICAL MANAGEMENT

Pediatric primary care providers are in a unique position to routinely inquire about gender development in children and adolescents as part of recommended well-child visits[50] and to be a reliable source of validation, support, and reassurance. They are often the first provider to be aware that a child may not identify as cisgender or that there may be distress related to a gender-diverse identity. The best way to approach gender with patients is to inquire directly and nonjudgmentally about their experience and feelings before applying any labels.[27,51]

Many medical interventions can be offered to youth who identify as TGD and their families. The decision of whether and when to initiate gender-affirmative treatment is personal and involves careful consideration of risks, benefits, and other factors unique to each patient and family. Many protocols suggest that clinical assessment of youth who identify as TGD is ideally conducted on an ongoing basis in the setting of a collaborative, multidisciplinary approach, which, in addition to the patient and family, may include the pediatric provider, a mental health provider (preferably with expertise in caring for youth who identify as TGD), social and legal supports, and a pediatric endocrinologist or adolescent-medicine gender specialist, if available.[6,28] There is no prescribed path, sequence, or end point. Providers can make every effort to be aware of the influence of their own biases. The medical options also vary depending on pubertal and developmental progression.

Clinical Setting

In the past year, 1 in 4 adults who identified as transgender avoided a necessary doctor's visit because of fear of being mistreated.[31] All clinical office staff have a role in affirming a patient's gender identity. Making flyers available or displaying posters related to LGBTQ health issues, including information for children who identify as TGD and families, reveals inclusivity and awareness. Generally, patients who identify as TGD feel most comfortable when they have access to a gender-neutral restroom. Diversity training that encompasses sensitivity when caring for youth who identify as TGD and their families can be helpful in educating clinical and administrative staff. A patient-asserted name and pronouns are used by staff and are ideally reflected in the electronic medical record without creating duplicate charts.[52,53] The US Centers for Medicare and Medicaid Services and the National Coordinator for Health Information Technology require all electronic health record systems certified under the Meaningful Use incentive program to have the capacity to confidentially collect information on gender identity.[54,55] Explaining and maintaining confidentiality procedures promotes openness and trust, particularly with youth who identify as LGBTQ.[1] Maintaining a safe clinical space can provide at least 1 consistent, protective refuge for patients and families, allowing authentic gender expression and exploration that builds resiliency.

Pubertal Suppression

Gonadotrophin-releasing hormones have been used to delay puberty since the 1980s for central precocious puberty.[56] These reversible treatments can also be used in adolescents who experience gender dysphoria to prevent development of secondary sex characteristics and provide time up until 16 years of age for the individual and the family to explore gender identity, access psychosocial supports, develop coping skills, and further define appropriate treatment goals. If pubertal suppression treatment is suspended, then endogenous puberty will resume.[20,57,58]

Often, pubertal suppression creates an opportunity to reduce distress that may occur with the development of secondary sexual characteristics and allow for gender-affirming care, including mental health support for the adolescent and the family. It reduces the need for later surgery because physical changes that are otherwise irreversible (protrusion of the Adam's apple, male pattern baldness, voice change, breast growth, etc) are prevented. The available data reveal that pubertal suppression in children who identify as TGD generally leads to improved psychological functioning in adolescence and young adulthood.[20,57–59]

Pubertal suppression is not without risks. Delaying puberty beyond one's peers can also be stressful and can lead to lower self-esteem and increased risk taking.[60] Some experts believe that genital underdevelopment may limit some potential reconstructive options.[61] Research on long-term risks, particularly in terms of bone metabolism[62] and fertility,[63] is currently limited and provides varied results.[57,64,65] Families often look to pediatric providers for help in considering whether pubertal suppression is indicated in the context of their child's overall well-being as gender diverse.

Gender Affirmation

As youth who identify as TGD reflect on and evaluate their gender identity, various interventions may be considered to better align their gender expression with their underlying identity. This process of reflection, acceptance, and, for some, intervention is known as "gender affirmation." It was formerly referred to as "transitioning," but many view the process as an affirmation and acceptance of who they have always been rather than a transition

TABLE 2 The Process of Gender Affirmation May Include ≥1 of the Following Components

Component	Definition	General Age Range[a]	Reversibility[a]
Social affirmation	Adopting gender-affirming hairstyles, clothing, name, gender pronouns, and restrooms and other facilities	Any	Reversible
Puberty blockers	Gonadotropin-releasing hormone analogues, such as leuprolide and histrelin	During puberty (Tanner stage 2–5)[b]	Reversible[c]
Cross-sex hormone therapy	Testosterone (for those who were assigned female at birth and are masculinizing); estrogen plus androgen inhibitor (for those who were assigned male at birth and are feminizing)	Early adolescence onward	Partially reversible (skin texture, muscle mass, and fat deposition); irreversible once developed (testosterone: Adam's apple protrusion, voice changes, and male pattern baldness; estrogen: breast development); unknown reversibility (effect on fertility)
Gender-affirming surgeries	"Top" surgery (to create a male-typical chest shape or enhance breasts); "bottom" surgery (surgery on genitals or reproductive organs); facial feminization and other procedures	Typically adults (adolescents on case-by-case basis[d])	Not reversible
Legal affirmation	Changing gender and name recorded on birth certificate, school records, and other documents	Any	Reversible

[a] Note that the provided age range and reversibility is based on the little data that are currently available.
[b] There is limited benefit to starting gonadotropin-releasing hormone after Tanner stage 5 for pubertal suppression. However, when cross-sex hormones are initiated with a gradually increasing schedule, the initial levels are often not high enough to suppress endogenous sex hormone secretion. Therefore, gonadotropin-releasing hormone may be continued in accordance with the Endocrine Society Guidelines.[68]
[c] The effect of sustained puberty suppression on fertility is unknown. Pubertal suppression can be, and often is indicated to be, followed by cross-sex hormone treatment. However, when cross-sex hormones are initiated without endogenous hormones, then fertility may be decreased.[68]
[d] Eligibility criteria for gender-affirmative surgical interventions among adolescents are not clearly defined between established protocols and practice. When applicable, eligibility is usually determined on a case-by-case basis with the adolescent and the family along with input from medical, mental health, and surgical providers.[68–71]

from 1 gender identity to another. Accordingly, some people who have gone through the process prefer to call themselves "affirmed females, males, etc" (or just "females, males, etc"), rather than using the prefix "trans-." Gender affirmation is also used to acknowledge that some individuals who identify as TGD may feel affirmed in their gender without pursuing medical or surgical interventions.[7,66]

Supportive involvement of parents and family is associated with better mental and physical health outcomes.[67] Gender affirmation among adolescents with gender dysphoria often reduces the emphasis on gender in their lives, allowing them to attend to other developmental tasks, such as academic success, relationship building, and future-oriented planning.[64] Most protocols for gender-affirming interventions incorporate World Professional Association of Transgender Health[35] and Endocrine Society[68] recommendations and include ≥1 of the following elements (Table 2):

1. Social Affirmation: This is a reversible intervention in which children and adolescents express partially or completely in their asserted gender identity by adapting hairstyle, clothing, pronouns, name, etc. Children who identify as transgender and socially affirm and are supported in their asserted gender show no increase in depression and only minimal (clinically insignificant) increases in anxiety compared with age-matched averages.[48] Social affirmation can be complicated given the wide range of social interactions children have (eg, extended families, peers, school, community, etc). There is little guidance on the best approach (eg, all at once, gradual, creating new social networks, or affirming within existing networks, etc). Pediatric providers can best support families by anticipating and discussing such complexity proactively, either in their own practice or through enlisting a qualified mental health provider.

2. Legal Affirmation: Elements of a social affirmation, such as a name and gender marker, become official on legal documents, such as birth certificates, passports, identification cards, school documents, etc. The processes for making these changes depend on state laws and may require specific documentation from pediatric providers.

3. Medical Affirmation: This is the process of using cross-sex hormones to allow adolescents who have initiated puberty to develop secondary sex characteristics of the opposite biological sex. Some changes are partially reversible if hormones are stopped, but others become

irreversible once they are fully developed (Table 2).

4. Surgical Affirmation: Surgical approaches may be used to feminize or masculinize features, such as hair distribution, chest, or genitalia, and may include removal of internal organs, such as ovaries or the uterus (affecting fertility). These changes are irreversible. Although current protocols typically reserve surgical interventions for adults,[35,68] they are occasionally pursued during adolescence on a case-by-case basis, considering the necessity and benefit to the adolescent's overall health and often including multidisciplinary input from medical, mental health, and surgical providers as well as from the adolescent and family.[69–71]

For some youth who identify as TGD whose natal gender is female, menstruation, breakthrough bleeding, and dysmenorrhea can lead to significant distress before or during gender affirmation. The American College of Obstetrics and Gynecology suggests that, although limited data are available to outline management, menstruation can be managed without exogenous estrogens by using a progesterone-only pill, a medroxyprogesterone acetate shot, or a progesterone-containing intrauterine or implantable device.[72] If estrogen can be tolerated, oral contraceptives that contain both progesterone and estrogen are more effective at suppressing menses.[73] The Endocrine Society guidelines also suggest that gonadotrophin-releasing hormones can be used for menstrual suppression before the anticipated initiation of testosterone or in combination with testosterone for breakthrough bleeding (enables phenotypic masculinization at a lower dose than if testosterone is used alone).[68] Masculinizing hormones in natal female patients may lead to a cessation of menses, but unplanned pregnancies have been reported, which emphasizes the need for ongoing contraceptive counseling with youth who identify as TGD.[72]

HEALTH DISPARITIES

In addition to societal challenges, youth who identify as TGD face several barriers within the health care system, especially regarding access to care. In 2015, a focus group of youth who identified as transgender in Seattle, Washington, revealed 4 problematic areas related to health care:

1. safety issues, including the lack of safe clinical environments and fear of discrimination by providers;
2. poor access to physical health services, including testing for sexually transmitted infections;
3. inadequate resources to address mental health concerns; and
4. lack of continuity with providers.[74]

This study reveals the obstacles many youth who identify as TGD face in accessing essential services, including the limited supply of appropriately trained medical and psychological providers, fertility options, and insurance coverage denials for gender-related treatments.[74]

Insurance denials for services related to the care of patients who identify as TGD are a significant barrier. Although the Office for Civil Rights of the US Department of Health and Human Services explicitly stated in 2012 that the nondiscrimination provision in the Patient Protection and Affordable Care Act includes people who identify as gender diverse,[75,76] insurance claims for gender affirmation, particularly among youth who identify as TGD, are frequently denied.[54,77] In 1 study, it was found that approximately 25% of individuals who identified as transgender were denied insurance coverage because of being transgender.[31] The burden of covering medical expenses that are not covered by insurance can be financially devastating, and even when expenses are covered, families describe high levels of stress in navigating and submitting claims appropriately.[78] In 2012, a large gender center in Boston, Massachusetts, reported that most young patients who identified as transgender and were deemed appropriate candidates for recommended gender care were unable to obtain it because of such denials, which were based on the premise that gender dysphoria was a mental disorder, not a physical one, and that treatment was not medically or surgically necessary.[24] This practice not only contributes to stigma, prolonged gender dysphoria, and poor mental health outcomes,[77] but it may also lead patients to seek nonmedically supervised treatments that are potentially dangerous.[24] Furthermore, insurance denials can reinforce a socioeconomic divide between those who can finance the high costs of uncovered care and those who cannot.[24,77]

The transgender youth group in Seattle likely reflected the larger TGD population when they described how obstacles adversely affect self-esteem and contribute to the perception that they are undervalued by society and the health care system.[74,77] Professional medical associations, including the AAP, are increasingly calling for equity in health care provisions regardless of gender identity or expression.[1,8,23,72] There is a critical need for investments in research on the prevalence, disparities, biological underpinnings, and standards of care relating to gender-diverse populations. Pediatric providers who work with state government and insurance officials can play an essential role in advocating for

stronger nondiscrimination policies and improved coverage.

There is a lack of quality research on the experience of youth of color who identify as transgender. One theory suggests that the intersection of racism, transphobia, and sexism may result in the extreme marginalization that is experienced among many women of color who identify as transgender,[79] including rejection from their family and dropping out of school at younger ages (often in the setting of rigid religious beliefs regarding gender),[80] increased levels of violence and body objectification,[81] 3 times the risk of poverty compared with the general population,[31] and the highest prevalence of HIV compared with other risk groups (estimated as high as 56.3% in 1 meta-analysis).[30] One model suggests that pervasive stigma and oppression can be associated with psychological distress (anxiety, depression, and suicide) and adoption of risk behaviors by such youth to obtain a sense of validation toward their complex identities.[79]

FAMILY ACCEPTANCE

Research increasingly suggests that familial acceptance or rejection ultimately has little influence on the gender identity of youth; however, it may profoundly affect young people's ability to openly discuss or disclose concerns about their identity. Suppressing such concerns can affect mental health.[82] Families often find it hard to understand and accept their child's gender-diverse traits because of personal beliefs, social pressure, and stigma.[49,83] Legitimate fears may exist for their child's welfare, safety, and acceptance that pediatric providers need to appreciate and address. Families can be encouraged to communicate their concerns and questions. Unacknowledged concerns can contribute to shame and hesitation in regard to offering support and understanding,[84] which is essential for the child's self-esteem, social involvement, and overall health as TGD.[48,85–87] Some caution has been expressed that unquestioning acceptance per se may not best serve questioning youth or their families. Instead, psychological evidence suggests that the most benefit comes when family members and youth are supported and encouraged to engage in reflective perspective taking and validate their own and the other's thoughts and feelings despite divergent views.[49,82]

In this regard, suicide attempt rates among 433 adolescents in Ontario who identified as "trans" were 4% among those with strongly supportive parents and as high as 60% among those whose parents were not supportive.[85] Adolescents who identify as transgender and endorse at least 1 supportive person in their life report significantly less distress than those who only experience rejection. In communities with high levels of support, it was found that nonsupportive families tended to increase their support over time, leading to dramatic improvement in mental health outcomes among their children who identified as transgender.[88]

Pediatric providers can create a safe environment for parents and families to better understand and listen to the needs of their children while receiving reassurance and education.[83] It is often appropriate to assist the child in understanding the parents' concerns as well. Despite expectations by some youth with transgender identity for immediate acceptance after "coming out," family members often proceed through a process of becoming more comfortable and understanding of the youth's gender identity, thoughts, and feelings. One model suggests that the process resembles grieving, wherein the family separates from their expectations for their child to embrace a new reality. This process may proceed through stages of shock, denial, anger, feelings of betrayal, fear, self-discovery, and pride.[89] The amount of time spent in any of these stages and the overall pace varies widely. Many family members also struggle as they are pushed to reflect on their own gender experience and assumptions throughout this process. In some situations, youth who identify as TGD may be at risk for internalizing the difficult emotions that family members may be experiencing. In these cases, individual and group therapy for the family members may be helpful.[49,78]

Family dynamics can be complex, involving disagreement among legal guardians or between guardians and their children, which may affect the ability to obtain consent for any medical management or interventions. Even in states where minors may access care without parental consent for mental health services, contraception, and sexually transmitted infections, parental or guardian consent is required for hormonal and surgical care of patients who identify as TGD.[72,90] Some families may take issue with providers who address gender concerns or offer gender-affirming care. In rare cases, a family may deny access to care that raises concerns about the youth's welfare and safety; in those cases, additional legal or ethical support may be useful to consider. In such rare situations, pediatric providers may want to familiarize themselves with relevant local consent laws and maintain their primary responsibility for the welfare of the child.

SAFE SCHOOLS AND COMMUNITIES

Youth who identify as TGD are becoming more visible because gender-diverse expression is increasingly admissible in the media, on social media, and in schools and communities. Regardless of whether a youth with a gender-diverse

identity ultimately identifies as transgender, challenges exist in nearly every social context, from lack of understanding to outright rejection, isolation, discrimination, and victimization. In the US Transgender Survey of nearly 28 000 respondents, it was found that among those who were out as or perceived to be TGD between kindergarten and eighth grade, 54% were verbally harassed, 24% were physically assaulted, and 13% were sexually assaulted; 17% left school because of maltreatment.[31] Education and advocacy from the medical community on the importance of safe schools for youth who identify as TGD can have a significant effect.

At the time of this writing,* only 18 states and the District of Columbia had laws that prohibited discrimination based on gender expression when it comes to employment, housing, public accommodations, and insurance benefits. Over 200 US cities have such legislation. In addition to basic protections, many youth who identify as TGD also have to navigate legal obstacles when it comes to legally changing their name and/or gender marker.[54] In addition to advocating and working with policy makers to promote equal protections for youth who identify as TGD, pediatric providers can play an important role by developing a familiarity with local laws and organizations that provide social work and legal assistance to youth who identify as TGD and their families.

School environments play a significant role in the social and emotional development of children. Every child has a right to feel safe and respected at school, but for youth who identify as TGD, this can be challenging. Nearly every aspect of school life may present safety concerns and require negotiations regarding their gender expression, including name/pronoun use, use of bathrooms and locker rooms, sports teams, dances and activities, overnight activities, and even peer groups. Conflicts in any of these areas can quickly escalate beyond the school's control to larger debates among the community and even on a national stage.

The formerly known Gay, Lesbian, and Straight Education Network (GLSEN), an advocacy organization for youth who identify as LGBTQ, conducts an annual national survey to measure LGBTQ well-being in US schools. In 2015, students who identified as LGBTQ reported high rates of being discouraged from participation in extracurricular activities. One in 5 students who identified as LGBTQ reported being hindered from forming or participating in a club to support lesbian, gay, bisexual, or transgender students (eg, a gay straight alliance, now often referred to as a genders and sexualities alliance) despite such clubs at schools being associated with decreased reports of negative remarks about sexual orientation or gender expression, increased feelings of safety and connectedness at school, and lower levels of victimization. In addition, >20% of students who identified as LGBTQ reported being blocked from writing about LGBTQ issues in school yearbooks or school newspapers or being prevented or discouraged by coaches and school staff from participating in sports because of their sexual orientation or gender expression.[91]

One strategy to prevent conflict is to proactively support policies and protections that promote inclusion and safety of all students. However, such policies are far from consistent across districts. In 2015, GLSEN found that 43% of children who identified as LGBTQ reported feeling unsafe at school because of their gender expression, but only 6% reported that their school had official policies to support youth who identified as TGD, and only 11% reported that their school's antibullying policies had specific protections for gender expression.[91] Consequently, more than half of the students who identified as transgender in the study were prevented from using the bathroom, names, or pronouns that aligned with their asserted gender at school. A lack of explicit policies that protected youth who identified as TGD was associated with increased reported victimization, with more than half of students who identified as LGBTQ reporting verbal harassment because of their gender expression. Educators and school administrators play an essential role in advocating for and enforcing such policies. GLSEN found that when students recognized actions to reduce gender-based harassment, both students who identified as transgender and cisgender reported a greater connection to staff and feelings of safety.[91] In another study, schools were open to education regarding gender diversity and were willing to implement policies when they were supported by external agencies, such as medical professionals.[92]

Academic content plays an important role in building a safe school environment as well. The 2015 GLSEN survey revealed that when positive representations of people who identified as LGBTQ were included in the curriculum, students who identified as LGBTQ reported less hostile school environments, less victimization and greater feelings of safety, fewer school absences because of feeling unsafe, greater feelings of connectedness to their school

* For more information regarding state-specific laws, please contact the AAP Division of State Government Affairs at stgov@ aap.org.

community, and an increased interest in high school graduation and postsecondary education.[91] At the time of this writing,* 8 states had laws that explicitly forbade teachers from even discussing LGBTQ issues.[54]

MEDICAL EDUCATION

One of the most important ways to promote high-quality health care for youth who identify as TGD and their families is increasing the knowledge base and clinical experience of pediatric providers in providing culturally competent care to such populations, as recommended by the recently released guidelines by the Association of American Medical Colleges.[93] This begins with the medical school curriculum in areas such as human development, sexual health, endocrinology, pediatrics, and psychiatry. In a 2009–2010 survey of US medical schools, it was found that the median number of hours dedicated to LGBTQ health was 5, with one-third of US medical schools reporting no LGBTQ curriculum during the clinical years.[94]

During residency training, there is potential for gender diversity to be emphasized in core rotations, especially in pediatrics, psychiatry, family medicine, and obstetrics and gynecology. Awareness could be promoted through the inclusion of topics relevant to caring for children who identify as TGD in the list of core competencies published by the American Board of Pediatrics, certifying examinations, and relevant study materials. Continuing education and maintenance of certification activities can include topics relevant to TGD populations as well.

* For more information regarding state-specific laws, please contact the AAP Division of State Government Affairs at stgov@ aap.org.

RECOMMENDATIONS

The AAP works toward all children and adolescents, regardless of gender identity or expression, receiving care to promote optimal physical, mental, and social well-being. Any discrimination based on gender identity or expression, real or perceived, is damaging to the socioemotional health of children, families, and society. In particular, the AAP recommends the following:

1. that youth who identify as TGD have access to comprehensive, gender-affirming, and developmentally appropriate health care that is provided in a safe and inclusive clinical space;
2. that family-based therapy and support be available to recognize and respond to the emotional and mental health needs of parents, caregivers, and siblings of youth who identify as TGD;
3. that electronic health records, billing systems, patient-centered notification systems, and clinical research be designed to respect the asserted gender identity of each patient while maintaining confidentiality and avoiding duplicate charts;
4. that insurance plans offer coverage for health care that is specific to the needs of youth who identify as TGD, including coverage for medical, psychological, and, when indicated, surgical gender-affirming interventions;
5. that provider education, including medical school, residency, and continuing education, integrate core competencies on the emotional and physical health needs and best practices for the care of youth who identify as TGD and their families;
6. that pediatricians have a role in advocating for, educating, and developing liaison relationships with school districts and other community organizations to promote acceptance and inclusion of all children without fear of harassment, exclusion, or bullying because of gender expression;
7. that pediatricians have a role in advocating for policies and laws that protect youth who identify as TGD from discrimination and violence;
8. that the health care workforce protects diversity by offering equal employment opportunities and workplace protections, regardless of gender identity or expression; and
9. that the medical field and federal government prioritize research that is dedicated to improving the quality of evidence-based care for youth who identify as TGD.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
GACM: gender-affirmative care model
GLSEN: Gay, Lesbian, and Straight Education Network
LGBTQ: lesbian, gay, bisexual, transgender, or questioning
TGD: transgender and gender diverse

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Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents

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Guidelines for Psychological Practice With Transgender and Gender Nonconforming People

American Psychological Association

Transgender and gender nonconforming[1] (TGNC) people are those who have a gender identity that is not fully aligned with their sex assigned at birth. The existence of TGNC people has been documented in a range of historical cultures (Coleman, Colgan, & Gooren, 1992; Feinberg, 1996; Miller & Nichols, 2012; Schmidt, 2003). Current population estimates of TGNC people have ranged from 0.17 to 1,333 per 100,000 (Meier & Labuski, 2013). The Massachusetts Behavioral Risk Factor Surveillance Survey found 0.5% of the adult population aged 18 to 64 years identified as TGNC between 2009 and 2011 (Conron, Scott, Stowell, & Landers, 2012). However, population estimates likely underreport the true number of TGNC people, given difficulties in collecting comprehensive demographic information about this group (Meier & Labuski, 2013). Within the last two decades, there has been a significant increase in research about TGNC people. This increase in knowledge, informed by the TGNC community, has resulted in the development of progressively more trans-affirmative practice across the multiple health disciplines involved in the care of TGNC people (Bockting, Knudson, & Goldberg, 2006; Coleman et al., 2012). Research has documented the extensive experiences of stigma and discrimination reported by TGNC people (Grant et al., 2011) and the mental health consequences of these experiences across the life span (Bockting, Miner, Swinburne Romine, Hamilton, & Coleman, 2013), including increased rates of depression (Fredriksen-Goldsen et al., 2014) and suicidality (Clements-Nolle, Marx, & Katz, 2006). TGNC people's lack of access to trans-affirmative mental and physical health care is a common barrier (Fredriksen-Goldsen et al., 2014; Garofalo, Deleon, Osmer, Doll, & Harper, 2006; Grossman & D'Augelli, 2006), with TGNC people sometimes being denied care because of their gender identity (Xavier et al., 2012).

In 2009, the American Psychological Association (APA) Task Force on Gender Identity and Gender Variance (TFGIGV) survey found that less than 30% of psychologist and graduate student participants reported familiarity with issues that TGNC people experience (APA TFGIGV, 2009). Psychologists and other mental health professionals who have limited training and experience in TGNC-affirmative care may cause harm to TGNC people (Mikalson, Pardo, & Green, 2012; Xavier et al., 2012). The significant level of societal stigma and discrimination that TGNC people face, the associated mental health consequences, and psychologists' lack of familiarity with trans-affirmative care led the APA Task Force to recommend that psychological practice guidelines be developed to help psychologists maximize the effectiveness of services offered and avoid harm when working with TGNC people and their families.

Purpose

The purpose of the *Guidelines for Psychological Practice with Transgender and Gender Nonconforming People* (hereafter *Guidelines*) is to assist psychologists in the provision of culturally competent, developmentally appropriate, and trans-affirmative psychological practice with TGNC people. Trans-affirmative practice is the provision

The American Psychological Association's (APA's) Task Force on Guidelines for Psychological Practice with Transgender and Gender Nonconforming People developed these guidelines. lore m. dickey, Louisiana Tech University, and Anneliese A. Singh, The University of Georgia, served as chairs of the Task Force. The members of the Task Force included Walter O. Bockting, Columbia University; Sand Chang, Independent Practice; Kelly Ducheny, Howard Brown Health Center; Laura Edwards-Leeper, Pacific University; Randall D. Ehrbar, Whitman Walker Health Center; Max Fuentes Fuhrmann, Independent Practice; Michael L. Hendricks, Washington Psychological Center, P.C.; and Ellen Magalhaes, Center for Psychological Studies at Nova Southeastern University and California School of Professional Psychology at Alliant International University.

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This document will expire as APA policy in 2022. After this date, users should contact the APA Public Interest Directorate to determine whether the guidelines in this document remain in effect as APA policy.

Correspondence concerning this article should be addressed to the Public Interest Directorate, American Psychological Association, 750 First Street, NE, Washington, DC 20002.

[1] For the purposes of these guidelines, we use the term *transgender and gender nonconforming* (TGNC). We intend for the term to be as broadly inclusive as possible, and recognize that some TGNC people do not ascribe to these terms. Readers are referred to Appendix A for a listing of terms that include various TGNC identity labels.

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of care that is respectful, aware, and supportive of the identities and life experiences of TGNC people (Korell & Lorah, 2007). The *Guidelines* are an introductory resource for psychologists who will encounter TGNC people in their practice, but can also be useful for psychologists with expertise in this area of practice to improve the care already offered to TGNC people. The *Guidelines* include a set of definitions for readers who may be less familiar with language used when discussing gender identity and TGNC populations (see Appendix A). Distinct from TGNC, the term "cisgender" is used to refer to people whose sex assigned at birth is aligned with their gender identity (E. R. Green, 2006; Serano, 2006).

Given the added complexity of working with TGNC and gender-questioning youth[2] and the limitations of the available research, the *Guidelines* focus primarily, though not exclusively, on TGNC adults. Future revisions of the *Guidelines* will deepen a focus on TGNC and gender-questioning children and adolescents. The *Guidelines* address the strengths of TGNC people, the challenges they face, ethical and legal issues, life span considerations, research, education, training, and health care. Because issues of gender identity are often conflated with issues of gender expression or sexual orientation, psychological practice with the TGNC population warrants the acquisition of specific knowledge about concerns unique to TGNC people that are not addressed by other practice guidelines (APA, 2012). It is important to note that these *Guidelines* are not intended to address some of the conflicts that cisgender people may experience due to societal expectations regarding gender roles (Butler, 1990), nor are they intended to address intersex people (Dreger, 1999; Preves, 2003).

Documentation of Need

In 2005, the APA Council of Representatives authorized the creation of the Task Force on Gender Identity and Gender Variance (TFGIGV), charging the Task Force to review APA policies related to TGNC people and to offer recommendations for APA to best meet the needs of TGNC people (APA TFGIGV, 2009). In 2009, the APA Council of Representatives adopted the Resolution on Transgender, Gender Identity, & Gender Expression Non-Discrimination, which calls upon psychologists in their professional roles to provide appropriate, nondiscriminatory treatment; encourages psychologists to take a leadership role in working against discrimination; supports the provision of adequate and necessary mental and medical health care; recognizes the efficacy, benefit, and medical necessity of gender transition; supports access to appropriate treatment in institutional settings; and supports the creation of educational resources for all psychologists (Anton, 2009). In 2009, in an extensive report on the current state of psychological practice with TGNC people, the TFGIGV determined that there was sufficient knowledge and expertise in the field to warrant the development of practice guidelines for TGNC populations (APA TFGIGV, 2009). The report identified that TGNC people constituted a population with unique needs and that the creation of practice guidelines would be a valuable resource for the field (APA TFGIGV, 2009). Psychologists' relative lack of knowledge about TGNC people and trans-affirmative care, the level of societal stigma and discrimination that TGNC people face, and the significant mental health consequences that TGNC people experience as a result offer a compelling need for psychological practice guidelines for this population.

Users

The intended audience for these *Guidelines* includes psychologists who provide clinical care, conduct research, or provide education or training. Given that gender identity issues can arise at any stage in a TGNC person's life (Lev, 2004), clinicians can encounter a TGNC person in practice or have a client's presenting problem evolve into an issue related to gender identity and gender expression. Researchers, educators, and trainers will benefit from use of these *Guidelines* to inform their work, even when not specifically focused on TGNC populations. Psychologists who focus on TGNC populations in their clinical practice, research, or educational and training activities will also benefit from the use of these *Guidelines*.

Distinction Between Standards and Guidelines

When using these *Guidelines*, psychologists should be aware that APA has made an important distinction between *standards* and *guidelines* (Reed, McLaughlin, & Newman, 2002). Standards are mandates to which all psychologists must adhere (e.g., the *Ethical Principles of Psychologists and Code of Conduct*; APA, 2010), whereas guidelines are aspirational. Psychologists are encouraged to use these *Guidelines* in tandem with the *Ethical Principles of Psychologists and Code of Conduct*, and should be aware that state and federal laws may override these *Guidelines* (APA, 2010).

In addition, these *Guidelines* refer to psychological practice (e.g., clinical work, consultation, education, research, and training) rather than treatment. Practice guidelines are practitioner-focused and provide guidance for professionals regarding "conduct and the issues to be considered in particular areas of clinical practice" (Reed et al., 2002, p. 1044). Treatment guidelines are client-focused and address intervention-specific recommendations for a clinical population or condition (Reed et al., 2002). The current *Guidelines* are intended to complement treatment guidelines for TGNC people seeking mental health services, such as those set forth by the World Professional Association for Transgender Health Standards of Care (Coleman et al., 2012) and the Endocrine Society (Hembree et al., 2009).

[2] For the purposes of these guidelines, "youth" refers to both children and adolescents under the age of 18.

Compatibility

These *Guidelines* are consistent with the APA *Ethical Principles of Psychologists and Code of Conduct* (APA, 2010), the *Standards of Accreditation for Health Service Psychology* (APA, 2015), the APA TFGIGV (2009) report, and the APA Council of Representatives Resolution on Transgender, Gender Identity, & Gender Expression Non-Discrimination (Anton, 2009).

Practice Guidelines Development Process

To address one of the recommendations of the APA TFGIGV (2009), the APA Committee on Sexual Orientation and Gender Diversity (CSOGD; then the Committee on Lesbian, Gay, Bisexual, and Transgender Concerns) and Division 44 (the Society for the Psychological Study of Lesbian, Gay, Bisexual and Transgender Issues) initiated a joint Task Force on Psychological Practice Guidelines with Transgender and Gender Nonconforming People in 2011. Task Force members were selected through an application and review process conducted by the leadership of CSOGD and Division 44. The Task Force included 10 members who had substantial psychological practice expertise with TGNC people. Of the 10 task force members, five individuals identified as TGNC with a range of gender identities and five identified as cisgender. In terms of race/ethnicity, six of the task force members identified as White and four identified as people of color (one Indian American, one Chinese American, one Latina American, and one mixed race).

The Task Force conducted a comprehensive review of the extant scholarship, identified content most pertinent to the practice of psychology with TGNC people, and evaluated the level of evidence to support guidance within each guideline. To ensure the accuracy and comprehensiveness of these *Guidelines*, Task Force members met with TGNC community members and groups and consulted with subject matter experts within and outside of psychology. When the Task Force discovered a lack of professional consensus, every effort was made to include divergent opinions in the field relevant to that issue. When this occurred, the Task Force described the various approaches documented in the literature. Additionally, these *Guidelines* were informed by comments received at multiple presentations held at professional conferences and comments obtained through two cycles of open public comment on earlier *Guideline* drafts.

This document contains 16 guidelines for TGNC psychological practice. Each guideline includes a Rationale section, which reviews relevant scholarship supporting the need for the guideline, and an Application section, which describes how the particular guideline may be applied in psychological practice. The *Guidelines* are organized into five clusters: (a) foundational knowledge and awareness; (b) stigma, discrimination, and barriers to care; (c) life span development; (d) assessment, therapy, and intervention; and (e) research, education, and training.

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Selection of Evidence

Although the number of publications on the topic of TGNC-affirmative practice has been increasing, this is still an emerging area of scholarly literature and research. When possible, the Task Force relied on peer-reviewed publications, but books, chapters, and reports that do not typically receive a high level of peer review have also been cited when appropriate. These sources are from a diverse range of fields addressing mental health, including psychology, counseling, social work, and psychiatry. Some studies of TGNC people utilize small sample sizes, which limits the generalizability of results. Few studies of TGNC people utilize probability samples or randomized control groups (e.g., Conron et al., 2012; Dhejne et al., 2011). As a result, the Task Force relied primarily on studies using convenience samples, which limits the generalizability of results to the population as a whole, but can be adequate for describing issues and situations that arise within the population.

Foundational Knowledge and Awareness

Guideline 1. Psychologists understand that gender is a nonbinary construct that allows for a range of gender identities and that a person's gender identity may not align with sex assigned at birth.

Rationale. Gender identity is defined as a person's deeply felt, inherent sense of being a girl, woman, or female; a boy, a man, or male; a blend of male or female; or an alternative gender (Bethea & McCollum, 2013; Institute of Medicine [IOM], 2011). In many cultures and religious traditions, gender has been perceived as a binary construct, with mutually exclusive categories of male or female, boy or girl, man or woman (Benjamin, 1966; Mollenkott, 2001; Tanis, 2003). These mutually exclusive categories include an assumption that gender identity is always in alignment with sex assigned at birth (Bethea & McCollum, 2013). For TGNC people, gender identity differs from sex assigned at birth to varying degrees, and may be experienced and expressed outside of the gender binary (Harrison, Grant, & Herman, 2012; Kuper, Nussbaum, & Mustanski, 2012).

Gender as a nonbinary construct has been described and studied for decades (Benjamin, 1966; Herdt, 1994; Kulick, 1998). There is historical evidence of recognition, societal acceptance, and sometimes reverence of diversity in gender identity and gender expression in several different cultures (Coleman et al., 1992; Feinberg, 1996; Miller

& Nichols, 2012; Schmidt, 2003). Many cultures in which gender nonconforming persons and groups were visible were diminished by westernization, colonialism, and systemic inequity (Nanda, 1999). In the 20th century, TGNC expression became medicalized (Hirschfeld, 1910/1991), and medical interventions to treat discordance between a person's sex assigned at birth, secondary sex characteristics, and gender identity became available (Meyerowitz, 2002).

As early as the 1950s, research found variability in how an individual described their[3] gender, with some participants reporting a gender identity different from the culturally defined, mutually exclusive categories of "man" or "woman" (Benjamin, 1966). In several recent large online studies of the TGNC population in the United States, 30% to 40% of participants identified their gender identity as other than man or woman (Harrison et al., 2012; Kuper et al., 2012). Although some studies have cultivated a broader understanding of gender (Conron, Scout, & Austin, 2008), the majority of research has required a forced choice between man and woman, thus failing to represent or depict those with different gender identities (IOM, 2011). Research over the last two decades has demonstrated the existence of a wide spectrum of gender identity and gender expression (Bockting, 2008; Harrison et al., 2012; Kuper et al., 2012), which includes people who identify as either man or woman, neither man nor woman, a blend of man and woman, or a unique gender identity. A person's identification as TGNC can be healthy and self-affirming, and is not inherently pathological (Coleman et al., 2012). However, people may experience distress associated with discordance between their gender identity and their body or sex assigned at birth, as well as societal stigma and discrimination (Coleman et al., 2012).

Between the late 1960s and the early 1990s, health care to alleviate gender dysphoria largely reinforced a binary conceptualization of gender (APA TFGIGV, 2009; Bolin, 1994; Hastings, 1974). At that time, it was considered an ideal outcome for TGNC people to conform to an identity that aligned with either sex assigned at birth or, if not possible, with the "opposite" sex, with a heavy emphasis on blending into the cisgender population or "passing" (APA TFGIGV, 2009; Bolin, 1994; Hastings, 1974). Variance from these options could raise concern for health care providers about a TGNC person's ability to transition successfully. These concerns could act as a barrier to accessing surgery or hormone therapy because medical and mental health care provider endorsement was required before surgery or hormones could be accessed (Berger et al., 1979). Largely because of self-advocacy of TGNC individuals and communities in the 1990s, combined with advances in research and models of trans-affirmative care, there is greater recognition and acknowledgment of a spectrum of gender diversity and corresponding individualized, TGNC-specific health care (Bockting et al., 2006; Coleman et al., 2012).

Application. A nonbinary understanding of gender is fundamental to the provision of affirmative care for TGNC people. Psychologists are encouraged to adapt or modify their understanding of gender, broadening the range of variation viewed as healthy and normative. By understanding the spectrum of gender identities and gender expressions that exist, and that a person's gender identity may not be in full alignment with sex assigned at birth, psychologists can increase their capacity to assist TGNC people, their families, and their communities (Lev, 2004). Respecting and supporting TGNC people in authentically articulating their gender identity and gender expression, as well as their lived experience, can improve TGNC people's health, well-being, and quality of life (Witten, 2003).

Some TGNC people may have limited access to visible, positive TGNC role models. As a result, many TGNC people are isolated and must cope with the stigma of gender nonconformity without guidance or support, worsening the negative effect of stigma on mental health (Fredriksen-Goldsen et al., 2014; Singh, Hays, & Watson, 2011). Psychologists may assist TGNC people in challenging gender norms and stereotypes, and in exploring their unique gender identity and gender expression. TGNC people, partners, families, friends, and communities can benefit from education about the healthy variation of gender identity and gender expression, and the incorrect assumption that gender identity automatically aligns with sex assigned at birth.

Psychologists may model an acceptance of ambiguity as TGNC people develop and explore aspects of their gender, especially in childhood and adolescence. A nonjudgmental stance toward gender nonconformity can help to counteract the pervasive stigma faced by many TGNC people and provide a safe environment to explore gender identity and make informed decisions about gender expression.

Guideline 2. Psychologists understand that gender identity and sexual orientation are distinct but interrelated constructs.

Rationale. The constructs of gender identity and sexual orientation are theoretically and clinically distinct, even though professionals and nonprofessionals frequently conflate them. Although some research suggests a potential link in the development of gender identity and sexual orientation, the mechanisms of such a relationship are unknown (Adelson & American Academy of Child and Adolescent Psychiatry [AACAP] Committee on Quality Issues [CQI], 2012; APA TFGIGV, 2009; A. H. Devor, 2004; Drescher & Byne, 2013). *Sexual orientation* is defined as a person's sexual and/or emotional attraction to another person (Shively & De Cecco, 1977), compared with *gender identity*, which is defined by a person's felt, inherent sense of gender. For most people, gender identity develops earlier than sexual orientation. Gender identity is often established in young toddlerhood (Adelson & AACAP CQI, 2012; Kohlberg, 1966), compared with aware-

[3] The third person plural pronouns "they," "them," and "their" in some instances function in these guidelines as third-person singular pronouns to model a common technique used to avoid the use of gendered pronouns when speaking to or about TGNC people.

ness of same-sex attraction, which often emerges in early adolescence (Adelson & AACAP CQI, 2012; D'Augelli & Hershberger, 1993; Herdt & Boxer, 1993; Ryan, 2009; Savin-Williams & Diamond, 2000). Although gender identity is usually established in childhood, individuals may become aware that their gender identity is not in full alignment with sex assigned at birth in childhood, adolescence, or adulthood. The developmental pathway of gender identity typically includes a progression through multiple stages of awareness, exploration, expression, and identity integration (Bockting & Coleman, 2007; A. H. Devor, 2004; Vanderburgh, 2007). Similarly, a person's sexual orientation may progress through multiple stages of awareness, exploration, and identity through adolescence and into adulthood (Bilodeau & Renn, 2005). Just as some people experience their sexual orientation as being fluid or variable (L. M. Diamond, 2013), some people also experience their gender identity as fluid (Lev, 2004).

The experience of questioning one's gender can create significant confusion for some TGNC people, especially for those who are unfamiliar with the range of gender identities that exist. To explain any discordance they may experience between their sex assigned at birth, related societal expectations, patterns of sexual and romantic attraction, and/or gender role nonconformity and gender identity, some TGNC people may assume that they must be gay, lesbian, bisexual, or queer (Bockting, Benner, & Coleman, 2009). Focusing solely on sexual orientation as the cause for discordance may obscure awareness of a TGNC identity. It can be very important to include sexual orientation and gender identity in the process of identity exploration as well as in the associated decisions about which options will work best for any particular person. In addition, many TGNC adults have disguised or rejected their experience of gender incongruence in childhood or adolescence to conform to societal expectations and minimize their fear of difference (Bockting & Coleman, 2007; Byne et al., 2012).

Because gender and patterns of attraction are used to identify a person's sexual orientation, the articulation of sexual orientation is made more complex when sex assigned at birth is not aligned with gender identity. A person's sexual orientation identity cannot be determined by simply examining external appearance or behavior, but must incorporate a person's identity and self-identification (Broido, 2000).

Application. Psychologists may assist people in differentiating gender identity and sexual orientation. As clients become aware of previously hidden or constrained aspects of their gender identity or sexuality, psychologists may provide acceptance, support, and understanding without making assumptions or imposing a specific sexual orientation or gender identity outcome (APA TFGIGV, 2009). Because of their roles in assessment, treatment, and prevention, psychologists are in a unique position to help TGNC people better understand and integrate the various aspects of their identities. Psychologists may assist TGNC people by introducing and normalizing differences in gender identity and expression. As a TGNC person finds a comfortable way to actualize and express their gender identity, psychologists may notice that previously incongruent aspects of their sexual orientation may become more salient, better integrated, or increasingly egosyntonic (Bockting et al., 2009; H. Devor, 1993; Schleifer, 2006). This process may allow TGNC people the comfort and opportunity to explore attractions or aspects of their sexual orientation that previously had been repressed, hidden, or in conflict with their identity. TGNC people may experience a renewed exploration of their sexual orientation, a widened spectrum of attraction, or a shift in how they identify their sexual orientation in the context of a developing TGNC identity (Coleman, Bockting, & Gooren, 1993; Meier, Pardo, Labuski, & Babcock, 2013; Samons, 2008).

Psychologists may need to provide TGNC people with information about TGNC identities, offering language to describe the discordance and confusion TGNC people may be experiencing. To facilitate TGNC people's learning, psychologists may introduce some of the narratives written by TGNC people that reflect a range of outcomes and developmental processes in exploring and affirming gender identity (e.g., Bornstein & Bergman, 2010; Boylan, 2013; J. Green, 2004; Krieger, 2011; Lawrence, 2014). These resources may potentially aid TGNC people in distinguishing between issues of sexual orientation and gender identity and in locating themselves on the gender spectrum. Psychologists may also educate families and broader community systems (e.g., schools, medical systems) to better understand how gender identity and sexual orientation are different but related; this may be particularly useful when working with youth (Singh & Burnes, 2009; Whitman, 2013). Because gender identity and sexual orientation are often conflated, even by professionals, psychologists are encouraged to carefully examine resources that claim to provide affirmative services for lesbian, gay, bisexual, transgender, and queer (LGBTQ) people, and to confirm which are knowledgeable about and inclusive of the needs of TGNC people before offering referrals or recommendations to TGNC people and their families.

Guideline 3. Psychologists seek to understand how gender identity intersects with the other cultural identities of TGNC people.

Rationale. Gender identity and gender expression may have profound intersections with other aspects of identity (Collins, 2000; Warner, 2008). These aspects may include, but are not limited to, race/ethnicity, age, education, socioeconomic status, immigration status, occupation, disability status, HIV status, sexual orientation, relational status, and religion and/or spiritual affiliation. Whereas some of these aspects of identity may afford privilege, others may create stigma and hinder empowerment (Burnes & Chen, 2012; K. M. de Vries, 2015). In addition, TGNC people who transition may not be prepared for changes in privilege or societal treatment based on gender identity and gender expression. To illustrate, an African American trans man may gain male privilege, but may face racism and

societal stigma particular to African American men. An Asian American/Pacific Islander trans woman may experience the benefit of being perceived as a cisgender woman, but may also experience sexism, misogyny, and objectification particular to Asian American/Pacific Islander cisgender women.

The intersection of multiple identities within TGNC people's lives is complex and may obstruct or facilitate access to necessary support (A. Daley, Solomon, Newman, & Mishna, 2008). TGNC people with less privilege and/or multiple oppressed identities may experience greater stress and restricted access to resources. They may also develop resilience and strength in coping with disadvantages, or may locate community-based resources available to specific groups (e.g., for people living with HIV; Singh et al., 2011). Gender identity affirmation may conflict with religious beliefs or traditions (Bockting & Cesaretti, 2001). Finding an affirmative expression of their religious and spiritual beliefs and traditions, including positive relationships with religious leaders, can be an important resource for TGNC people (Glaser, 2008; Porter, Ronneberg, & Witten, 2013; Xavier, 2000).

Application. In practice, psychologists strive to recognize the salient multiple and intersecting identities of TGNC people that influence coping, discrimination, and resilience (Burnes & Chen, 2012). Improved rapport and therapeutic alliance are likely to develop when psychologists avoid overemphasizing gender identity and gender expression when not directly relevant to TGNC people's needs and concerns. Even when gender identity is the main focus of care, psychologists are encouraged to understand that a TGNC person's experience of gender may also be shaped by other important aspects of identity (e.g., age, race/ethnicity, sexual orientation), and that the salience of different aspects of identity may evolve as the person continues psychosocial development across the life span, regardless of whether they complete a social or medical transition.

At times, a TGNC person's intersection of identities may result in conflict, such as a person's struggle to integrate gender identity with religious and/or spiritual upbringing and beliefs (Kidd & Witten, 2008; Levy & Lo, 2013; Rodriguez & Follins, 2012). Psychologists may aid TGNC people in understanding and integrating identities that may be differently privileged within systems of power and systemic inequity (Burnes & Chen, 2012). Psychologists may also highlight and strengthen the development of TGNC people's competencies and resilience as they learn to manage the intersection of stigmatized identities (Singh, 2012).

Guideline 4. Psychologists are aware of how their attitudes about and knowledge of gender identity and gender expression may affect the quality of care they provide to TGNC people and their families.

Rationale. Psychologists, like other members of society, come to their personal understanding and acceptance of different aspects of human diversity through a process of socialization. Psychologists' cultural biases, as well as the cultural differences between psychologists and their clients, have a clinical impact (Israel, Gorcheva, Burnes, & Walther, 2008; Vasquez, 2007). The assumptions, biases, and attitudes psychologists hold regarding TGNC people and gender identity and/or gender expression can affect the quality of services psychologists provide and their ability to develop an effective therapeutic alliance (Bess & Stabb, 2009; Rachlin, 2002). In addition, a lack of knowledge or training in providing affirmative care to TGNC people can limit a psychologist's effectiveness and perpetuate barriers to care (Bess & Stabb, 2009; Rachlin, 2002). Psychologists experienced with lesbian, gay, or bisexual (LGB) people may not be familiar with the unique needs of TGNC people (Israel, 2005; Israel et al., 2008). In community surveys, TGNC people have reported that many mental health care providers lack basic knowledge and skills relevant to care of TGNC people (Bradford, Xavier, Hendricks, Rives, & Honnold, 2007; Xavier, Bobbin, Singer, & Budd, 2005) and receive little training to prepare them to work with TGNC people (APA TFGIGV, 2009; Lurie, 2005). The National Transgender Discrimination Survey (Grant et al., 2011) reported that 50% of TGNC respondents shared that they had to educate their health care providers about TGNC care, 28% postponed seeking medical care due to antitrans bias, and 19% were refused care due to discrimination.

The APA ethics code (APA, 2010) specifies that psychologists practice in areas only within the boundaries of their competence (Standard 2.01), participate in proactive and consistent ways to enhance their competence (Standard 2.03), and base their work upon established scientific and professional knowledge (Standard 2.04). Competence in working with TGNC people can be developed through a range of activities, such as education, training, supervised experience, consultation, study, or professional experience.

Application. Psychologists may engage in practice with TGNC people in various ways; therefore, the depth and level of knowledge and competence required by a psychologist depends on the type and complexity of service offered to TGNC people. Services that psychologists provide to TGNC people require a basic understanding of the population and its needs, as well as the ability to respectfully interact in a trans-affirmative manner (L. Carroll, 2010).

APA emphasizes the use of evidence-based practice (APA Presidential Task Force on Evidence-Based Practice, 2006). Given how easily assumptions or stereotypes could influence treatment, evidence-based practice may be especially relevant to psychological practice with TGNC people. Until evidence-based practices are developed specifically for TGNC people, psychologists are encouraged to utilize existing evidence-based practices in the care they provide. APA also promotes collaboration with clients concerning clinical decisions, including issues related to costs, potential benefits, and the existing options and resources related to treatment (APA Presidential Task Force on Evidence-Based Practice, 2006). TGNC people could benefit from such collaboration and active engagement in decision

making, given the historical disenfranchisement and disempowerment of TGNC people in health care.

In an effort to develop competence in working with TGNC people, psychologists are encouraged to examine their personal beliefs regarding gender and sexuality, gender stereotypes, and TGNC identities, in addition to identifying gaps in their own knowledge, understanding, and acceptance (American Counseling Association [ACA], 2010). This examination may include exploring one's own gender identity and gendered experiences related to privilege, power, or marginalization, as well as seeking consultation and training with psychologists who have expertise in working with TGNC people and communities.

Psychologists are further encouraged to develop competence in working with TGNC people and their families by seeking up-to-date basic knowledge and understanding of gender identity and expression, and learning how to interact with TGNC people and their families respectfully and without judgment. Competence in working with TGNC people may be achieved and maintained in formal and informal ways, ranging from exposure in the curriculum of training programs for future psychologists and continuing education at professional conferences, to affirmative involvement as allies in the TGNC community. Beyond acquiring general competence, psychologists who choose to specialize in working with TGNC people presenting with gender-identity-related concerns are strongly encouraged to obtain advanced training, consultation, and professional experience (ACA, 2010; Coleman et al., 2012).

Psychologists may gain knowledge about the TGNC community and become more familiar with the complex social issues that affect the lives of TGNC people through first-hand experiences (e.g., attending community meetings and conferences, reading narratives written by TGNC people). If psychologists have not yet developed competence in working with TGNC people, it is recommended that they refer TGNC people to other psychologists or providers who are knowledgeable and able to provide trans-affirmative care.

Stigma, Discrimination, and Barriers to Care

Guideline 5. Psychologists recognize how stigma, prejudice, discrimination, and violence affect the health and well-being of TGNC people.

Rationale. Many TGNC people experience discrimination, ranging from subtle to severe, when accessing housing, health care, employment, education, public assistance, and other social services (Bazargan & Galvan, 2012; Bradford, Reisner, Honnold, & Xavier, 2013; Dispenza, Watson, Chung, & Brack, 2012; Grant et al., 2011). Discrimination can include assuming a person's assigned sex at birth is fully aligned with that person's gender identity, not using a person's preferred name or pronoun, asking TGNC people inappropriate questions about their bodies, or making the assumption that psychopathology exists given a specific gender identity or gender expression (Nadal, Rivera, & Corpus, 2010; Nadal, Skolnik, & Wong, 2012). Discrimination may also include refusing access to housing or employment or extreme acts of violence (e.g., sexual assault, murder). TGNC people who hold multiple marginalized identities are more vulnerable to discrimination and violence. TGNC women and people of color disproportionately experience severe forms of violence and discrimination, including police violence, and are less likely to receive help from law enforcement (Edelman, 2011; National Coalition of Anti-Violence Programs, 2011; Saffin, 2011).

TGNC people are at risk of experiencing antitrans prejudice and discrimination in educational settings. In a national representative sample of 7,898 LGBT youth in K-12 settings, 55.2% of participants reported verbal harassment, 22.7% reported physical harassment, and 11.4% reported physical assault based on their gender expression (Kosciw, Greytak, Palmer, & Boesen, 2014). In a national community survey of TGNC adults, 15% reported prematurely leaving educational settings ranging from kindergarten through college as a result of harassment (Grant et al., 2011). Many schools do not include gender identity and gender expression in their school nondiscrimination policies; this leaves TGNC youth without needed protections from bullying and aggression in schools (Singh & Jackson, 2012). TGNC youth in rural settings may be even more vulnerable to bullying and hostility in their school environments due to antitrans prejudice (Kosciw et al., 2014).

Inequities in educational settings and other forms of TGNC-related discrimination may contribute to the significant economic disparities TGNC people have reported. Grant and colleagues (2011) found that TGNC people were four times more likely to have a household income of less than $10,000 compared with cisgender people, and almost half of a sample of TGNC older adults reported a household income at or below 200% of poverty (Fredriksen-Goldsen et al., 2014). TGNC people often face workplace discrimination both when seeking and maintaining employment (Brewster, Velez, Mennicke, & Tebbe, 2014; Dispenza et al., 2012; Mizock & Mueser, 2014). In a nonrepresentative national study of TGNC people, 90% reported having "directly experienced harassment or mistreatment at work and felt forced to take protective actions that negatively impacted their careers or their well-being, such as hiding who they were to avoid workplace repercussions" (Grant et al., 2011, p. 56). In addition, 78% of respondents reported experiencing some kind of direct mistreatment or discrimination at work (Grant et al., 2011). Employment discrimination may be related to stigma based on a TGNC person's appearance, discrepancies in identity documentation, or being unable to provide job references linked to that person's pretransition name or gender presentation (Bender-Baird, 2011).

Issues of employment discrimination and workplace harassment are particularly salient for TGNC military personnel and veterans. Currently, TGNC people cannot serve openly in the U.S. military. Military regulations cite "transsexualism" as a medical exclusion from service (Department of Defense, 2011; Elders & Steinman, 2014). When

enlisted, TGNC military personnel are faced with very difficult decisions related to coming out, transition, and seeking appropriate medical and mental health care, which may significantly impact or end their military careers. Not surprisingly, research documents very high rates of suicidal ideation and behavior among TGNC military and veteran populations (Blosnich et al., 2013; Matarazzo et al., 2014). Being open about their TGNC identity with health care providers can carry risk for TGNC military personnel (OutServe-Servicemembers Legal Defense Network, n.d.). Barriers to accessing health care noted by TGNC veterans include viewing the VA health care system as an extension of the military, perceiving the VA as an unwelcoming environment, and fearing providers' negative reactions to their identity (Sherman, Kauth, Shipherd, & Street, 2014; Shipherd, Mizock, Maguen, & Green, 2012). A recent study shows 28% of LGBT veterans perceived their VA as welcoming and one third as unwelcoming (Sherman et al., 2014). Multiple initiatives are underway throughout the VA system to improve the quality and sensitivity of services to LGBT veterans.

Given widespread workplace discrimination and possible dismissal following transition, TGNC people may engage in sex work or survival sex (e.g., trading sex for food), or sell drugs to generate income (Grant et al., 2011; Hwahng & Nuttbrock, 2007; Operario, Soma, & Underhill, 2008; Stanley, 2011). This increases the potential for negative interactions with the legal system, such as harassment by the police, bribery, extortion, and arrest (Edelman, 2011; Testa et al., 2012), as well as increased likelihood of mental health symptoms and greater health risks, such as higher incidence of sexually transmitted infections, including HIV (Nemoto, Operario, Keatley, & Villegas, 2004).

Incarcerated TGNC people report harassment, isolation, forced sex, and physical assault, both by prison personnel and other inmates (American Civil Liberties Union National Prison Project, 2005; Brotheim, 2013; C. Daley, 2005). In sex-segregated facilities, TGNC people may be subjected to involuntary solitary confinement (also called "administrative segregation"), which can lead to severe negative mental and physical health consequences and may block access to services (Gallagher, 2014; National Center for Transgender Equality, 2012). Another area of concern is for TGNC immigrants and refugees. TGNC people in detention centers may not be granted access to necessary care and experience significant rates of assault and violence in these facilities (Gruberg, 2013). TGNC people may seek asylum in the United States to escape danger as a direct result of lack of protections in their country of origin (APA Presidential Task Force on Immigration, 2012; Cerezo, Morales, Quintero, & Rothman, 2014; Morales, 2013).

TGNC people have difficulty accessing necessary health care (Fredriksen-Goldsen et al., 2014; Lambda Legal, 2012) and often feel unsafe sharing their gender identity or their experiences of antitrans prejudice and discrimination due to historical and current discrimination from health care providers (Grant et al., 2011; Lurie, 2005; Singh & McKleroy, 2011). Even when TGNC people have health insurance, plans may explicitly exclude coverage related to gender transition (e.g., hormone therapy, surgery). TGNC people may also have difficulty accessing trans-affirmative primary health care if coverage for procedures is denied based on gender. For example, trans men may be excluded from necessary gynecological care based on the assumption that men do not need these services. These barriers often lead to a lack of preventive health care for TGNC people (Fredriksen-Goldsen et al., 2014; Lambda Legal, 2012). Although the landscape is beginning to change with the recent revision of Medicare policy (National Center for Transgender Equality, 2014) and changes to state laws (Transgender Law Center, n.d.), many TGNC people are still likely to have little to no access to TGNC-related health care as a result of the exclusions in their insurance.

Application. Awareness of and sensitivity to the effects of antitrans prejudice and discrimination can assist psychologists in assessing, treating, and advocating for their TGNC clients. When a TGNC person faces discrimination based on gender identity or gender expression, psychologists may facilitate emotional processing of these experiences and work with the person to identify supportive resources and possible courses of action. Specific needs of TGNC people might vary from developing self-advocacy strategies, to navigating public spaces, to seeking legal recourse for harassment and discrimination in social services and other systems. Additionally, TGNC people who have been traumatized by physical or emotional violence may need therapeutic support.

Psychologists may be able to assist TGNC people in accessing relevant social service systems. For example, psychologists may be able to assist in identifying health care providers and housing resources that are affirming and affordable, or locating affirming religious and spiritual communities (Glaser, 2008; Porter et al., 2013). Psychologists may also assist in furnishing documentation or official correspondence that affirms gender identity for the purpose of accessing appropriate public accommodations, such as bathroom use or housing (Lev, 2009; W. J. Meyer, 2009).

Additionally, psychologists may identify appropriate resources, information, and services to help TGNC people in addressing workplace discrimination, including strategies during a social and/or medical transition for identity disclosure at work. For those who are seeking employment, psychologists may help strategize about how and whether to share information about gender history. Psychologists may also work with employers to develop supportive policies for workplace gender transition or to develop training to help employees adjust to the transition of a coworker.

For TGNC military and veteran populations, psychologists may help to address the emotional impact of navigating TGNC identity development in the military system. Psychologists are encouraged to be aware that issues of confidentiality may be particularly sensitive with active duty or reserve status service members, as the consequences of being identified as TGNC may prevent the client's disclosure of gender identity in treatment.

In educational settings, psychologists may advocate for TGNC youth on a number of levels (APA & National

Association of School Psychologists, 2014; Boulder Valley School District, 2012). Psychologists may consult with administrators, teachers, and school counselors to provide resources and trainings on antitrans prejudice and developing safer school environments for TGNC students (Singh & Burnes, 2009). Peer support from other TGNC people has been shown to buffer the negative effect of stigma on mental health (Bockting et al., 2013). As such, psychologists may consider and develop peer-based interventions to facilitate greater understanding and respectful treatment of TGNC youth by cisgender peers (Case & Meier, 2014). Psychologists may work with TGNC youth and their families to identify relevant resources, such as school policies that protect gender identity and gender expression (APA & National Association of School Psychologists, 2014; Gonzalez & McNulty, 2010), referrals to TGNC-affirmative organizations, and online resources, which may be especially helpful for TGNC youth in rural settings.

Guideline 6. Psychologists strive to recognize the influence of institutional barriers on the lives of TGNC people and to assist in developing TGNC-affirmative environments.

Rationale. Antitrans prejudice and the adherence of mainstream society to the gender binary adversely affect TGNC people within their families, schools, health care, legal systems, workplaces, religious traditions, and communities (American Civil Liberties Union National Prison Project, 2005; Bradford et al., 2013; Brewster et al., 2014; Levy & Lo, 2013; McGuire, Anderson, & Toomey, 2010). TGNC people face challenges accessing gender-inclusive restrooms, which may result in discomfort when being forced to use a men's or women's restroom (Transgender Law Center, 2005). In addition to the emotional distress the forced binary choice that public restrooms may create for some, TGNC people are frequently concerned with others' reactions to their presence in public restrooms, including potential discrimination, harassment, and violence (Herman, 2013).

Many TGNC people may be distrustful of care providers due to previous experiences of being pathologized (Benson, 2013). Experiences of discrimination and prejudice with health care providers may be complicated by power differentials within the therapeutic relationship that may greatly affect or complicate the care that TGNC people experience. TGNC people have routinely been asked to obtain an endorsement letter from a psychologist attesting to the stability of their gender identity as a prerequisite to access an endocrinologist, surgeon, or legal institution (e.g., driver's license bureau; Lev, 2009). The need for such required documentation from a psychologist may influence rapport, resulting in TGNC people fearing prejudicial treatment in which this documentation is withheld or delayed by the treating provider (Bouman et al., 2014). Whether a TGNC person has personally experienced interactions with providers as disempowering or has learned from community members to expect such a dynamic, psychologists are encouraged to be prepared for TGNC people to be very cautious when entering into a therapeutic relationship. When TGNC people feel validated and empowered within the environment in which a psychologist practices, the therapeutic relationship will benefit and the person may be more willing to explore their authentic selves and share uncertainties and ambiguities that are a common part of TGNC identity development.

Application. Because many TGNC people experience antitrans prejudice or discrimination, psychologists are encouraged to ensure that their work settings are welcoming and respectful of TGNC people, and to be mindful of what TGNC people may perceive as unwelcoming. To do so, psychologists may educate themselves about the many ways that cisgender privilege and antitrans prejudice may be expressed. Psychologists may also have specific conversations with TGNC people about their experiences of the mental health system and implement feedback to foster TGNC-affirmative environments. As a result, when TGNC people access various treatment settings and public spaces, they may experience less harm, disempowerment, or pathologization, and thus will be more likely to avail themselves of resources and support.

Psychologists are encouraged to be proactive in considering how overt or subtle cues in their workplaces and other environments may affect the comfort and safety of TGNC people. To increase the comfort of TGNC people, psychologists are encouraged to display TGNC-affirmative resources in waiting areas and to avoid the display of items that reflect antitrans attitudes (Lev, 2009). Psychologists are encouraged to examine how their language (e.g., use of incorrect pronouns and names) may reinforce the gender binary in overt or subtle and unintentional ways (Smith, Shin, & Officer, 2012). It may be helpful for psychologists to provide training for support staff on how to respectfully interact with TGNC people. A psychologist may consider making changes to paperwork, forms, or outreach materials to ensure that these materials are more inclusive of TGNC people (Spade, 2011b). For example, demographic questionnaires can communicate respect through the use of inclusive language and the inclusion of a range of gender identities. In addition, psychologists may also work within their institutions to advocate for restrooms that are inclusive and accessible for people of all gender identities and/or gender expressions.

When working with TGNC people in a variety of care and institutional settings (e.g., inpatient medical and psychiatric hospitals, substance abuse treatment settings, nursing homes, foster care, religious communities, military and VA health care settings, and prisons), psychologists may become liaisons and advocates for TGNC people's mental health needs and for respectful treatment that addresses their gender identity in an affirming manner. In playing this role, psychologists may find guidance and best practices that have been published for particular institutional contexts to be helpful (e.g., Department of Veterans Affairs, Veterans' Health Administration, 2013; Glezer, McNiel, & Binder, 2013; Merksamer, 2011).

Guideline 7: Psychologists understand the need to promote social change that reduces the negative effects of stigma on the health and well-being of TGNC people.

Rationale. The lack of public policy that addresses the needs of TGNC people creates significant hardships for them (Taylor, 2007). Although there have been major advances in legal protections for TGNC people in recent years (Buzuvis, 2013; Harvard Law Review Association, 2013), many TGNC people are still not afforded protections from discrimination on the basis of gender identity or expression (National LGBTQ Task Force, 2013; Taylor, 2007). For instance, in many states, TGNC people do not have employment or housing protections and may be fired or lose their housing based on their gender identity. Many policies that protect the rights of cisgender people, including LGB people, do not protect the rights of TGNC people (Currah, & Minter, 2000; Spade, 2011a).

TGNC people can experience challenges obtaining gender-affirming identity documentation (e.g., birth certificate, passport, social security card, driver's license). For TGNC people experiencing poverty or economic hardship, requirements for obtaining this documentation may be impossible to meet, in part due to the difficulty of securing employment without identity documentation that aligns with their gender identity and gender expression (Sheridan, 2009). Additionally, systemic barriers related to binary gender identification systems prevent some TGNC people from changing their documents, including those who are incarcerated, undocumented immigrants, and people who live in jurisdictions that explicitly forbid such changes (Spade, 2006). Documentation requirements can also assume a universal TGNC experience that marginalizes some TGNC people, especially those who do not undergo a medical transition. This may affect a TGNC person's social and psychological well-being and interfere with accessing employment, education, housing and shelter, health care, public benefits, and basic life management resources (e.g., opening a bank account).

Application. Psychologists are encouraged to inform public policy to reduce negative systemic impact on TGNC people and to promote positive social change. Psychologists are encouraged to identify and improve systems that permit violence; educational, employment, and housing discrimination; lack of access to health care; unequal access to other vital resources; and other instances of systemic inequity that TGNC people experience (ACA, 2010). Many TGNC people experience stressors from constant barriers, inequitable treatment, and forced release of sensitive and private information about their bodies and their lives (Hendricks & Testa, 2012). To obtain proper identity documentation, TGNC people may be required to provide court orders, proof of having had surgery, and documentation of psychotherapy or a psychiatric diagnosis. Psychologists may assist TGNC people by normalizing their reactions of fatigue and traumatization while interacting with legal systems and requirements; TGNC people may also benefit from guidance about alternate avenues of recourse, self-advocacy, or appeal. When TGNC people feel that it is unsafe to advocate for themselves, psychologists may work with their clients to access appropriate resources in the community.

Psychologists are encouraged to be sensitive to the challenges of attaining gender-affirming identity documentation and how the receipt or denial of such documentation may affect social and psychological well-being, the person's ability to obtain education and employment, find safe housing, access public benefits, obtain student loans, and access health insurance. It may be of significant assistance for psychologists to understand and offer information about the process of a legal name change, gender marker change on identification, or the process for accessing other gender-affirming documents. Psychologists may consult the National Center for Transgender Equality, the Sylvia Rivera Law Project, or the Transgender Law Center for additional information on identity documentation for TGNC people.

Psychologists may choose to become involved with an organization that seeks to revise law and public policy to better protect the rights and dignities of TGNC people. Psychologists may participate at the local, state, or national level to support TGNC-affirmative health care accessibility, human rights in sex-segregated facilities, or policy change regarding gender-affirming identity documentation. Psychologists working in institutional settings may also expand their roles to work as collaborative advocates for TGNC people (Gonzalez & McNulty, 2010). Psychologists are encouraged to provide written affirmations supporting TGNC people and their gender identity so that they may access necessary services (e.g., hormone therapy).

Life Span Development

Guideline 8. Psychologists working with gender-questioning [4] and TGNC youth understand the different developmental needs of children and adolescents, and that not all youth will persist in a TGNC identity into adulthood.

Rationale. Many children develop stability (constancy across time) in their gender identity between Ages 3 to 4 (Kohlberg, 1966), although gender consistency (recognition that gender remains the same across situations) often does not occur until Ages 4 to 7 (Siegal & Robinson, 1987). Children who demonstrate gender nonconformity in preschool and early elementary years may not follow this trajectory (Zucker & Bradley, 1995). Existing research suggests that between 12% and 50% of children diagnosed with gender dysphoria may persist in their identification with a gender different than sex assigned at birth into late adolescence and young adulthood (Drummond, Bradley,

[4] Gender-questioning youth are differentiated from TGNC youth in this section of the guidelines. Gender-questioning youth may be questioning or exploring their gender identity but have not yet developed a TGNC identity. As such, they may not be eligible for some services that would be offered to TGNC youth. Gender-questioning youth are included here because gender questioning may lead to a TGNC identity.

Peterson-Badaali, & Zucker, 2008; Steensma, McGuire, Kreukels, Beekman, & Cohen-Kettenis, 2013; Wallien & Cohen-Kettenis, 2008). However, several research studies categorized 30% to 62% of youth who did not return to the clinic for medical intervention after initial assessment, and whose gender identity may be unknown, as "desisters" who no longer identified with a gender different than sex assigned at birth (Steensma et al., 2013; Wallien & Cohen-Kettenis, 2008; Zucker, 2008a). As a result, this research runs a strong risk of inflating estimates of the number of youth who do not persist with a TGNC identity. Research has suggested that children who identify more intensely with a gender different than sex assigned at birth are more likely to persist in this gender identification into adolescence (Steensma et al., 2013), and that when gender dysphoria persists through childhood and intensifies into adolescence, the likelihood of long-term TGNC identification increases (A. L. de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2011; Steensma et al., 2013; Wallien & Cohen-Kettenis, 2008; Zucker, 2008b). Gender-questioning children who do not persist may be more likely to later identify as gay or lesbian than non-gender-questioning children (Bailey & Zucker, 1995; Drescher, 2014; Wallien & Cohen-Kettenis, 2008).

A clear distinction between care of TGNC and gender-questioning children and adolescents exists in the literature. Due to the evidence that not all children persist in a TGNC identity into adolescence or adulthood, and because no approach to working with TGNC children has been adequately, empirically validated, consensus does not exist regarding best practice with prepubertal children. Lack of consensus about the preferred approach to treatment may be due in part to divergent ideas regarding what constitutes optimal treatment outcomes for TGNC and gender-questioning youth (Hembree et al., 2009). Two distinct approaches exist to address gender identity concerns in children (Hill, Menvielle, Sica, & Johnson, 2010; Wallace & Russell, 2013), with some authors subdividing one of the approaches to suggest three (Byne et al., 2012; Drescher, 2014; Stein, 2012).

One approach encourages an affirmation and acceptance of children's expressed gender identity. This may include assisting children to socially transition and to begin medical transition when their bodies have physically developed, or allowing a child's gender identity to unfold without expectation of a specific outcome (A. L. de Vries & Cohen-Kettenis, 2012; Edwards-Leeper & Spack, 2012; Ehrensaft, 2012; Hidalgo et al., 2013; Tishelman et al., 2015). Clinicians using this approach believe that an open exploration and affirmation will assist children to develop coping strategies and emotional tools to integrate a positive TGNC identity should gender questioning persist (Edwards-Leeper & Spack, 2012).

In the second approach, children are encouraged to embrace their given bodies and to align with their assigned gender roles. This includes endorsing and supporting behaviors and attitudes that align with the child's sex assigned at birth prior to the onset of puberty (Zucker, 2008a; Zucker, Wood, Singh, & Bradley, 2012). Clinicians using this approach believe that undergoing multiple medical interventions and living as a TGNC person in a world that stigmatizes gender nonconformity is a less desirable outcome than one in which children may be assisted to happily align with their sex assigned at birth (Zucker et al., 2012). Consensus does not exist regarding whether this approach may provide benefit (Zucker, 2008a; Zucker et al., 2012) or may cause harm or lead to psychosocial adversities (Hill et al., 2010; Pyne, 2014; Travers et al., 2012; Wallace & Russell, 2013). When addressing psychological interventions for children and adolescents, the World Professional Association for Transgender Health Standards of Care identify interventions "aimed at trying to change gender identity and expression to become more congruent with sex assigned at birth" as unethical (Coleman et al., 2012, p. 175). It is hoped that future research will offer improved guidance in this area of practice (Adelson & AACAP CQI, 2012; Malpas, 2011).

Much greater consensus exists regarding practice with adolescents. Adolescents presenting with gender identity concerns bring their own set of unique challenges. This may include having a late-onset (i.e., postpubertal) presentation of gender nonconforming identification, with no history of gender role nonconformity or gender questioning in childhood (Edwards-Leeper & Spack, 2012). Complicating their clinical presentation, many gender-questioning adolescents also present with co-occurring psychological concerns, such as suicidal ideation, self-injurious behaviors (Liu & Mustanski, 2012; Mustanski, Garofalo, & Emerson, 2010), drug and alcohol use (Garofalo et al., 2006), and autism spectrum disorders (A. L. de Vries, Noens, Cohen-Kettenis, van Berckelaer-Onnes, & Doreleijers, 2010; Jones et al., 2012). Additionally, adolescents can become intensely focused on their immediate desires, resulting in outward displays of frustration and resentment when faced with any delay in receiving the medical treatment from which they feel they would benefit and to which they feel entitled (Angello, 2013; Edwards-Leeper & Spack, 2012). This intense focus on immediate needs may create challenges in assuring that adolescents are cognitively and emotionally able to make life-altering decisions to change their name or gender marker, begin hormone therapy (which may affect fertility), or pursue surgery.

Nonetheless, there is greater consensus that treatment approaches for adolescents affirm an adolescents' gender identity (Coleman et al., 2012). Treatment options for adolescents extend beyond social approaches to include medical approaches. One particular medical intervention involves the use of puberty-suppressing medication or "blockers" (GnRH analogue), which is a reversible medical intervention used to delay puberty for appropriately screened adolescents with gender dysphoria (Coleman et al., 2012; A. L. C. de Vries et al., 2014; Edwards-Leeper, & Spack, 2012). Because of their age, other medical interventions may also become available to adolescents, and psychologists are frequently consulted to provide an assessment of whether such procedures would be advisable (Coleman et al., 2012).

Application. Psychologists working with TGNC and gender-questioning youth are encouraged to regularly review the most current literature in this area, recognizing the limited available research regarding the potential benefits and risks of different treatment approaches for children and for adolescents. Psychologists are encouraged to offer parents and guardians clear information about available treatment approaches, regardless of the specific approach chosen by the psychologist. Psychologists are encouraged to provide psychological service to TGNC and gender-questioning children and adolescents that draws from empirically validated literature when available, recognizing the influence psychologists' values and beliefs may have on the treatment approaches they select (Ehrbar & Gorton, 2010). Psychologists are also encouraged to remain aware that what one youth and/or parent may be seeking in a therapeutic relationship may not coincide with a clinician's approach (Brill & Pepper, 2008). In cases in which a youth and/or parent identify different preferred treatment outcomes than a clinician, it may not be clinically appropriate for the clinician to continue working with the youth and family, and alternative options, including referral, might be considered. Psychologists may also find themselves navigating family systems in which youth and their caregivers are seeking different treatment outcomes (Edwards-Leeper & Spack, 2012). Psychologists are encouraged to carefully reflect on their personal values and beliefs about gender identity development in conjunction with the available research, and to keep the best interest of the child or adolescent at the forefront of their clinical decisions at all times.

Because gender nonconformity may be transient for younger children in particular, the psychologist's role may be to help support children and their families through the process of exploration and self-identification (Ehrensaft, 2012). Additionally, psychologists may provide parents with information about possible long-term trajectories children may take in regard to their gender identity, along with the available medical interventions for adolescents whose TGNC identification persists (Edwards-Leeper & Spack, 2012).

When working with adolescents, psychologists are encouraged to recognize that some TGNC adolescents will not have a strong history of childhood gender role nonconformity or gender dysphoria either by self-report or family observation (Edwards-Leeper & Spack, 2012). Some of these adolescents may have withheld their feelings of gender nonconformity out of a fear of rejection, confusion, conflating gender identity and sexual orientation, or a lack of awareness of the option to identify as TGNC. Parents of these adolescents may need additional assistance in understanding and supporting their youth, given that late-onset gender dysphoria and TGNC identification may come as a significant surprise. Moving more slowly and cautiously in these cases is often advisable (Edwards-Leeper & Spack, 2012). Given the possibility of adolescents' intense focus on immediate desires and strong reactions to perceived delays or barriers, psychologists are encouraged to validate these concerns and the desire to move through the process quickly while also remaining thoughtful and deliberate in treatment. Adolescents and their families may need support in tolerating ambiguity and uncertainty with regard to gender identity and its development (Brill & Pepper, 2008). It is encouraged that care should be taken not to foreclose this process.

For adolescents who exhibit a long history of gender nonconformity, psychologists may inform parents that the adolescent's self-affirmed gender identity is most likely stable (A. L. de Vries et al., 2011). The clinical needs of these adolescents may be different than those who are in the initial phases of exploring or questioning their gender identity. Psychologists are encouraged to complete a comprehensive evaluation and ensure the adolescent's and family's readiness to progress while also avoiding unnecessary delay for those who are ready to move forward.

Psychologists working with TGNC and gender-questioning youth are encouraged to become familiar with medical treatment options for adolescents (e.g., puberty-suppressing medication, hormone therapy) and work collaboratively with medical providers to provide appropriate care to clients. Because the ongoing involvement of a knowledgeable mental health provider is encouraged due to the psychosocial implications, and is often also a required part of the medical treatment regimen that may be offered to TGNC adolescents (Coleman et al., 2012; Hembree et al., 2009), psychologists often play an essential role in assisting in this process.

Psychologists may encourage parents and caregivers to involve youth in developmentally appropriate decision making about their education, health care, and peer networks, as these relate to children's and adolescents' gender identity and gender expression (Ryan, Russell, Huebner, Diaz, & Sanchez, 2010). Psychologists are also encouraged to educate themselves about the advantages and disadvantages of social transition during childhood and adolescence, and to discuss these factors with both their young clients and clients' parents. Emphasizing to parents the importance of allowing their child the freedom to return to a gender identity that aligns with sex assigned at birth or another gender identity at any point cannot be overstated, particularly given the research that suggests that not all young gender nonconforming children will ultimately express a gender identity different from that assigned at birth (Wallien, & Cohen-Kettenis, 2008; Zucker & Bradley, 1995). Psychologists are encouraged to acknowledge and explore the fear and burden of responsibility that parents and caregivers may feel as they make decisions about the health of their child or adolescent (Grossman, D'Augelli, Howell, & Hubbard, 2006). Parents and caregivers may benefit from a supportive environment to discuss feelings of isolation, explore loss and grief they may experience, vent anger and frustration at systems that disrespect or discriminate against them and their youth, and learn how to communicate with others about their child's or adolescent's gender identity or gender expression (Brill & Pepper, 2008).

Guideline 9. Psychologists strive to understand both the particular challenges that TGNC elders experience and the resilience they can develop.

Rationale. Little research has been conducted about TGNC elders, leaving much to be discovered about this life stage for TGNC people (Auldridge, Tamar-Mattis, Kennedy, Ames, & Tobin, 2012). Socialization into gender role behaviors and expectations based on sex assigned at birth, as well as the extent to which TGNC people adhere to these societal standards, is influenced by the chronological age at which a person self-identifies as TGNC, the age at which a person comes out or socially and/or medically transitions (Birren & Schaie, 2006; Bockting & Coleman, 2007; Cavanaugh & Blanchard-Fields, 2010; Nuttbrock et al., 2010; Wahl, Iwarsson, & Oswald, 2012), and a person's generational cohort (e.g., 1950 vs. 2010; Fredriksen-Goldsen et al., 2011).

Even decades after a medical or social transition, TGNC elders may still subscribe to the predominant gender role expectations that existed at the time of their transition (Knochel, Croghan, Moore, & Quam, 2011). Prior to the 1980s, TGNC people who transitioned were strongly encouraged by providers to pass in society as cisgender and heterosexual and to avoid associating with other TGNC people (Benjamin, 1966; R. Green & Money, 1969; Hastings, 1974; Hastings & Markland, 1978). Even TGNC elders who were comfortable telling others about their TGNC identity when they were younger may choose not to reveal their identity at a later stage of life (Ekins & King, 2005; Ippolito & Witten, 2014). Elders' unwillingness to disclose their TGNC identity can result from feelings of physical vulnerability or increased reliance on others who may discriminate against them or treat them poorly as a result of their gender identity (Bockting & Coleman, 2007), especially if the elder resides in an institutionalized setting (i.e., nursing home, assisted living facility) and relies on others for many daily needs (Auldridge et al., 2012). TGNC elders are also at a heightened risk for depression, suicidal ideation, and loneliness compared with LGB elders (Auldridge et al., 2012; Fredriksen-Goldsen et al., 2011).

A Transgender Law Center survey found that TGNC and LGB elders had less financial well-being than their younger cohorts, despite having a higher than average educational level for their age group compared with the general population (Hartzell, Frazer, Wertz, & Davis, 2009). Survey research has also revealed that TGNC elders experience underemployment and gaps in employment, often due to discrimination (Auldridge et al., 2012; Beemyn & Rankin, 2011; Factor & Rothblum, 2007). In the past, some TGNC people with established careers may have been encouraged by service providers to find new careers or jobs to avoid undergoing a gender transition at work or being identified as TGNC, potentially leading to a significant loss of income and occupational identity (Cook-Daniels, 2006). Obstacles to employment can increase economic disparities that result in increased needs for supportive housing and other social services (National Center for Transgender Equality, 2012; Services and Advocacy for GLBT Elders & National Center for Transgender Equality, 2012).

TGNC elders may face obstacles to seeking or accessing resources that support their physical, financial, or emotional well-being. For instance, they may be concerned about applying for social security benefits, fearing that their TGNC identity may become known (Hartzell et al., 2009). A TGNC elder may avoid medical care, increasing the likelihood of later needing a higher level of medical care (e.g., home-based care, assisted living, or nursing home) than their same-age cisgender peers (Hartzell et al., 2009; Ippolito & Witten, 2014; Mikalson et al., 2012). Nursing homes and assisted living facilities are rarely sensitive to the unique medical needs of TGNC elders (National Senior Citizens Law Center, 2011). Some TGNC individuals who enter congregate housing, assisted living, or long-term care settings may feel the need to reverse their transition to align with sex assigned at birth to avoid discrimination and persecution by other residents and staff (Ippolito & Witten, 2014).

Older age may both facilitate and complicate medical treatment related to gender transition. TGNC people who begin hormone therapy later in life may have a smoother transition due to waning hormone levels that are a natural part of aging (Witten & Eyler, 2012). Age may also influence the decisions TGNC elders make regarding sex-affirmation surgeries, especially if physical conditions exist that could significantly increase risks associated with surgery or recovery.

Much has been written about the resilience of elders who have endured trauma (Fuhrmann & Shevlowitz, 2006; Hardy, Concato, & Gill, 2004; Mlinac, Sheeran, Blissmer, Lees, & Martins, 2011; Rodin & Stewart, 2012). Although some TGNC elders have experienced significant psychological trauma related to their gender identity, some also have developed resilience and effective ways of coping with adversity (Fruhauf & Orel, 2015). Despite the limited availability of LGBTQ-affirmative religious organizations in many local communities, TGNC elders make greater use of these resources than their cisgender peers (Porter et al., 2013).

Application. Psychologists are encouraged to seek information about the biopsychosocial needs of TGNC elders to inform case conceptualization and treatment planning to address psychological, social, and medical concerns. Many TGNC elders are socially isolated. Isolation can occur as a result of a loss of social networks through death or through disclosure of a TGNC identity. Psychologists may assist TGNC elders in establishing new social networks that support and value their TGNC identity, while also working to strengthen existing family and friend networks after a TGNC identity has been disclosed. TGNC elders may find special value in relationships with others in their generational cohort or those who may have similar coming-out experiences. Psychologists may encourage TGNC elders to identify ways they can mentor and improve the resilience of younger TGNC generations, creating a sense of generativity (Erikson, 1968) and contribu-

tion while building new supportive relationships. Psychologists working with TGNC elders may help them recognize the sources of their resilience and encourage them to connect with and be active in their communities (Fuhrmann & Craffey, 2014).

For TGNC elders who have chosen not to disclose their gender identity, psychologists may provide support to address shame, guilt, or internalized antitrans prejudice, and validate each person's freedom to choose their pattern of disclosure. Clinicians may also provide validation and empathy when TGNC elders have chosen a model of transition that avoids any disclosure of gender identity and is heavily focused on passing as cisgender.

TGNC elders who choose to undergo a medical or social transition in older adulthood may experience antitrans prejudice from people who question the value of transition at an older age or who believe that these elders are not truly invested in their transition or in a TGNC identity given the length of time they have waited (Auldridge et al., 2012). Some TGNC elders may also grieve lost time and missed opportunities. Psychologists may validate elders' choices to come out, transition, or evolve their gender identity or gender expression at any age, recognizing that such choices may have been much less accessible or viable at earlier stages of TGNC elders' lives.

Psychologists may assist congregate housing, assisted living, or long-term care settings to best meet TGNC elders' needs through respectful communication and affirmation of each person's gender identity and gender expression. Psychologists may work with TGNC people in hospice care systems to develop an end-of-life plan that respects the person's wishes about disclosure of gender identity during and after death.

Assessment, Therapy, and Intervention

Guideline 10. Psychologists strive to understand how mental health concerns may or may not be related to a TGNC person's gender identity and the psychological effects of minority stress.

Rationale. TGNC people may seek assistance from psychologists in addressing gender-related concerns, other mental health issues, or both. Mental health problems experienced by a TGNC person may or may not be related to that person's gender identity and/or may complicate assessment and intervention of gender-related concerns. In some cases, there may not be a relationship between a person's gender identity and a co-occurring condition (e.g., depression, PTSD, substance abuse). In other cases, having a TGNC identity may lead or contribute to a co-occurring mental health condition, either directly by way of gender dysphoria, or indirectly by way of minority stress and oppression (Hendricks & Testa, 2012; I. H. Meyer, 1995, 2003). In extremely rare cases, a co-occurring condition can mimic gender dysphoria (i.e., a psychotic process that distorts the perception of one's gender; Baltieri & De Andrade, 2009; Hepp, Kraemer, Schnyder, Miller, & Delsignore, 2004).

Regardless of the presence or absence of an etiological link, gender identity may affect how a TGNC person experiences a co-occurring mental health condition, and/or a co-occurring mental health condition may complicate the person's gender expression or gender identity. For example, an eating disorder may be influenced by a TGNC person's gender expression (e.g., rigid eating patterns used to manage body shape or menstruation may be related to gender identity or gender dysphoria; Ålgars, Alanko, Santtila, & Sandnabba, 2012; Murray, Boon, & Touyz, 2013). In addition, the presence of autism spectrum disorder may complicate a TGNC person's articulation and exploration of gender identity (Jones et al., 2012). In cases in which gender dysphoria is contributing to other mental health concerns, treatment of gender dysphoria may be helpful in alleviating those concerns as well (Keo-Meier et al., 2015).

A relationship also exists between mental health conditions and the psychological sequelae of minority stress that TGNC people can experience. Given that TGNC people experience physical and sexual violence (Clements-Nolle et al., 2006; Kenagy & Bostwick, 2005; Lombardi, Wilchins, Priesing, & Malouf, 2001; Xavier et al., 2005), general harassment and discrimination (Beemyn & Rankin, 2011; Factor & Rothblum, 2007), and employment and housing discrimination (Bradford et al., 2007), they are likely to experience significant levels of minority stress. Studies have demonstrated the disproportionately high levels of negative psychological sequelae related to minority stress, including suicidal ideation and suicide attempts (Center for Substance Abuse Treatment, 2012; Clements-Nolle et al., 2006; Cochran & Cauce, 2006; Nuttbrock et al., 2010; Xavier et al., 2005) and completed suicides (Dhejne et al., 2011; van Kesteren, Asscheman, Megens, & Gooren, 1997). Recent studies have begun to demonstrate an association between sources of external stress and psychological distress (Bockting et al., 2013; Nuttbrock et al., 2010), including suicidal ideation and attempts and self-injurious behavior (dickey, Reisner, & Juntunen, 2015; Goldblum et al., 2012; Testa et al., 2012).

The minority stress model accounts for both the negative mental health effects of stigma-related stress and the processes by which members of the minority group may develop resilience and resistance to the negative effects of stress (I. H. Meyer, 1995, 2003). Although the minority stress model was developed as a theory of the relationship between sexual orientation and mental disorders, the model has been adapted to TGNC populations (Hendricks & Testa, 2012).

Application. Because of the increased risk of stress-related mental health conditions, psychologists are encouraged to conduct a careful diagnostic assessment, including a differential diagnosis, when working with TGNC people (Coleman et al., 2012). Taking into account the intricate interplay between the effects of mental health symptoms and gender identity and gender expression, psychologists are encouraged to neither ignore mental health problems a TGNC person is experiencing, nor erroneously

assume that those mental health problems are a result of the person's gender identity or gender expression. Psychologists are strongly encouraged to be cautious before determining that gender nonconformity or dysphoria is due to an underlying psychotic process, as this type of causal relationship is rare.

When TGNC people seek to access transition-related health care, a psychosocial assessment is often part of this process (Coleman et al., 2012). A comprehensive and balanced assessment typically includes not only information about a person's past experiences of antitrans prejudice or discrimination, internalized messages related to these experiences, and anticipation of future victimization or rejection (Coolhart, Provancher, Hager, & Wang, 2008), but also coping strategies and sources of resilience (Hendricks & Testa, 2012; Singh et al., 2011). Gathering information about negative life events directly related to a TGNC person's gender identity and gender expression may assist psychologists in understanding the sequelae of stress and discrimination, distinguishing them from concurrent and potentially unrelated mental health problems. Similarly, when a TGNC person has a primary presenting concern that is not gender focused, a comprehensive assessment takes into account that person's experience relative to gender identity and gender expression, including any discrimination, just as it would include assessing other potential trauma history, medical concerns, previous experience with helping professionals, important future goals, and important aspects of identity. Strategies a TGNC person uses to navigate antitrans discrimination could be sources of strength to deal with life challenges or sources of distress that increase challenges and barriers.

Psychologists are encouraged to help TGNC people understand the pervasive influence of minority stress and discrimination that may exist in their lives, potentially including internalized negative attitudes about themselves and their TGNC identity (Hendricks & Testa, 2012). With this support, clients can better understand the origins of their mental health symptoms and normalize their reactions when faced with TGNC-related inequities and discrimination. Minority stress models also identify potentially important sources of resilience. TGNC people can develop resilience when they connect with other TGNC people who provide information on how to navigate antitrans prejudice and increase access to necessary care and resources (Singh et al., 2011). TGNC people may need help developing social support systems to nurture their resilience and bolster their ability to cope with the adverse effects of antitrans prejudice and/or discrimination (Singh & McKleroy, 2011).

Feminizing or masculinizing hormone therapy can positively or negatively affect existing mood disorders (Coleman et al., 2012). Psychologists may also help TGNC people who are in the initial stages of hormone therapy adjust to normal changes in how they experience emotions. For example, trans women who begin estrogens and antiandrogens may experience a broader range of emotions than they are accustomed to, or trans men beginning testosterone might be faced with adjusting to a higher libido and feeling more emotionally reactive in stressful situations. These changes can be normalized as similar to the emotional adjustments that cisgender women and men experience during puberty. Some TGNC people will be able to adapt existing coping strategies, whereas others may need help developing additional skills (e.g., emotional regulation or assertiveness). Readers are encouraged to refer to the World Professional Association for Transgender Health Standards of Care for discussion of the possible effects of hormone therapy on a TGNC person's mood, affect, and behavior (Coleman et al., 2012).

Guideline 11. Psychologists recognize that TGNC people are more likely to experience positive life outcomes when they receive social support or trans-affirmative care.

Rationale. Research has primarily shown positive treatment outcomes when TGNC adults and adolescents receive TGNC-affirmative medical and psychological services (i.e., psychotherapy, hormones, surgery; Byne et al., 2012; R. Carroll, 1999; Cohen-Kettenis, Delemarre-van de Waal, & Gooren, 2008; Davis & Meier, 2014; De Cuypere et al., 2006; Gooren, Giltay, & Bunck, 2008; Kuhn et al., 2009), although sample sizes are frequently small with no population-based studies. In a meta-analysis of the hormone therapy treatment literature with TGNC adults and adolescents, researchers reported that 80% of participants receiving trans-affirmative care experienced an improved quality of life, decreased gender dysphoria, and a reduction in negative psychological symptoms (Murad et al., 2010).

In addition, TGNC people who receive social support about their gender identity and gender expression have improved outcomes and quality of life (Brill & Pepper, 2008; Pinto, Melendez, & Spector, 2008). Several studies indicate that family acceptance of TGNC adolescents and adults is associated with decreased rates of negative outcomes, such as depression, suicide, and HIV risk behaviors and infection (Bockting et al., 2013; Dhejne et al., 2011; Grant et al., 2011; Liu & Mustanski, 2012; Ryan, 2009). Family support is also a strong protective factor for TGNC adults and adolescents (Bockting et al., 2013; Moody & Smith, 2013; Ryan et al., 2010). TGNC people, however, frequently experience blatant or subtle antitrans prejudice, discrimination, and even violence within their families (Bradford et al., 2007). Such family rejection is associated with higher rates of HIV infection, suicide, incarceration, and homelessness for TGNC adults and adolescents (Grant et al., 2011; Liu & Mustanski, 2012). Family rejection and lower levels of social support are significantly correlated with depression (Clements-Nolle et al., 2006; Ryan, 2009). Many TGNC people seek support through peer relationships, chosen families, and communities in which they may be more likely to experience acceptance (Gonzalez & McNulty, 2010; Nuttbrock et al., 2009). Peer support from other TGNC people has been found to be a moderator between antitrans discrimination and mental health, with higher levels of peer support associated with better mental health (Bockting et al., 2013). For some TGNC people, support from religious and spiritual communities provides

an important source of resilience (Glaser, 2008; Kidd & Witten, 2008; Porter et al., 2013).

Application. Given the strong evidence for the positive influence of affirmative care, psychologists are encouraged to facilitate access to and provide trans-affirmative care to TGNC people. Whether through the provision of assessment and psychotherapy, or through assisting clients to access hormone therapy or surgery, psychologists may play a critical role in empowering and validating TGNC adults' and adolescents' experiences and increasing TGNC people's positive life outcomes (Bess & Stabb, 2009; Rachlin, 2002).

Psychologists are also encouraged to be aware of the importance of affirmative social support and assist TGNC adults and adolescents in building social support networks in which their gender identity is accepted and affirmed. Psychologists may assist TGNC people in negotiating family dynamics that may arise in the course of exploring and establishing gender identity. Depending on the context of psychological practice, these issues might be addressed in individual work with TGNC clients, conjoint sessions including members of their support system, family therapy, or group therapy. Psychologists may help TGNC people decide how and when to reveal their gender identity at work or school, in religious communities, and to friends and contacts in other settings. TGNC people who decide not to come out in all aspects of their lives can still benefit from TGNC-affirmative in-person or online peer support groups.

Clients may ask psychologists to assist family members in exploring feelings about their loved one's gender identity and gender expression. Published models of family adjustment (Emerson & Rosenfeld, 1996) may be useful to help normalize family members' reactions upon learning that they have a TGNC family member, and to reduce feelings of isolation. When working with family members or significant others, it may be helpful to normalize feelings of loss or fear of what may happen to current relationships as TGNC people disclose their gender identity and expression to others. Psychologists may help significant others adjust to changing relationships and consider how to talk to extended family, friends, and other community members about TGNC loved ones. Providing significant others with referrals to TGNC-affirmative providers, educational resources, and support groups can have a profound impact on their understanding of gender identity and their communication with TGNC loved ones. Psychologists working with couples and families may also help TGNC people identify ways to include significant others in their social or medical transition.

Psychologists working with TGNC people in rural settings may provide clients with resources to connect with other TGNC people online or provide information about in-person support groups in which they can explore the unique challenges of being TGNC in these geographic areas (Walinsky & Whitcomb, 2010). Psychologists serving TGNC military and veteran populations are encouraged to be sensitive to the barriers these individuals face, especially for people who are on active duty in the U.S. military (OutServe-Servicemembers Legal Defense Network, n.d.). Psychologists may help TGNC military members and veterans establish specific systems of support that create a safe and affirming space to reduce isolation and to create a network of peers with a shared military experience. Psychologists who work with veterans are encouraged to educate themselves on recent changes to VA policy that support equal access to VA medical and mental health services (Department of Veterans Affairs, Veterans' Health Administration, 2013).

Guideline 12. Psychologists strive to understand the effects that changes in gender identity and gender expression have on the romantic and sexual relationships of TGNC people.

Rationale. Relationships involving TGNC people can be healthy and successful (Kins, Hoebeke, Heylens, Rubens, & De Cuyprere, 2008; Meier, Sharp, Michonski, Babcock, & Fitzgerald, 2013) as well as challenging (Brown, 2007; Iantaffi & Bockting, 2011). A study of successful relationships between TGNC men and cisgender women found that these couples attributed the success of their relationship to respect, honesty, trust, love, understanding, and open communication (Kins et al., 2008). Just as relationships between cisgender people can involve abuse, so can relationships between TGNC people and their partners (Brown, 2007), with some violent partners threatening to disclose a TGNC person's identity to exact control in the relationship (FORGE, n.d.).

In the early decades of medical and social transition for TGNC people, only those whose sexual orientations would be heterosexual posttransition (e.g., trans woman with a cisgender man) were deemed eligible for medical and social transition (Meyerowitz, 2002). This restriction prescribed only certain relationship partners (American Psychiatric Association, 1980; Benjamin, 1966; Chivers & Bailey, 2000), denied access to surgery for trans men identifying as gay or bisexual (Coleman & Bockting, 1988), or trans women identifying as lesbian or bisexual, and even required that TGNC people's existing legal marriages be dissolved before they could gain access to transition care (Lev, 2004).

Disclosure of a TGNC identity can have an important impact on the relationship between TGNC people and their partners. Disclosure of TGNC status earlier in the relationship tends to be associated with better relationship outcomes, whereas disclosure of TGNC status many years into an existing relationship may be perceived as a betrayal (Erhardt, 2007). When a TGNC person comes out in the context of an existing relationship, it can also be helpful if both partners are involved in decision making about the use of shared resources (i.e., how to balance the financial costs of transition with other family needs) and how to share this news with shared supports (i.e., friends and family). Sometimes relationship roles are renegotiated in the context of a TGNC person coming out to their partner (Samons, 2008). Assumptions about what it means to be a "husband" or a "wife" can shift if the gender identity of one's spouse shifts

(Erhardt, 2007). Depending on when gender issues are disclosed and how much of a change this creates in the relationship, partners may grieve the loss of aspects of their partner and the way the relationship used to be (Lev, 2004).

Although increasing alignment between gender identity and gender expression, whether it be through dress, behavior, or through medical interventions (i.e., hormones, surgery), does not necessarily affect to whom a TGNC person is attracted (Coleman et al., 1993), TGNC people may become more open to exploring their sexual orientation, may redefine sexual orientation as they move through transition, or both (Daskalos, 1998; H. Devor, 1993; Schleifer, 2006). Through increased comfort with their body and gender identity, TGNC people may explore aspects of their sexual orientation that were previously hidden or that felt discordant with their sex assigned at birth. Following a medical and/or social transition, a TGNC person's sexual orientation may remain constant or shift, either temporarily or permanently (e.g., renewed exploration of sexual orientation in the context of TGNC identity, shift in attraction or choice of sexual partners, widened spectrum of attraction, shift in sexual orientation identity; Meier, Sharp et al., 2013; Samons, 2008). For example, a trans man previously identified as a lesbian may later be attracted to men (Coleman et al., 1993; dickey, Burnes, & Singh, 2012), and a trans woman attracted to women pretransition may remain attracted to women posttransition (Lev, 2004).

Some TGNC people and their partners may fear the loss of mutual sexual attraction and other potential effects of shifting gender identities in the relationship. Lesbian-identified partners of trans men may struggle with the idea that being in a relationship with a man may cause others to perceive them as a heterosexual couple (Califia, 1997). Similarly, women in heterosexual relationships who later learn that their partners are trans women may be unfamiliar with navigating stigma associated with sexual minority status when viewed as a lesbian couple (Erhardt, 2007). Additionally, partners may find they are not attracted to a partner after transition. As an example, a lesbian whose partner transitions to a male identity may find that she is no longer attracted to this person because she is not sexually attracted to men. Partners of TGNC people may also experience grief and loss as their partners engage in social and/or medical transitions.

Application. Psychologists may help foster resilience in relationships by addressing issues specific to partners of TGNC people. Psychologists may provide support to partners of TGNC people who are having difficulty with their partner's evolving gender identity or transition, or are experiencing others having difficulty with the partner's transition. Partner peer support groups may be especially helpful in navigating internalized antitrans prejudice, shame, resentment, and relationship concerns related to a partner's gender transition. Meeting or knowing other TGNC people, other partners of TGNC people, and couples who have successfully navigated transition may also help TGNC people and their partners and serve as a protective factor (Brown, 2007). When TGNC status is disclosed during an existing relationship, psychologists may help couples explore which relationship dynamics they want to preserve and which they might like to change.

In working with psychologists, TGNC people may explore a range of issues in their relationships and sexuality (dickey et al., 2012), including when and how to come out to current or potential romantic and sexual partners, communicating their sexual desires, renegotiating intimacy that may be lost during the TGNC partner's transition, adapting to bodily changes caused by hormone use or surgery, and exploring boundaries regarding touch, affection, and safer sex practices (Iantaffi & Bockting, 2011; Sevelius, 2009). TGNC people may experience increased sexual self-efficacy through transition. Although psychologists may aid partners in understanding a TGNC person's transition decisions, TGNC people may also benefit from help in cultivating awareness of the ways in which these decisions influence the lives of loved ones.

Guideline 13. Psychologists seek to understand how parenting and family formation among TGNC people take a variety of forms.

Rationale. Psychologists work with TGNC people across the life span to address parenting and family issues (Kenagy & Hsieh, 2005). There is evidence that many TGNC people have and want children (Wierckx et al., 2012). Some TGNC people conceive a child through sexual intercourse, whereas others may foster, adopt, pursue surrogacy, or employ assisted reproductive technologies, such as sperm or egg donation, to build or expand a family (De Sutter, Kira, Verschoor, & Hotimsky, 2002). Based on a small body of research to date, there is no indication that children of TGNC parents suffer long-term negative impacts directly related to parental gender change (R. Green, 1978, 1988; White & Ettner, 2004). TGNC people may find it both challenging to find medical providers who are willing to offer them reproductive treatment and to afford the cost (Coleman et al., 2012). Similarly, adoption can be quite costly, and some TGNC people may find it challenging to find foster care or adoption agencies that will work with them in a nondiscriminatory manner. Current or past use of hormone therapy may limit fertility and restrict a TGNC person's reproductive options (Darnery, 2008; Wierckx et al., 2012). Other TGNC people may have children or families before coming out as TGNC or beginning a gender transition.

TGNC people may present with a range of parenting and family-building concerns. Some will seek support to address issues within preexisting family systems, some will explore the creation or expansion of a family, and some will need to make decisions regarding potential fertility issues related to hormone therapy, pubertal suppression, or surgical transition. The medical and/or social transition of a TGNC parent may shift family dynamics, creating challenges and opportunities for partners, children, and other family members. One study of therapists' reflections on their experiences with TGNC clients suggested that family constellation and the parental relationship was more significant for children than the parent's social and/or medical

transition itself (White & Ettner, 2004). Although research has not documented that the transitions of TGNC people have an effect on their parenting abilities, preexisting partnerships or marriages may not survive the disclosure of a TGNC identity or a subsequent transition (dickey et al., 2012). This may result in divorce or separation, which may affect the children in the family. A positive relationship between parents, regardless of marital status, has been suggested to be an important protective factor for children (Amato, 2001; White & Ettner, 2007). This seems to be the case especially when children are reminded of the parent's love and assured of the parent's continued presence in their life (White & Ettner, 2007). Based on a small body of literature available, it is generally the case that younger children are best able to incorporate the transition of a parent, followed by adult children, with adolescents generally having the most difficulty (White & Ettner, 2007). If separated or divorced from their partners or spouses, TGNC parents may be at risk for loss of custody or visitation rights because some courts presume that there is a nexus between their gender identity or gender expression and parental fitness (Flynn, 2006). This type of prejudice is especially common for TGNC people of color (Grant et al., 2011).

Application. Psychologists are encouraged to attend to the parenting and family-building concerns of TGNC people. When working with TGNC people who have previous parenting experience, psychologists may help TGNC people identify how being a parent may influence decisions to come out as TGNC or to begin a transition (Freeman, Tasker, & Di Ceglie, 2002; Grant et al., 2011; Wierckx et al., 2012). Some TGNC people may choose to delay disclosure until their children have grown and left home (Bethea & McCollum, 2013). Clinical guidelines jointly developed by a Vancouver, British Columbia, TGNC community organization and a health care provider organization encourage psychologists and other mental health providers working with TGNC people to plan for disclosure to a partner, previous partner, or children, and to pay particular attention to resources that assist TGNC people to discuss their identity with children of various ages in developmentally appropriate ways (Bockting et al., 2006). Lev (2004) uses a developmental stage framework for the process that family members are likely to go through in coming to terms with a TGNC family member's identity that some psychologists may find helpful. Awareness of peer support networks for spouses and children of TGNC people can also be helpful (e.g., PFLAG, TransYouth Family Allies). Psychologists may provide family counseling to assist a family in managing disclosure, improve family functioning, and maintain family involvement of the TGNC person, as well as aiding the TGNC person in attending to the ways that their transition process has affected their family members (Samons, 2008). Helping parents to continue to work together to focus on the needs of their children and to maintain family bonds is likely to lead to the best results for the children (White & Ettner, 2007).

For TGNC people with existing families, psychologists may support TGNC people in seeking legal counsel regarding parental rights in adoption or custody. Depending on the situation, this may be desirable even if the TGNC parent is biologically related to the child (Minter & Wald, 2012). Although being TGNC is not a legal impediment to adoption in the United States, there is the potential for overt and covert discrimination and barriers, given the widespread prejudice against TGNC people. The question of whether to disclose TGNC status on an adoption application is a personal one, and a prospective TGNC parent would benefit from consulting a lawyer for legal advice, including what the laws in their jurisdiction say about disclosure. Given the extensive background investigation frequently conducted, it may be difficult to avoid disclosure. Many lawyers favor disclosure to avoid any potential legal challenges during the adoption process (Minter & Wald, 2012).

In discussing family-building options with TGNC people, psychologists are encouraged to remain aware that some of these options require medical intervention and are not available everywhere, in addition to being quite costly (Coleman et al., 2012). Psychologists may work with clients to manage feelings of loss, grief, anger, and resentment that may arise if TGNC people are unable to access or afford the services they need for building a family (Bockting et al., 2006; De Sutter et al., 2002).

When TGNC people consider beginning hormone therapy, psychologists may engage them in a conversation about the possibly permanent effects on fertility to better prepare TGNC people to make a fully informed decision. This may be of special importance with TGNC adolescents and young adults who often feel that family planning or loss of fertility is not a significant concern in their current daily lives, and therefore disregard the long-term reproductive implications of hormone therapy or surgery (Coleman et al., 2012). Psychologists are encouraged to discuss contraception and safer sex practices with TGNC people, given that they may still have the ability to conceive even when undergoing hormone therapy (Bockting, Robinson, & Rosser, 1998). Psychologists may play a critical role in educating TGNC adolescents and young adults and their parents about the long-term effects of medical interventions on fertility and assist them in offering informed consent prior to pursuing such interventions. Although hormone therapy may limit fertility (Coleman et al., 2012), psychologists may encourage TGNC people to refrain from relying on hormone therapy as the sole means of birth control, even when a person has amenorrhea (Gorton & Grubb, 2014). Education on safer sex practices may also be important, as some segments of the TGNC community (e.g., trans women and people of color) are especially vulnerable to sexually transmitted infections and have been shown to have high prevalence and incidence rates of HIV infection (Kellogg, Clements-Nolle, Dilley, Katz, & McFarland, 2001; Nemoto, Operario, Keatley, Han, & Soma, 2004).

Depending on the timing and type of options selected, psychologists may explore the physical, social, and emotional implications should TGNC people choose to delay or

stop hormone therapy, undergo fertility treatment, or become pregnant. Psychological effects of stopping hormone therapy may include depression, mood swings, and reactions to the loss of physical masculinization or feminization facilitated by hormone therapy (Coleman et al., 2012). TGNC people who choose to halt hormone therapy during attempts to conceive or during a pregnancy may need additional psychological support. For example, TGNC people and their families may need help in managing the additional antitrans prejudice and scrutiny that may result when a TGNC person with stereotypically masculine features becomes visibly pregnant. Psychologists may also assist TGNC people in addressing their loss when they cannot engage in reproductive activities that are consistent with their gender identity, or when they encounter barriers to conceiving, adopting, or fostering children not typically faced by other people (Vanderburgh, 2007). Psychologists are encouraged to assess the degree to which reproductive health services are TGNC-affirmative prior to referring TGNC people to them. Psychologists are also encouraged to provide TGNC-affirmative information to reproductive health service personnel when there is a lack of trans-affirmative knowledge.

Guideline 14. Psychologists recognize the potential benefits of an interdisciplinary approach when providing care to TGNC people and strive to work collaboratively with other providers.

Rationale. Collaboration across disciplines can be crucial when working with TGNC people because of the potential interplay of biological, psychological, and social factors in diagnosis and treatment (Hendricks & Testa, 2012). The challenges of living with a stigmatized identity and the need of many TGNC people to transition, socially and/or medically, may call for the involvement of health professionals from various disciplines, including psychologists, psychiatrists, social workers, primary health care providers, endocrinologists, nurses, pharmacists, surgeons, gynecologists, urologists, electrologists, speech therapists, physical therapists, pastoral counselors and chaplains, and career or educational counselors. Communication, cooperation, and collaboration will ensure optimal coordination and quality of care. Just as psychologists often refer TGNC people to medical providers for assessment and treatment of medical issues, medical providers may rely on psychologists to assess readiness and assist TGNC clients to prepare for the psychological and social aspects of transition before, during, and after medical interventions (Coleman et al., 2012; Hembree et al., 2009; Lev, 2009). Outcome research to date supports the value and effectiveness of an interdisciplinary, collaborative approach to TGNC-specific care (see Coleman et al., 2012 for a review).

Application. Psychologists' collaboration with colleagues in medical and associated health disciplines involved in TGNC clients' care (e.g., hormonal and surgical treatment, primary health care; Coleman et al., 2012; Lev, 2009) may take many forms and should occur in a timely manner that does not complicate access to needed services (e.g., considerations of wait time). For example, a psychologist working with a trans man who has a diagnosis of bipolar disorder may need to coordinate with his primary care provider and psychiatrist to adjust his hormone levels and psychiatric medications, given that testosterone can have an activating effect, in addition to treating gender dysphoria. At a basic level, collaboration may entail the creation of required documentation that TGNC people present to surgeons or medical providers to access gender-affirming medical interventions (e.g., surgery, hormone therapy; Coleman et al., 2012). Psychologists may offer support, information, and education to interdisciplinary colleagues who are unfamiliar with issues of gender identity and gender expression to assist TGNC people in obtaining TGNC-affirmative care (Holman & Goldberg, 2006; Lev, 2009). For example, a psychologist who is assisting a trans woman with obtaining gender-affirming surgery may, with her consent, contact her new gynecologist in preparation for her first medical visit. This contact could include sharing general information about her gender history and discussing how both providers could most affirmatively support appropriate health checks to ensure her best physical health (Holman & Goldberg, 2006).

Psychologists in interdisciplinary settings could also collaborate with medical professionals prescribing hormone therapy by educating TGNC people and ensuring TGNC people are able to make fully informed decisions prior to starting hormone treatment (Coleman et al., 2012; Deutsch, 2012; Lev, 2009). Psychologists working with children and adolescents play a particularly important role on the interdisciplinary team due to considerations of cognitive and social development, family dynamics, and degree of parental support. This role is especially crucial when providing psychological evaluation to determine the appropriateness and timeliness of a medical intervention. When psychologists are not part of an interdisciplinary setting, especially in isolated or rural communities, they can identify interdisciplinary colleagues with whom they may collaborate and/or refer (Walinsky & Whitcomb, 2010). For example, a rural psychologist could identify a trans-affirmative pediatrician in a surrounding area and collaborate with the pediatrician to work with parents raising concerns about their TGNC and questioning children and adolescents.

In addition to working collaboratively with other providers, psychologists who obtain additional training to specialize in work with TGNC people may also serve as consultants in the field (e.g., providing additional support to providers working with TGNC people or assisting school and workplaces with diversity training). Psychologists who have expertise in working with TGNC people may play a consultative role with providers in inpatient settings seeking to provide affirmative care to TGNC clients. Psychologists may also collaborate with social service colleagues to provide TGNC people with affirmative referrals related to housing, financial support, vocational/educational counseling and training, TGNC-affirming religious or spiritual communities, peer support, and other community resources (Gehi & Arkles, 2007). This collaboration might also in-

clude assuring that TGNC people who are minors in the care of the state have access to culturally appropriate care.

Research, Education, and Training

Guideline 15. Psychologists respect the welfare and rights of TGNC participants in research and strive to represent results accurately and avoid misuse or misrepresentation of findings.

Rationale. Historically, in a set of demographic questions, psychological research has included one item on either sex or gender, with two response options—male and female. This approach wastes an opportunity to increase knowledge about TGNC people for whom neither option may fit their identity, and runs the risk of alienating TGNC research participants (IOM, 2011). For example, there is little knowledge about HIV prevalence, risks, and prevention needs of TGNC people because most of the research on HIV has not included demographic questions to identify TGNC participants within their samples. Instead, TGNC people have been historically subsumed within larger demographic categories (e.g., men who have sex with men, women of color), rendering the impact of the HIV epidemic on the TGNC population invisible (Herbst et al., 2008). Scholars have noted that this invisibility fails to draw attention to the needs of TGNC populations that experience the greatest health disparities, including TGNC people who are of color, immigrants, low income, homeless, veterans, incarcerated, live in rural areas, or have disabilities (Bauer et al., 2009; Hanssmann, Morrison, Russian, Shiu-Thornton, & Bowen, 2010; Shipherd et al., 2012; Walinsky & Whitcomb, 2010).

There is a great need for more research to inform practice, including affirmative treatment approaches with TGNC people. Although sufficient evidence exists to support current standards of care (Byne et al., 2012; Coleman et al., 2012), much is yet to be learned to optimize quality of care and outcome for TGNC clients, especially as it relates to the treatment of children (IOM, 2011; Mikalson et al., 2012). In addition, some research with TGNC populations has been misused and misinterpreted, negatively affecting TGNC people's access to health services to address issues of gender identity and gender expression (Namaste, 2000). This has resulted in justifiable skepticism and suspicion in the TGNC community when invited to participate in research initiatives. In accordance with the APA ethics code (APA, 2010), psychologists conduct research and distribute research findings with integrity and respect for their research participants. As TGNC research increases, some TGNC communities may experience being oversampled in particular geographic areas and/or TGNC people of color may not be well-represented in TGNC studies (Hwahng & Lin, 2009; Namaste, 2000).

Application. All psychologists conducting research, even when not specific to TGNC populations, are encouraged to provide a range of options for capturing demographic information about TGNC people so that TGNC people may be included and accurately represented (Conron et al., 2008; Deutsch et al., 2013). One group of experts has recommended that population research, and especially government-sponsored surveillance research, use a two-step method, first asking for sex assigned at birth, and then following with a question about gender identity (GenIUSS, 2013). For research focused on TGNC people, including questions that assess both sex assigned at birth and current gender identity allows the disaggregation of subgroups within the TGNC population and has the potential to increase knowledge of differences within the population. In addition, findings about one subgroup of TGNC people may not apply to other subgroups. For example, results from a study of trans women of color with a history of sex work who live in urban areas (Nemoto, Operario, Keatley, & Villegas, 2004) may not generalize to all TGNC women of color or to the larger TGNC population (Bauer, Travers, Scanlon, & Coleman, 2012; Operario et al., 2008).

In conducting research with TGNC people, psychologists will confront the challenges associated with studying a relatively small, geographically dispersed, diverse, stigmatized, hidden, and hard-to-reach population (IOM, 2011). Because TGNC individuals are often hard to reach (IOM, 2011) and TGNC research is rapidly evolving, it is important to consider the strengths and limitations of the methods that have been or may be used to study the TGNC population, and to interpret and represent findings accordingly. Some researchers have strongly recommended collaborative research models (e.g., participatory action research) in which TGNC community members are integrally involved in these research activities (Clements-Nolle & Bachrach, 2003; Singh, Richmond, & Burnes, 2013). Psychologists who seek to educate the public by communicating research findings in the popular media will also confront challenges, because most journalists have limited knowledge about the scientific method and there is potential for the media to misinterpret, exploit, or sensationalize findings (Garber, 1992; Namaste, 2000).

Guideline 16. Psychologists Seek to Prepare Trainees in Psychology to Work Competently With TGNC People.

Rationale. The *Ethical Principles of Psychologists and Code of Conduct* (APA, 2010) include gender identity as one factor for which psychologists may need to obtain training, experience, consultation, or supervision in order to ensure their competence (APA, 2010). In addition, when APA-accredited programs are required to demonstrate a commitment to cultural and individual diversity, gender identity is specifically included (APA, 2015). Yet surveys of TGNC people suggest that many mental health care providers lack even basic knowledge and skills required to offer trans-affirmative care (Bradford et al., 2007; O'Hara, Dispenza, Brack, & Blood, 2013; Xavier et al., 2005). The APA Task Force on Gender Identity and Gender Variance (2009) projected that many, if not most, psychologists and graduate psychology students will at some point encounter TGNC people among their clients, colleagues, and trainees. Yet professional education and training in psychology includes little or no preparation for

working with TGNC people (Anton, 2009; APA TFGIGV, 2009), and continuing professional education available to practicing mental health clinicians is also scant (Lurie, 2005). Only 52% percent of psychologists and graduate students who responded to a survey conducted by an APA Task Force reported having had the opportunity to learn about TGNC issues in school; of those respondents, only 27% reported feeling adequately familiar with gender concerns (n = 294; APA TFGIGV, 2009).

Training on gender identity in professional psychology has frequently been subsumed under discussions of sexual orientation or in classes on human sexuality. Some scholars have suggested that psychologists and students may mistakenly believe that they have obtained adequate knowledge and awareness about TGNC people through training focused on LGB populations (Harper & Schneider, 2003). However, Israel and colleagues have found important differences between the therapeutic needs of TGNC people and those of LGB people in the perceptions of both clients and providers (Israel et al., 2008; Israel, Walther, Gorcheva, & Perry, 2011). Nadal and colleagues have suggested that the absence of distinct, accurate information about TGNC populations in psychology training not only perpetuates misunderstanding and marginalization of TGNC people by psychologists but also contributes to continued marginalization of TGNC people in society as a whole (Nadal et al., 2010, 2012).

Application. Psychologists strive to continue their education on issues of gender identity and gender expression with TGNC people as a foundational component of affirmative psychological practice. In addition to these guidelines, which educators may use as a resource in developing curricula and training experiences, ACA (2010) has also adopted a set of competencies that may be a helpful resource for educators. In addition to including TGNC people and their issues in foundational education in health service psychology (e.g., personality development, multiculturalism, research methods), some psychology programs may also provide coursework and training for students interested in developing more advanced expertise on issues of gender identity and gender expression.

Because of the high level of societal ignorance and stigma associated with TGNC people, ensuring that psychological education, training, and supervision is affirmative, and does not sensationalize (Namaste, 2000), exploit, or pathologize TGNC people (Lev, 2004), will require care on the part of educators. Students will benefit from support from their educators in developing a professional, nonjudgmental attitude toward people who may have a different experience of gender identity and gender expression from their own. A number of training resources have been published that may be helpful to psychologists in integrating information about TGNC people into the training they offer (e.g., Catalano, McCarthy, & Shlasko, 2007; Stryker, 2008; Wentling, Schilt, Windsor, & Lucal, 2008). Because most psychologists have had little or no training on TGNC populations and do not perceive themselves as having sufficient understanding of issues related to gender identity and gender expression (APA TFGIGV, 2009), psychologists with relevant expertise are encouraged to develop and distribute continuing education and training to help to address these gaps. Psychologists providing education can incorporate activities that increase awareness of cisgender privilege, antitrans prejudice and discrimination, host a panel of TGNC people to offer personal perspectives, or include narratives of TGNC people in course readings (ACA, 2010). When engaging these approaches, it is important to include a wide variety of TGNC experiences to reflect the inherent diversity within the TGNC community.

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Appendix A
Definitions

Terminology within the health care field and transgender and gender nonconforming (TGNC) communities is constantly evolving (Coleman et al., 2012). The evolution of terminology has been especially rapid in the last decade, as the profession's awareness of gender diversity has increased, as more literature and research in this area has been published, and as voices of the TGNC community have strengthened. Some terms or definitions are not universally accepted, and there is some disagreement among professionals and communities as to the "correct" words or definitions, depending on theoretical orientation, geographic region, generation, or culture, with some terms seen as affirming and others as outdated or demeaning. American Psychological Association (APA) Task Force for *Guidelines for Psychological Practice with Transgender and Gender Nonconforming People* developed the definitions below by reviewing existing definitions put forward by professional organizations (e.g., APA Task Force on Gender Identity and Gender Variance, 2009; the Institute of Medicine, 2011; and the World Professional Association for Transgender Health [Coleman et al., 2012]), health care agencies serving TGNC clients (e.g., Fenway Health Center), TGNC community resources (Gender Equity Resource Center, National Center for Transgender Equality), and professional literature. Psychologists are encouraged to refresh their knowledge and familiarity with evolving terminology on a regular basis as changes emerge in the community and/or the professional literature. The definitions below include terms frequently used within the *Guidelines*, by the TGNC community, and within professional literature.

Ally: a cisgender person who supports and advocates for TGNC people and/or communities.

(*Appendices continue*)

Antitrans prejudice (transprejudice, transnegativity, transphobia): prejudicial attitudes that may result in the devaluing, dislike, and hatred of people whose gender identity and/or gender expression do not conform to their sex assigned at birth. Antitrans prejudice may lead to discriminatory behaviors in such areas as employment and public accommodations, and may lead to harassment and violence. When TGNC people hold these negative attitudes about themselves and their gender identity, it is called *internalized transphobia* (a construct analogous to internalized homophobia). Transmisogyny describes a simultaneous experience of sexism and antitrans prejudice with particularly adverse effects on trans women.

Cisgender: an adjective used to describe a person whose gender identity and gender expression align with sex assigned at birth; a person who is not TGNC.

Cisgenderism: a systemic bias based on the ideology that gender expression and gender identities are determined by sex assigned at birth rather than self-identified gender identity. Cisgenderism may lead to prejudicial attitudes and discriminatory behaviors toward TGNC people or to forms of behavior or gender expression that lie outside of the traditional gender binary.

Coming out: a process by which individuals affirm and actualize a stigmatized identity. Coming out as TGNC can include disclosing a gender identity or gender history that does not align with sex assigned at birth or current gender expression. Coming out is an individual process and is partially influenced by one's age and other generational influences.

Cross dressing: wearing clothing, accessories, and/or make-up, and/or adopting a gender expression not associated with a person's assigned sex at birth according to cultural and environmental standards (Bullough & Bullough, 1993). Cross-dressing is not always reflective of gender identity or sexual orientation. People who cross-dress may or may not identify with the larger TGNC community.

Disorders of sex development (DSD, Intersex): term used to describe a variety of medical conditions associated with atypical development of an individual's physical sex characteristics (Hughes, Houk, Ahmed, & Lee, 2006). These conditions may involve differences of a person's internal and/or external reproductive organs, sex chromosomes, and/or sex-related hormones that may complicate sex assignment at birth. DSD conditions may be considered variations in biological diversity rather than disorders (M. Diamond, 2009); therefore some prefer the terms *intersex*, *intersexuality*, or *differences in sex development* rather than "disorders of sex development" (Coleman et al., 2012).

Drag: the act of adopting a gender expression, often as part of a performance. Drag may be enacted as a political comment on gender, as parody, or as entertainment, and is not necessarily reflective of gender identity.

Female-to-male (FTM): individuals assigned a female sex at birth who have changed, are changing, or wish to change their body and/or gender identity to a more masculine body or gender identity. FTM persons are also often referred to as *transgender men*, *transmen*, or *trans men*.

Gatekeeping: the role of psychologists and other mental health professionals of evaluating a TGNC person's eligibility and readiness for hormone therapy or surgery according to the Standards of Care set forth by the World Professional Association for Transgender Health (Coleman et al., 2012). In the past, this role has been perceived as limiting a TGNC adult's autonomy and contributing to mistrust between psychologists and TGNC clients. Current approaches are sensitive to this history and are more affirming of a TGNC adult's autonomy in making decisions with regard to medical transition (American Counseling Association, 2010; Coleman et al., 2012; Singh & Burnes, 2010).

Gender-affirming surgery (sex reassignment surgery or gender reassignment surgery): surgery to change primary and/or secondary sex characteristics to better align a person's physical appearance with their gender identity. Gender-affirming surgery can be an important part of medically necessary treatment to alleviate gender dysphoria and may include mastectomy, hysterectomy, metoidioplasty, phalloplasty, breast augmentation, orchiectomy, vaginoplasty, facial feminization surgery, and/or other surgical procedures.

Gender binary: the classification of gender into two discrete categories of boy/man and girl/woman.

Gender dysphoria: discomfort or distress related to incongruence between a person's gender identity, sex assigned at birth, gender identity, and/or primary and secondary sex characteristics (Knudson, De Cuypere, & Bockting, 2010). In 2013, the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM–5*; American Psychiatric Association, 2013) adopted the term *gender dysphoria* as a diagnosis characterized by "a marked incongruence between" a person's gender assigned at birth and gender identity (American Psychiatric Association, 2013, p. 453). Gender dysphoria replaced the diagnosis of gender identity disorder (GID) in the previous version of the *DSM* (American Psychiatric Association, 2000).

Gender expression: the presentation of an individual, including physical appearance, clothing choice and accessories, and behaviors that express aspects of gender identity or role. Gender expression may or may not conform to a person's gender identity.

(*Appendices continue*)

Gender identity: a person's deeply felt, inherent sense of being a boy, a man, or male; a girl, a woman, or female; or an alternative gender (e.g., genderqueer, gender nonconforming, gender neutral) that may or may not correspond to a person's sex assigned at birth or to a person's primary or secondary sex characteristics. Because gender identity is internal, a person's gender identity is not necessarily visible to others. "Affirmed gender identity" refers to a person's gender identity after coming out as TGNC or undergoing a social and/or medical transition process.

Gender marker: an indicator (M, F) of a person's sex or gender found on identification (e.g., driver's license, passport) and other legal documents (e.g., birth certificate, academic transcripts).

Gender nonconforming (GNC): an adjective used as an umbrella term to describe people whose gender expression or gender identity differs from gender norms associated with their assigned birth sex. Subpopulations of the TGNC community can develop specialized language to represent their experience and culture, such as the term "masculine of center" (MOC; Cole & Han, 2011) that is used in communities of color to describe one's GNC identity.

Gender questioning: an adjective to describe people who may be questioning or exploring their gender identity and whose gender identity may not align with their sex assigned at birth.

Genderqueer: a term to describe a person whose gender identity does not align with a binary understanding of gender (i.e., a person who does not identify fully as either a man or a woman). People who identify as genderqueer may redefine gender or decline to define themselves as gendered altogether. For example, people who identify as genderqueer may think of themselves as both man and woman (bigender, pangender, androgyne); neither man nor woman (genderless, gender neutral, neutrois, agender); moving between genders (genderfluid); or embodying a third gender.

Gender role: refers to a pattern of appearance, personality, and behavior that, in a given culture, is associated with being a boy/man/male or being a girl/woman/female. The appearance, personality, and behavior characteristics may or may not conform to what is expected based on a person's sex assigned at birth according to cultural and environmental standards. Gender role may also refer to the *social* role in which one is living (e.g., as a woman, a man, or another gender), with some role characteristics conforming and others not conforming to what is associated with girls/women or boys/men in a given culture and time.

Hormone therapy (gender-affirming hormone therapy, hormone replacement therapy): the use of hormones to masculinize or feminize a person's body to better align that person's physical characteristics with their gender identity. People wishing to feminize their body receive antiandrogens and/or estrogens; people wishing to masculinize their body receive testosterone. Hormone therapy may be an important part of medically necessary treatment to alleviate gender dysphoria.

Male-to-female (MTF): individuals whose assigned sex at birth was male and who have changed, are changing, or wish to change their body and/or gender role to a more feminized body or gender role. MTF persons are also often referred to as *transgender women*, *transwomen*, or *trans women*.

Passing: the ability to blend in with cisgender people without being recognized as transgender based on appearance or gender role and expression; being perceived as cisgender. Passing may or may not be a goal for all TGNC people.

Puberty suppression (puberty blocking, puberty delaying therapy): a treatment that can be used to temporarily suppress the development of secondary sex characteristics that occur during puberty in youth, typically using gonadotropin-releasing hormone (GnRH) analogues. Puberty suppression may be an important part of medically necessary treatment to alleviate gender dysphoria. Puberty suppression can provide adolescents time to determine whether they desire less reversible medical intervention and can serve as a diagnostic tool to determine if further medical intervention is warranted.

Sex (sex assigned at birth): sex is typically assigned at birth (or before during ultrasound) based on the appearance of external genitalia. When the external genitalia are ambiguous, other indicators (e.g., internal genitalia, chromosomal and hormonal sex) are considered to assign a sex, with the aim of assigning a sex that is most likely to be congruent with the child's gender identity (MacLaughlin & Donahoe, 2004). For most people, gender identity is congruent with sex assigned at birth (see *cisgender*); for TGNC individuals, gender identity differs in varying degrees from sex assigned at birth.

Sexual orientation: a component of identity that includes a person's sexual and emotional attraction to another person and the behavior and/or social affiliation that may result from this attraction. A person may be attracted to men, women, both, neither, or to people who are genderqueer, androgynous, or have other gender identities. Individuals may identify as lesbian, gay, heterosexual, bisexual, queer, pansexual, or asexual, among others.

Stealth (going stealth): a phrase used by some TGNC people across the life span (e.g., children, adolescents) who choose to make a transition in a new environment (e.g., school) in their affirmed gender without openly sharing their identity as a TGNC person.

(*Appendices continue*)

TGNC: an abbreviation used to refer to people who are transgender or gender nonconforming.

Trans: common short-hand for the terms transgender, transsexual, and/or gender nonconforming. Although the term "trans" is commonly accepted, not all transsexual or gender nonconforming people identify as trans.

Trans-affirmative: being respectful, aware and supportive of the needs of TGNC people.

Transgender: an adjective that is an umbrella term used to describe the full range of people whose gender identity and/or gender role do not conform to what is typically associated with their sex assigned at birth. Although the term "transgender" is commonly accepted, not all TGNC people self-identify as transgender.

Transgender man, trans man, or transman: a person whose sex assigned at birth was female, but who identifies as a man (see FTM).

Transgender woman, trans woman, or transwoman: a person whose sex assigned at birth was male, but who identifies as a woman (see MTF).

Transition: a process some TGNC people progress through when they shift toward a gender role that differs from the one associated with their sex assigned at birth. The length, scope, and process of transition are unique to each person's life situation. For many people, this involves developing a gender role and expression that is more aligned with their gender identity. A transition typically occurs over a period of time; TGNC people may proceed through a social transition (e.g., changes in gender expression, gender role, name, pronoun, and gender marker) and/or a medical transition (e.g., hormone therapy, surgery, and/or other interventions).

Transsexual: term to describe TGNC people who have changed or are changing their bodies through medical interventions (e.g., hormones, surgery) to better align their bodies with a gender identity that is different than their sex assigned at birth. Not all people who identify as transsexual consider themselves to be TGNC. For example, some transsexual individuals identify as female or male, without identifying as TGNC. Transsexualism is used as a medical diagnosis in the World Health Organization's (2015) International Classification of Diseases version 10.

Two-spirit: term used by some Native American cultures to describe people who identify with both male and female gender roles; this can include both gender identity and sexual orientation. Two-spirit people are often respected and carry unique spiritual roles for their community.

Appendix B
Guidelines for Psychological Practice With Transgender and Gender Nonconforming People

Foundational Knowledge and Awareness

Guideline 1. Psychologists understand that gender is a nonbinary construct that allows for a range of gender identities and that a person's gender identity may not align with sex assigned at birth.

Guideline 2. Psychologists understand that gender identity and sexual orientation are distinct but interrelated constructs.

Guideline 3. Psychologists seek to understand how gender identity intersects with the other cultural identities of TGNC people.

Guideline 4. Psychologists are aware of how their attitudes about and knowledge of gender identity and gender expression may affect the quality of care they provide to TGNC people and their families.

Stigma, Discrimination, and Barriers to Care

Guideline 5. Psychologists recognize how stigma, prejudice, discrimination, and violence affect the health and well-being of TGNC people.

Guideline 6. Psychologists strive to recognize the influence of institutional barriers on the lives of TGNC people and to assist in developing TGNC-affirmative environments.

Guideline 7. Psychologists understand the need to promote social change that reduces the negative effects of stigma on the health and well-being of TGNC people.

(*Appendices continue*)

Life Span Development

Guideline 8. Psychologists working with gender-questioning and TGNC youth understand the different developmental needs of children and adolescents and that not all youth will persist in a TGNC identity into adulthood.

Guideline 9. Psychologists strive to understand both the particular challenges that TGNC elders experience and the resilience they can develop.

Assessment, Therapy, and Intervention

Guideline 10. Psychologists strive to understand how mental health concerns may or may not be related to a TGNC person's gender identity and the psychological effects of minority stress.

Guideline 11. Psychologists recognize that TGNC people are more likely to experience positive life outcomes when they receive social support or trans-affirmative care.

Guideline 12. Psychologists strive to understand the effects that changes in gender identity and gender expression have on the romantic and sexual relationships of TGNC people.

Guideline 13. Psychologists seek to understand how parenting and family formation among TGNC people take a variety of forms.

Guideline 14. Psychologists recognize the potential benefits of an interdisciplinary approach when providing care to TGNC people and strive to work collaboratively with other providers.

Research, Education, and Training

Guideline 15. Psychologists respect the welfare and rights of TGNC participants in research and strive to represent results accurately and avoid misuse or misrepresentation of findings.

Guideline 16. Psychologists Seek to Prepare Trainees in Psychology to Work Competently With TGNC People.

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DEFENDANT'S EXHIBIT 26

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER, *et al.*,	)	
Plaintiffs,	)	
v.	)	No. 2:22-cv-00184-LCB-SRW
KAY IVEY, in her official capacity as Governor of the State of Alabama, *et al.*,	)	
Defendants.	)	

DECLARATION OF CORINNA COHN

My name is Corinna Cohn. I am over the age of 19, I am qualified to give this declaration, and, I have personal knowledge of the matters set forth herein.

In or about 2nd grade, I saw a psychologist for problems related to being bullied and emotional regulation. After less than a year, my parents chose to discontinue therapy. I continued to be bullied and had problems forming friendships. Other boys excluded me from social activities. Later in elementary school I began to pray to be made into a girl, which I thought would allow me to fit in better. This became a fixation for me.

In high school, I confessed to my parents that I wanted to become a woman. They brought me to see the same psychologist I'd had as a child, and she diagnosed me with having gender identity disorder. Upon receiving this diagnosis, my parents again chose to discontinue my therapy. I continued to have problems socializing at school and experienced depression and anxiety on a daily basis.

At the age of 17, I gained access to the Internet. This was prior to the popularization of the World Wide Web, but I was able to use message boards and chat in order to find other members of what today would be called the "trans community". Adult transgender women befriended me, supplied me with validation and support, and provided information on how I could transition to also become a transgender woman.

At the age of 18, I resumed my sessions with my psychologist with the goal of receiving a prescription for cross-sex hormones and eventual sex reassignment surgery. Due to my prior relationship with my psychologist, I was able to gain a letter of recommendation to an endocrinologist and was prescribed estrogen. The endocrinologist was referred to me by transgender friends on the Internet. I began living as a woman and had my legal identification updated to reflect my chosen name.

I had sex reassignment surgery in Neenah, Wisconsin in 1994. I was only 19 years old. Securing the appointment required letters from two therapists along with a letter from my endocrinologist. My surgeon told me I was the second-youngest patient he had operated on. The surgery involved removal of my testicles, penectomy, and vaginoplasty. It was successful and without complication.

After healing from my sex change surgery I thought that my transition journey was over. I discontinued therapy, and I began focusing on my career. I found it was easier to socialize and make new friends with my new confidence and feelings of being my authentic self. As I reached my late twenties, my friends began pairing off and starting families. I discovered that it was very difficult to find a partner who wanted to do the same with me.

Although I was in denial for several years, I eventually realized that my depression and anxiety related to my gender identity had not resolved. It was not unusual for me to spend entire weekends in my room crying and entertaining thoughts of suicide.

In my mid-thirties I became interested in radical feminism. I am not a feminist, nor have I ever been, but I wanted to reconcile how feminist concepts applied to people like myself: males who try to turn ourselves into women. One of the concepts I found pivotal was the feminist criticism of biological essentialism, which challenges the idea that men and women are destined to fulfill rigid sex roles. Once I understood this criticism I realized that my more stereotypically feminine attitudes and behaviors did not therefore make me a woman, but rather a feminine man. In retrospect, my self-perception of being a woman also required that I overlook or discount traits that are more stereotypically masculine. Although it took time for this realization to fully sink in, a side effect was that I stopped having bouts of depression and anxiety related to my gender identity. I have not had any depressive episodes related to gender identity in ten years. As a teenager I was unprepared to understand the consequences of my decision to medicalize my transition despite the rigorous controls that were then in place to ensure that patients would not be harmed from gender affirming care.

In 2019, I co-founded a non-profit dedicated to advocating for patients of gender care services. Through the Gender Care Consumer Advocacy Network (GCCAN), I have spoken with other patients and gender clinicians to identify opportunities that can benefit patients and improve the quality of care delivered. The gender clinicians I have spoken with have admitted that they do not follow the World Professional Association of Transgender Health standards of care because they are viewed to be needlessly restrictive. It is GCCAN's position to oppose

criminalization of gender affirmative care, but it is evident that gender clinicians treating adolescents are not abiding by the existing standards of care and that they are not self-regulating. Individuals are in a difficult position to be made whole when injured as it is common for transgender patients to rationalize or forgive poor treatment lest they lose access to their providers altogether. The reticence of gender clinicians to avoid harming their patients has created a vacuum for legislators to address.

I wish I could persuade other boys who wish to become women that the changes they seek are only superficial. Hormones and surgery are unable to reveal an authentic self, and anyone who promises otherwise is, in my opinion, deliberately misleading young people to follow a one-way track to a lifetime of medicalization. Although some people may choose to transition, and may even enjoy a higher quality of life, there is no reason why this irreversible decision needs to be made in adolescence. Adults who advocate for adolescent transition do so without understanding what tradeoffs early transition entails, which includes the loss of fertility, the likelihood of sexual dysfunction, and the likelihood of surgical complication inflicted at an early age from elective procedures. Unfortunately, I do understand some of these tradeoffs. While I would not want to see well-meaning family doctors prosecuted for trying to help a dysphoric child, until such a time as there is clear evidence that adolescent transition is likely to help, adolescent gender affirming care should be heavily scrutinized.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed on April 26, 2022.

Corinna Cohn

DEFENDANT'S EXHIBIT 27

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Sydney Wright In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, Sydney Wright, declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") is a necessary, potentially life-saving law that will protect vulnerable children and their parents from the heartbreaking regret, irreversible physical changes, and emotional pain that I have experienced after undertaking medical interventions aimed at "transitioning" me from a female to a male.

3. I'm a 23-year-old woman who spent a year as a "transman" after being rushed into taking mega doses of testosterone at age 18.

4. I began to identify as transgender in 2017 during counseling after reading about transgenderism on the internet. I had not experienced feelings of gender dysphoria prior to this time.

5. A neighborhood boy engaged in sexually touching with me from age 5 to 12. This awakened sexual feelings at too young an age and caused me to feel unsafe.

6. I was very tomboyish growing up and was sometimes bullied. I began having same-sex attractions as a teen. I was raised in a strict religious home, where homosexuality was frowned upon. When my father learned that I had same-sex attractions he kicked me out of his house (my parents divorced when I was 12) and I went to live with my mother.

7. I was first introduced to transgenderism on social media at around age 18. I began to question if I was really a man because I was attracted to girls.

8. I cut my long blond hair, which caused me to look more masculine. This made me want to move quickly through transition.

9. I started seeing a counselor on June 13, 2017. I disclosed to the counselor that I had been sexually molested for years as a child, about my parents' contentious divorce, and about my dysfunctional relationship with both parents. I also disclosed that I was in a dysfunctional marriage to a physically abusive woman who brought and sold drugs.

10. The counselor did not explore how any of this history might be contributing to my dysphoria, but simply asked some questions and diagnosed me with gender dysphoria and gave me a recommendation to a physician for testosterone treatment within five weeks of our first meeting.

11. My frame of mind at the time, at age 18, was that I believed I might have been "born in the wrong body" and needed to correct it. But I was also unsure,

confused, and in need of guidance. Had a professional told me the truth and helped me explore why I was distressed by being a girl (and a lesbian) in a nonjudgmental way, I would not have proceeded with testosterone.

12. However, that was not the case, and I met with the doctor to whom the counselor referred me. The visit lasted less than 10 minutes, during which time the doctor was curt and rude. He asked me for my "hormone letter," but did not open it or read it. He did not ask any questions to confirm that I had gender dysphoria or any questions concerning my medical history or past or present physical condition or symptoms.

13. I told the doctor that I was nervous, and he curtly asked, "Do you want to do this?" and told me I could pick up the testosterone that day. I asked the doctor if he would administer the injections in the office. He said no and told me to go home and look on You Tube to find out how to give myself the shots, indicating "There's no wrong way to do it. I later learned that the shots were supposed to be administered intramuscularly after administering them subcutaneously in my stomach which caused pain and bubbles to form under the skin.

14. My voice began to deepen, which I have found out is going to be a permanent, irreversible change.

15. I gained over 50 pounds and became pre-diabetic. When I mentioned this to the physician during a follow up appointment he just told me to start working out.

16. After about a year on testosterone, test results revealed that my blood was starting to thicken, my red blood cell count was too high, and I was developing a blood disorder that could lead to a heart attack or stroke if not controlled. I did some research and believe this was polycythemia. I began experiencing chest pains and was told I had developed tachycardia.

17. I begam suffering excruciating and constant abdominal pain and could not eat. Testing did not reveal any disorders. I was later diagnosed with irritable bowel syndrome, which I continue to suffer with.

18. The pain was becoming so excruciating that I became suicidal. My mental health was deteriorating as I was suffering from depression, irritability, insecurity, and exhaustion.

19. The changes brought on by the testosterone caused my family tremendous emotional distress. Finally, my grandfather sat me down with tears in his eyes and asked me to stop what I was doing to myself. That was a saving grace. I would have let the treatment kill me before admitting that I had made a mistake. My grandfather's intervention saved my life.

20. I stopped taking testosterone and resumed living as a female. My physical and mental health have improved, but I continue to suffer adverse effects from the treatments, including a deepened voice and digestive issues that I've been told will be permanent.

21. I also suffer extreme regret for the choices I made as a teenager. I trusted the doctors' advice. They were the experts, who was I as a confused and scared 18 year old not to listen to them?

22. But telling an 18-year-old girl that mega-doses of testosterone would fix her mental health problems? They didn't even to talk to me about other treatment options! No doctor or therapist suggested I give myself time to grow up, or suggested counseling for what was causing my feelings – no doctor or therapist told me most young people outgrow their feelings of wanting to be the opposite sex. The only advice I got was to take mega-doses of testosterone.

23. Unfortunately, there are more and more young people like me being deceived every day, being told that the solution to their insecurity and identity problems is to get a "sex change." The problem is, a person's sex can't really be changed. You can take hormones and have cosmetic surgeries, but that doesn't really change your sex, or solve your problems. I wish I knew that when I was younger.

24. The VCCAP Act is a critical and necessary law that will help spare my fellow Alabama citizens from being similar misled and suffering the distress I am

continuing to suffer because of the availability of medical interventions to minors under age 19. This law will save lives.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 04/29/2022 2022

Sydney Wright

Sydney Wright

Signature: Sydney E Wright
Sydney E Wright (Apr 29, 2022 18:57 EDT)

Email: [redacted]

DEFENDANT'S EXHIBIT 28

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Carol Frietas In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, Carol Frietas, declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") is a necessary, potentially life-saving law that will protect vulnerable children and their parents from the heartbreaking regret, irreversible physical changes, and emotional pain that I have experienced after undertaking medical and surgical interventions aimed at "transitioning" me from a female to a "male."

3. As a youth, I was what today is called "gender non-conforming," but I lived in a household where gender expression was strictly aligned with cultural stereotypes. I was not allowed to wear boys' clothes or play boys' sports.

4. At puberty I realized I was same-sex attracted with crushes on girls. I became depressed and anxiety-ridden as I feared what "being gay" might mean to how I lived my life and my family relationships. I dropped out of school.

5. At age 20, I began to meet other LGBT youth and my life stabilized. However, I also learned that many masculine females, like me, felt that they were "born in the wrong body" and were transitioning, so I adopted that persona.

6. I went to a gender therapist who diagnosed me with gender dysphoria and told me that transition was the only treatment that would alleviate my discomfort and anxiety.

7. However, at that time there were gatekeeping standards for gender transition, which required that I first live as man for six months, including using a male name, showing a male appearance, and using male spaces. I had very large breasts and could not pass for a male in male spaces, so I did not pursue testosterone at that time. I viewed myself as a male trapped in the "wrong body," but my mental health otherwise was stable.

8. In 2014, I revisited the idea of transitioning, believing it would make me feel better because I was undergoing trauma in various forms. My grandmother who had practically raised me died. I had suffered severe abuse and neglect in childhood, and in retrospect believe I was experiencing symptoms of PTSD from that. I had just become a new mother a couple of months before my brother-in-law committed suicide.

9. I spiraled downward and wanted out. I couldn't commit suicide because I was a mother, so I returned to the idea of transition, believing it would help me feel better. By that time the requirements for testosterone had lessened. I went to Planned Parenthood for testosterone and was given it right away, with no information. I was not given any information on uterine atrophy, vaginal atrophy,

or other effects of testosterone and the staff did not talk about any of my emotional or mental health issues.

10. Four months after starting testosterone, I went to a plastic surgeon for a mastectomy. I needed a letter from a therapist and received one from the therapist who had affirmed me and originally recommended transition. As was true with testosterone, I was not given any information about the procedure. Instead I had a consultation with the surgeon, who said "this is what we are going to do," drew on my chest, took pictures and asked me what I wanted out of the surgery. He said "we'll create a masculine looking chest, you'll look great."

11. During the first four months on testosterone menstruation stopped, my sex drive went way up, my voice deepened, and facial and body hair came in. As I continued on testosterone, my personality changed drastically and my verbal abilities declined. Testosterone lowered and muted my emotions and empathy, but also gave me a lot of energy and a sense of a high. My depression and anxiety worsened to the point that I was having such severe panic attacks that I could not leave home. I told my doctors that I thought the testosterone was making the anxiety worse, but they said no.

12. I went to a psychiatrist to specifically to deal with the depression and I was provided with an anti-depressant that really worked. I felt mentally stable and able to address the trauma that led me to transition.

13. Within a month of starting the anti-depressant, I realized that I had not needed to transition. It was the biggest mistake I had ever made. I did not detransition for a year because I couldn't believe that it was so easy, *i.e.*, that anti-depressants alleviated my depression and enabled me to think clearly and reason better. This allowed me address my internalized homophobia and childhood abuse through therapeutic means.

14. Meanwhile, my health began going downhill. Before going on testosterone, I had no health problems. After being on it for four years, I was pre-diabetic, had high cholesterol, and had a high red blood cell count to the point that doctors were recommending that I donate blood to reduce the volume.

15. I stopped taking testosterone and four months later my blood work was back down to normal. I thought to myself "How do they [doctors] not know about this?" Going off testosterone allowed me to finally sleep. I felt like I never slept all the time that I was taking testosterone. Going off testosterone also helped with empathy and other emotions. My personal relationships, including my relationship with my wife, were better.

16. I believe that healthcare providers did not ask me about mental health issues because they believed that those issues were caused by gender dysphoria and that transitioning would fix the problem. In fact, the opposite was true.

17. I would have been spared physical, psychological, and emotional losses if I had received a proper diagnosis and treatment for PTSD and depression before undergoing years of medical and surgical interventions. Alabama's VCCAP Act is necessary and essential because it will give children and adolescents the chance to work through and address their underlying issues such as depression or PTSD effectively without being pulled onto the affirmation conveyor belt. Hormones and surgery are irreversible decisions that children and adolescents are incapable of making.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 29, 2022.

Carol Freitas

DEFENDANT'S EXHIBIT 29

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Barbara F.*
In Support of Defendants'
Opposition to Plaintiffs'
Motion for Preliminary Injunction

I, Barbara F.[1] declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") provides parents necessary protections against manipulation and coercion on the part of health care providers, ex-spouses and confused children to comply with demands for medical and surgical interventions aimed at "affirming" a child's professed discordant gender identity under threats of alienation or loss of a child to suicide.

3. Because there is no such parent and child-protective law in place in my home state, I have been subjected to alienation from my daughter, coercion, manipulation, and blatant disregard for my parental right to make medical and mental health decisions for my child. The VCCAP will prevent parents and children in Alabama from suffering similar harms. It will actually restore the rights of all parents, not just those who agree with demands for "gender-affirming" medical

[1] Declarant is submitting this Declaration using a pseudonym to protect the privacy of her children and other family members.

interventions, to make medical and mental health care decisions for their children that are truly in the best interest of their child's healthy development.

4. When my daughter, B., was 11 years old she said she identified as a boy and wanted to be referred to by an alternate male name. This occurred after she had endured ridicule from her father (my ex-husband) for laughing like me and witnessed her brother getting preferential treatment from her father.

5. B's father championed her new 'male" identity and began harassing me for not affirming it. He accused me of emotional abuse and called child protection services against me. B's father convinced B. to not participate in visitations with me unless I affirmed the discordant identity.

6. Shortly after B announced that she identified as a boy, I acted on the advice of our family physician and took B to a gender clinic. I naively believed that I would have an opportunity to seek a psychological evaluation and psychological counseling for B. and discuss her sudden identification as a boy prior to any interventions aimed at "affirming" her choice.

7. However, when my daughter and I arrived at the clinic the staff psychologist did an evaluation, but said that she did not have time to see B. regularly to give more in depth psychological help. I stated that believed that B. needed to have psychological counseling before any medical interventions were begun.

8. I told the clinic staff that I did not consent to further consultations regarding medical intervention. I had done some research on the puberty blockers and hormone therapy being suggested for my daughter and was concerned about their unproven safety and efficacy.

9. The clinic staff ignored my directions and, without telling me, an endocrinologist met with my 12-year-old daughter privately and with her father to discuss beginning puberty blockers. The endocrinologist then came in to meet with my daughter and me. When I raised concerns about the puberty blockers, the endocrinologist said that there are "no studies that show the drugs aren't safe." She also told me *in front of* my daughter that I needed "to get on board [with providing puberty blockers and hormones] if I don't want my daughter to commit suicide."

10. I have repeatedly notified clinic staff orally and in writing that I do not consent to their treating my daughter. My ex-husband and I have shared decision-making authority for our children's medical care, so no care is supposed to be provided unless both of us consent. Nevertheless, the clinic and B.'s father have continued with regular consultations with my daughter without my consent.

11. I have reviewed documents from the clinic in which staff say that they plan to "convince me" to consent to the medical interventions, completely disregarding my legal rights and role as B's mother.

12. The availability and promotion of "gender affirming" medical interventions for minors such as my daughter has been used to drive a wedge between B. and me, to prevent B. from receiving counseling for underlying mental health issues and to expose her to unknown long-term medical and mental health consequences without my consent. The notion of "informed consent" or parental decision-making is non-existent.

13. The VCCAP Act prevents such coercive manipulation and potential harm against Alabama's vulnerable children and should be upheld for the protection of children and their families.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 28, 2022.

/s/ Barbara F.
Barbara F. (pseudonym)
[original signature available on request]

DEFENDANT'S EXHIBIT 30

UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of John Doe*
In Support of Defendants'
Opposition to Plaintiffs'
Motion for Preliminary Injunction

I, John Doe[1], declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. I am the father of two sons including a 17-year-old, C. (a pseudonym), who is being seen by Dr. Stephen Rosenthal and his team at UCSF, who is an expert witness who has been retained by the Plaintiffs in this case.

3. I have read Dr. Rosenthal's Declaration. I can testify that his statements regarding the standard of care for transgender children, and particularly his claims that parents have the opportunity to exercise informed consent regarding medical interventions for their child are not true with regard to my son.

4. Dr. Rosenthal claims that medical treatment is done in consultation with the patient's family. In my case this is not true. Dr. Rosenthal's institution has actively worked to prevent my participation in my son's care to the point of providing information to the attorney representing my son in family court aimed at

[1] Declarant is submitting this Declaration using a pseudonym for himself and his son to protect the privacy of his child and family.

stripping me of custody because I would not affirm my son in a discordant gender identity.

5. In fact, I knew nothing about my son receiving life-altering medical interventions until I received a statement from my insurance carrier showing that it had paid more than $209,000 to a child and adolescent gender clinic at UCSF. Even then, I did not know what the payment was for until I asked my ex-wife. She emailed me that she was "pleased" to report that our son had been given an implant of Supprelin (used to suppress testosterone) and was receiving estradiol (estrogen) pills.

6. My research on these substances showed that they chemically castrate patients and are even used specifically for that purpose in some cases for sex offenders. Yet here my 17-year-old son was receiving these drugs from Dr. Rosenthal ostensibly to improve his health and well-being.

7. I have learned that Supprelin is Dr. Rosenthal's preferred method for administering puberty blockers for adolescents like my son. Supprelin requires surgical implantation, meaning that it is a surgical intervention administered to children under the age of 18, which is contrary to Dr. Rosenthal's testimony that surgical interventions are not prescribed for minors and not recommended by the "Standards of Care."

8. I contend that Dr. Rosenthal's surgical implantation of Supprelin into my son also violates the family court's custody order, which UCSF has a copy of, which states that my son is not permitted to "undergo any gender identity related surgery" until he is 18 absent a written agreement of **both parents** or order of the court. I did not agree to the surgical implantation, nor is there any court order permitting it, yet C.'s records show a surgical procedure performed on him to insert the Supprelin. This further calls into question Dr. Rosenthal's testimony regarding the "standards of care" employed in "gender-affirming" interventions.

9. Dr. Rosenthal's testimony also contradicts his actions with my son in that after UCSF surgically implanted my 17 year old son with Supprelin LA (without my knowledge or consent but paid for by my health insurance), Dr. Rosenthal discussed follow-up surgical options with him without both parents present. Dr. Rosenthal discussed breast implants, facial feminization and bottom surgery with my son at age 17 years and 5 months.

10. Rosenthal claims to "provide the patient and their family the information they need to make an informed decision about whether to proceed with the treatment." Again, that is not true regarding the treatment prescribed for my son. When I sought information about alternatives, such as "watchful waiting," and whether patients are assessed by Ray Blanchard's typology of transsexuals, instead

of receiving an answer I was subjected to actions in the family court aimed at stripping me of custody because of my questioning of the protocols at UCSF.

11. Similarly, when I provided Dr. Rosenthal with research that I had found which suggests that puberty blockers can cause cognitive harm and asked questions I received no response, contrary to his testimony that parents are involved to ensure everyone involved has the information they need to make an informed decision.

12. Further contradicting his claim of "informed" decision-making is seen in the form presented to and discussed with my then 16 year old son. The form did not indicate that permanent and irreversible sterility is a potential and likely outcome of the recommended treatment, particularly when puberty blockers are combined with estrogen as is the case with C.

13. Dr. Rosenthal's actions with regard to the treatment of my son differ significantly from the "safe and effective" protocols that he claims are part of "gender-affirming" treatments. His refusal to respond to my questions as the concerned father of his patient belie his testimony about the information-rich and collaborative environment he claims is part of the "gender-affirming" care he provides.

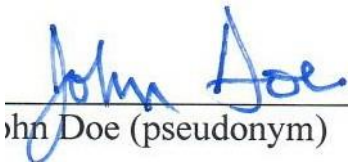
14. My experiences with Dr. Rosenthal instead point to an ideologically driven conveyor belt onto which vulnerable children like my son are placed and processed without the safeguards usually inherent in medical procedures.

15. Parental participation is tolerated only so long as it is affirming of the ideology. If, as in my case, the parent asks questions instead of immediately affirming the agenda, then that parent is disregarded even to the point, as in my case, of having their rights stripped away.

16. The availability of "gender-affirming" medical interventions for vulnerable children experiencing distress about changes in their bodies enables the ideological conveyor belt to proceed unhindered, leaving in its wake sterilized, drug-dependent and dysfunctional young adults, shattered relationships, and distrust in the medical profession.

17. Alabama's efforts to ban these treatments for minors in the VCCAP is necessary to prevent the irreversible and incalculable harms caused by the unchecked gender medicine machine. The VCCAP law will save Alabama families from similar devastation.

Dated: April 28, 2022.



ohn Doe (pseudonym)

DEFENDANT'S EXHIBIT 31

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of John Roe*
In Support of Defendants'
Opposition to Plaintiffs'
Motion for Preliminary Injunction

I, John Roe[1] declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am a resident of Alabama and the father of a son who said he was gender dysphoric and who was socially transitioned at school without our knowledge and referred for "gender transition" medical treatments. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") will protect vulnerable children and provide parents necessary protections against manipulation and coercion on the part of health care providers and confused children to comply with demands for medical and surgical interventions aimed at "affirming" a child's professed discordant gender identity under threats of alienation or loss of a child to suicide.

3. The VCCAP will provide parents with the information necessary to exercise their rights to make mental health and medical care decisions for their children without the secrecy and interference from the government, particularly

[1] Declarant is submitting this Declaration using a pseudonym to protect the privacy of his child and other family members.

public school and coercive influence of mental health professionals, that I experienced.

4. My son, J., has been diagnosed with ADHD and anxiety. He never expressed any distress about his sex until middle school, his eighth grade year. During that time, J. spent a lot of time online and was interested in anime and role-playing games. He also became friends with a girl who identified as trans, which piqued his curiosity.

5. Between eighth and ninth grade, J. left a note for his mother stating that that he was "transgender." He signed the note "your daughter." My wife did not tell me about the note at that time. She spoke with J. who said he "felt more female than male."

6. J. later left me a similar note saying that he had gender dysphoria as long as he can remember.

7. During a therapy session J. said he started feeling that he was transgender in the 8th grade, but then "did his research" through online searches and confirmed his conclusion. I learned that he had watched internet trans influencers, viewed YouTube videos, and answered online questionnaires to self-diagnose gender dysphoria in eighth grade.

8. I learned after the fact that J.'s public school had facilitated J. socially transitioning to a female gender identity without the knowledge or consent or my

wife or me. Without informing us, the school went along with J.'s wishes to be called by a female name and pronouns in ninth grade. We also later learned that J. was wearing a skirt at school without our knowledge. I found out about the new female name being used by the school as if by accident through communication with a teacher and learned that J. was using female pronouns at school through an art project.

9. We took J. to a therapist who did not do a psychological evaluation, but diagnosed him with OCD, anxiety, and depression as well as the previously diagnosed ADHD.

10. During a family therapy session, the therapist ignored J.'s other co-morbidities and focused solely on gender dysphoria. The therapist called J. "courageous." The therapist printed out a handout from an advocacy group. She was trying to bring my wife and I on board with letting our child lead with diagnosis and treatment.

11. The therapist said that kids have a sense of their identity by age 3 or 4, but provided no scientific support.

12. *With J. present*, the therapist told me and my wife that kids are more likely to attempt suicide and run away from home if they are not affirmed in their chosen identity.

13. After the third or fourth visit the therapist recommended that we take J. to Magic City gender clinic to receive puberty blockers or cross-sex hormones.

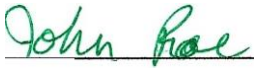
14. We did not follow up on that recommendation. I researched the clinic and the proposed interventions and was concerned about what the interventions would steer my son toward. I believed that for a child of J.'s age struggling as he was with self-esteem, amplified by his other co-morbidities, these medical interventions were not going to solve his real underlying issues long-term. I believed that the interventions were permanent changes with life-long consequences to a child's body for a problem of the mind that could be solved by a less invasive route.

15. I believed my son needed to understand that his body was not the problem, but that his thoughts were and that they could be assisted to bring him more peace with his body through therapy.

16. A total ban on these treatments for children, such as provided in the VCCAP Act is necessary because the medical gatekeepers are not doing their job. They are not following proper professional protocols, are not safeguarding confused adolescents, and not self-regulating. They are allowing adolescents, who are prone to making rash decisions, to self-harm and harm their future. They are also pressuring parents with talk of suicide in front of the adolescent. These treatments have unknown long-term effects and are experimenting on children.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 28, 2022.



John Roe (pseudonym)

DEFENDANT'S EXHIBIT 32

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Kristine W.*
In Support of Defendants'
Opposition to Plaintiffs'
Motion for Preliminary Injunction

I, Kristine W. [1] declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") provides parents necessary protections against manipulation and coercion on the part of health care providers and children to comply with demands for medical and surgical interventions aimed at "affirming" a child's professed discordant gender identity under threats of alienation or loss of a child to suicide and pitting children against their parents.

3. Because there is no such parent and child-protective law in place in my home state, I have been subjected to coercion, manipulation, alienation from my daughter and blatant disregard for my parental right to make medical and mental health decisions. The VCCAP will prevent parents and children in Alabama from suffering similar harms. It will actually restore the rights of all parents, not just those who agree with demands for "gender-affirming" medical interventions, to make

[1] Declarant is submitting this Declaration using a pseudonym to protect the privacy of her children and other family members.

medical and mental health care decisions for their children that are in the best interests of their children and their healthy development into adulthood.

4. My daughter, S., had been diagnosed with OCD, Tourette's Syndrome and bulimia when she began intensive outpatient psychiatric treatment for suicidal ideation. She had spent copious amounts of time online during the pandemic lockdown and was influenced by transgender ideology presentations on the internet.

5. At age 13, S. suddenly declared, in a manner which sounded scripted, that she believed she was a boy and wanted to use a male name. When I spoke to her caregivers, they focused on S. wanting to go by a male name and pronouns. I asked them to address S.'s self-harm, anxiety and bulimia, but they refused. Instead, they told me that I needed to ask, "How can we help you with your gender identity?"

6. The staff told me that "transgender identity is very trendy in the hospital setting right now." They continued to confirm S's obsessive thoughts. During one visit, with S present, the caregivers stated that "trans" people are more likely to commit suicide if not affirmed. In another instance, staff at the hospital said, "You must affirm or she will kill herself. Do you want live son or dead daughter?" The school counselor made similar statements.

7. Following the psychiatric treatment, S. returned to seeing psychiatrists and counselors that she had previously been seeing. Her medication was adjusted, she stopped self-harming and her tics were better controlled.

8. After doing more research and believing it important to ground our child in reality, S's father and I no longer used her preferred male name and pronouns at home. I told S. that she could change her name if she desired when she was an adult but until then she did not get to choose her name.

9. S.'s pediatrician told her father, *in front of S.*, that he needed to use the "chosen" name and to not do so was damaging to her emotionally. That conversation put a wedge between father and daughter. We have switched her to our adult practice so we would not have to deal with doctors pushing the transgender agenda on our child.

10. S. asked why her own parents would not use her new name but everyone else did. She felt that we cared more about the name than her feelings of suicide because of the comments made by doctors about how fragile trans kids are. I explained to her that no one loved her as much and cared about her mental health more than do her father and I, who want to do what was best for her in the long run, which was to hold reality for her.

11. S. had asked for testosterone, but after doing my own research I became concerned about the potential harms to my female child and resisted. S. has since announced "I'm not a boy – boys are awful" and is dressing on and off as a girl. Her mental health is improving.

12. S. has a few separate friend groups across three different schools. Of 10-15 children, only one identifies as her natal sex. These numbers mimic known social contagions such as anorexia and cutting behavior. It is statistically impossible and improbable that all these children will continue to identify as another gender into adulthood.

13. S uses a "chosen" name at school. When enrolling her, I had no choice but to go along with it because the school's policy was to do whatever the child wanted regardless of parental wishes. So I registered her with the "chosen" name as a nickname. (The counselor has since confided to me that it is a huge problem for those who change the whole name when applying to college because the transcripts have different names). I believe that if the school and teachers used her given name, it would be easier for her to completely drop the trans narrative.

14. To allow the medical establishment to push children into irreversible treatments and to pit objecting parents against their children is a great tragedy. Families are being ruined. "Gender-affirming" medical interventions should not be available for children.

15. The VCCAP Act prevents coercive manipulation and potential harm against Alabama's vulnerable children and should be upheld for the protection of children and their families.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 28, 2022.

Kristine W. (pseudonym)

DEFENDANT'S EXHIBIT 33

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Yaacov Sheinfeld In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, Yaacov Sheinfeld, declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") provides parents necessary protections against manipulation and coercion on the part of health care providers and their own distress and confused children to comply with demands for medical and surgical interventions aimed at "affirming" a child's professed discordant gender identity under threats of alienation or loss of a child to suicide. Most importantly, this law protects vulnerable children and young people from grievous harm.

3. Had a law like VCCAP been in effect in my state, my daughter might still be alive today.

4. My daughter, S. had been in counseling for depression since age 15, but had never said anything about gender dysphoria to her counselor.

5. At age 17, S.'s mother told me that S. was transgender. I thought it was a bad idea to pursue transitioning, nevertheless, I told S. that I would help her in any other way.

6. S. had suffered a lot of rejection in school and was seeking affirmation. Five of her friends announced that they were transgender. When S. said she was transgender too it was seen as fashionable and she finally had the peer acceptance she had not previously experienced in high school.

7. When S. went to college at age 18, unbeknownst to me, she began taking testosterone. When I met with her at school, I noticed she was very depressed.

8. A social worker who was also present at my meeting with S. told me that S. was going to get a double mastectomy.

9. When I objected to her taking such a drastic step at such a young age, the social worker told me I was an "Israeli chauvinist", a typical chauvinist male, who doesn't love his child enough. Her approach was that this is what we're going to do and you need to just get on board.

10. The social worker assured me that everything would be fine if I just loved my daughter.

11. After this meeting S. refused to talk to me and began threatening that she would kill herself if she did not get the surgery she wanted. She had a double mastectomy at age 19.

12. I witnessed distressing physical changes in S. The changes in her because of the testosterone were so distressing that I even considered suicide at one time. S. gained and lost lots of weight, had pain all over her body, suffered from

mood swings, could not concentrate, and was briefly hospitalized in a psychiatric hospital.

13. S. was deeply depressed and taking a significant number of medications along with testosterone. I kept assuring her that I would do whatever I could to help her.

14. S.'s pain became so intense that she began taking Fentanyl. S. was found dead on August 6, 2021 with Fentanyl and alcohol in her system. She was 28.

15. Alabama's VCCAP and similar laws to ban medical interventions for minors are critical important because children, especially children with mental health issues such as S, cannot make clear mature decisions about their future, particularly when neither they nor their parents are provided with full information about the effects of these interventions. We know from research that the brain is not fully formed until a person reaches her mid-20s, so even a healthy 18-year-old does not have the mental maturity to make significant decisions such as taking cross-sex hormones that will sterilize them and surgically mutilating their bodies. This is particularly true when, as was true with my daughter, neither the child nor the parents are informed about the medical side effects and harms that the medical interventions cause.

16. The medical interventions that were promoted to my daughter with a promise that they would relieve her problems, in fact, increased them and led to her death.

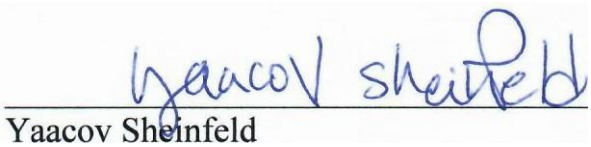
17. Parents should not be put in the position to make decisions for their child that result in sterilization, losing healthy body parts, or other life-long harms, especially when children have mental health issues that are not being addressed.

18. Laws like VCCAP protect parents from being coerced into making these decisions through manipulation and threats like the one leveled at me that my child would commit suicide if she did not get the intervention she demanded.

19. I further declare that certain people in our society think and act in a shameful and destructive way such as this cult, peer group pressure, pitching children against their parents, anarchist ideas. The way my child was treated is like an experiment in bad, unfounded pseudosexual theories that do not hold water. They are dangerous, harmful, destroy the subject of treatment, harm their body, and in many cases- kill them. So much for therapy! Ha! What I went through was hell on earth. I say to you all: Stop this madness now!

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 29, 2022.



Yaacov Sheinfeld

DEFENDANT'S EXHIBIT 34

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Martha S.*
In Support of Defendants'
Opposition to Plaintiffs'
Motion for Preliminary Injunction

I, Martha S.[1] declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") provides parents necessary protections against manipulation and coercion on the part of health care providers and even our own mentally compromised children to comply with demands for medical and surgical interventions aimed at "affirming" a child's professed discordant gender identity under threats of alienation or loss of a child to suicide.

3. The VCCAP will actually restore the rights of all parents, not just those who agree with demands for "gender-affirming" medical interventions, to make medical and mental health care decisions for their children that will protect their healthy physical and mental development and long-term well-being.

4. At age 16, my son, M., began acting out after suffering two traumatic events. When his behavior improved after receiving antibiotics for a sinus infection,

[1] Declarant is submitting this Declaration using a pseudonym to protect the privacy of her children and other family members.

he was diagnosed with Pediatric Auto-immune Neuropsychological Disorder Associated with Strep (PANDAS). PANDAS causes the same kind of psychiatric symptoms that are seen in trans-identified children, *e.g.*, severe anxiety, ADHD, schizophrenia, OCD, and eating disorders.

5. M., who is Caucasian, blonde-haired and blue-eyed, identified as African-American for a semester in high school. Later that year M. told me that he was transgender. When he was home from school during the pandemic M. was depressed and spent a lot of time on the internet asking questions about why he felt so miserable. He was told by sources on Reddit that he was transgender.

6. Our pediatrician referred us to a gender clinic with the expectation that the "experts" at the clinic would help us sort out the issues. Instead the gender clinic staff told me that M. needed to be seen by a gender therapist to get a diagnosis of gender dysphoria.

7. M. had three visits with a gender therapist who did not do any testing and did not address any underlying issues. After the third visit, the therapist prepared a pro forma letter for the clinic that contained an inaccurate history and stated that M. was suffering from gender dysphoria and ready for medical interventions.

8. We saw a psychologist at the gender clinic who after one visit with M. and filling out some questionnaires said that she would recommend that M. see the endocrinologist to be prescribed hormones. She said M. would be put on

spironolactone to block the testosterone instead of puberty blockers, because he was already past most of puberty and on estrogen.

9. I questioned why M. would be recommended for hormone therapy when he did not have a history of gender dysphoria until after he was diagnosed with PANDAS and suffered trauma. The psychologist said, "You have to honor your young person." I replied, "He is not our young person -- he is our child."

10. My husband and I asked to speak to the endocrinologist first to find out about side effects. However, the therapist said we could not see the endocrinologist unless we were ready to get prescriptions for hormones for our son. We said we needed more information.

11. Then a neuropsychologist who was not associated with the gender clinic evaluated our whole family and diagnosed M. with bipolar or possibly dissociative disorder, but not with gender dysphoria. She recommended psychiatric treatment, rather than hormonal treatment without first addressing the other disorders.

12. M. kept demanding hormones because he had been convinced this was what he needed. My husband and I did not follow through on that demand.

However, after M. turned 18 and went away to college, he found a practitioner who prescribed a testosterone suppressor and an estrogen patch. M soon stopped the suppressor because he did not like the effects. He returned home for online

learning in the spring, went on antibiotics and his health improved. He then discontinued the estrogen patch.

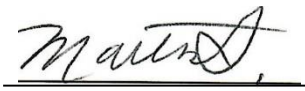
14. The availability of medical and surgical interventions for minors puts parents in a terrible bind. Parents are put in a difficult position when we have a mentally and physically ill child who is convinced that he needs an intervention recommended by a physician that is not based on sound science.

15. This experience has damaged both my and M.'s trust in the medical community. If physicians are legally prevented from recommending these interventions, then parents will not be not put at cross purposes with their child and the medical community.

16. The VCCAP Act prevents coercive manipulation and potential harm against Alabama's vulnerable children and should be upheld for the protection of children and their families.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 28, 2022.



Martha S. (pseudonym)

DEFENDANT'S EXHIBIT 35

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of KathyGrace Duncan In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, KathyGrace Duncan, declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") is a necessary, potentially life-saving law that will protect vulnerable children and their parents from the heartbreaking regret, irreversible physical changes, sexual dysfunction and emotional pain that I have experienced after undertaking medical and surgical interventions aimed at "transitioning" me from a female to a "male."

3. From a very young age, I was what is called today "gender non-conforming." I preferred male clothing, I thought I was a "boy" and I wanted to live as one.

4. I grew up in a dysfunctional family in which my mother was often the victim of my father's emotional and verbal abuse. As a result I internalized the message that "my dad would love me if I were a boy."

5. Sexual abuse by a family member between the ages of 10 and 12 further convinced me that being a girl meant being unsafe and unlovable.

6. In sixth grade, I learned about female to male transsexuals. I believed that my distress was caused by not having the "right" body and the only way to live a normal life was to medically transition and become a heterosexual male.

7. At age 19, I began living as a man named Keith and went to a therapist who formally diagnosed me with gender dysphoria. I began testosterone and a year later had a mastectomy. At the time, I believed it was necessary so that what I saw in the mirror matched what I felt on the inside.

8. I never viewed my condition as touching on mental health issues, and neither did the therapist who diagnosed me. The question of whether my self-perception and desire to transition was related to her mental health issues was never explored.

9. After 11 years passing as a man and living what I thought was a relatively "happy" and stable life (which included having a number of girlfriends), I realized that I was living a lie built upon years of repressed pain and abuse. Hormones and surgery had not helped me resolve underlying issues of rejection, abuse, and sexual assault. I came to understand that my desire to live as a man was a symptom of deeper unmet needs.

10. With the help of life coaches and a supportive community, I returned to my female identity and began addressing the underlying issues that had been hidden

in my attempt to live as a man. I experienced depression that I had repressed for years and grieved over the irreversible changes to my body.

11. If someone had walked with me through my feelings instead of affirming my desire to transition, then I would have been able to address my issues more effectively and not spend so many years making and recovering from a grave mistake.

12. Alabama's VCCAP Act is necessary and essential because it will give children and adolescents a chance to walk through their feelings and address their underlying issues effectively without being pulled onto the affirmation conveyor belt. Hormones and surgery are irreversible decisions that children and adolescents are incapable of making.

13. VCCAP is also necessary to protect parents from the coercion and manipulation of their confused children and over-zealous medical practitioners who try to convince parents to consent to the treatments by threatening that their children might be removed from their care or even commit suicide. If the treatments are banned until the children reach majority, then children and health care providers will not be able to use the treatments as a bargaining chip, but will have to explore other alternatives for helping the children.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 29, 2022.

KathyGrace Duncan

DEFENDANT'S EXHIBIT 36

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Jeanne Crowley* In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, Jeanne Crowley[1] declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") provides parents necessary protections against manipulation and coercion on the part of health care providers and children to comply with demands for medical and surgical interventions aimed at "affirming" a child's professed discordant gender identity under threats of alienation or loss of a child to suicide and without providing parents and children the information needed to understanding the long-term implications and potential harms to children's developing bodies.

3. Because there is no such parent and child-protective law in place in my home state, I have been subjected to coercion, manipulation, alienation from my daughter and blatant disregard for my parental right to make medical and mental health decisions for my child. The VCCAP will prevent parents and children in Alabama from suffering similar harms. It will actually restore the rights of all

[1] Declarant is submitting this Declaration using a pseudonym to protect the privacy of her children and other family members.

parents, not just those who agree with demands for "gender-affirming" medical interventions, to make medical and mental health care decisions for their children that will protect their children's developing bodies and long-term mental health.

4. My husband and I were repeatedly told that the puberty blockers our pre-teen daughter, M., was clamoring for were the answer for her anxiety and distress about her changing body. We were advised that children like M. had high rates of suicide and self-harm and puberty blockers would help by stopping the development of secondary sex characteristics that cause children distress and "give the children time to explore their identity."

5. Gender-affirming mental health and medical professionals assured us that acceding to our daughter's demand for puberty blockers was necessary for her mental health. We were repeatedly assured that the puberty blockers were nothing more than a "pause button" and completely reversible. We were not told that these treatments could cause harm to our child's developing bones or that there were no clinical studies establishing them to be safe and effective as a "treatment" for gender dysphoria in children.

6. Based on these assurances we consented to M. receiving a long-lasting puberty-blocking implant. Once the implant was in place, there was no follow up. I had to initiate contact with the clinic to replace the implant and get necessary lab work.

7. M. previously had psychological evaluations that revealed depression, Autism Spectrum Disorder (ASD) with sensory issues, dyslexia, and dysgraphia. M. had also experienced social trauma. However, none of these issues was addressed by health care professionals once they determined M. had gender dysphoria. Nor did they offer any other treatment options.

8. I learned through my own research that puberty blockers were shown to cause loss of bone density and diminished cognitive development. Healthcare professionals did not inform my husband and me about those harms. When we raised the issue, the doctors responded that they have been prescribing the blockers for many years to treat precocious puberty and the reported bone loss was "nothing to worry about."

9. I had a bone density scan done for M. It revealed that M. has an 11 percent loss of bone density in one hip, 14 percent loss in the other, and a 7 percent loss in the lumbar region. She has developed osteopenia at a time in her life when her bone density should be increasing and her body building a reservoir of strong developing bones as an important protection against osteoporosis in adulthood.

10. When my husband and I confronted the physician to have the puberty blocker implant removed, the doctor recommended that M. continue on to cross-sex hormones, *i.e.*, testosterone. We were not informed this would very likely *sterilize*

our child. I declined, pointing out to the doctor that it is estrogen, not testosterone, that improves bone density.

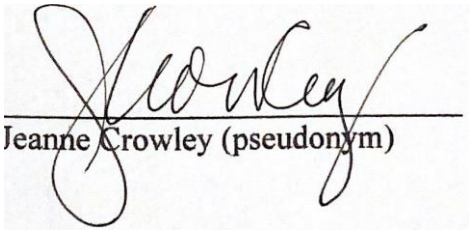
11. Throughout the time that M. was on puberty blockers, we had difficulty finding a therapist to explore M.'s underlying mental health issues. Therapists were unwilling to address anything other than affirming M. as transgender. M. is currently improving working with a psychotherapist we were finally able to find that is willing to explore the underlying issues with M. However, she continues to have loss of bone density that will significantly affect her physical health and growth and having lasting effects possibly for the rest of her life.

12. The availability of these medical interventions for a pre-teen girl distressed by changes in her body meant that neither M nor her healthcare providers would consider other alternatives. VCCAP can overcome that obstacle for parents in Alabama.

13. The VCCAP Act prevents coercive manipulation and potential harm against Alabama's vulnerable children and should be upheld for the protection of children and their families.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 28, 2022.



DEFENDANT'S EXHIBIT 37

UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Ted H Halley In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, Ted H Halley, declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") is a necessary, potentially life-saving law that will protect vulnerable children and their parents from the heartbreaking regret, irreversible physical changes, sexual dysfunction and emotional pain that I have experienced after undertaking medical and surgical interventions aimed at "transitioning" me from a male to a "female."

3. Like many of the children who seek the medical and surgical interventions banned by VCCAP, I experienced distress about my sex beginning in my pre-teens. I wanted God to make me a girl and at age eight I fantasized about cross-dressing in my mother's clothes.

4. I continued to experience feelings of wanting to be a woman and struggling with my gender identity between adolescence and age 50, but as a married father of 5 and active duty member of the Air Force I suppressed those feelings.

5. At age 50 I began attending a heterosexual cross-dressing group, and that confirmed for me that I wanted to go further to fully transition.

6. I had facial feminization surgery in 2009 and a second feminization surgery in 2010.

7. In 2010, I also began taking estrogen and spironolactone, which is a testosterone suppressor.

8. In December 2011, I had genital reassignment surgery in which my male genitalia was removed and a "neo vagina" was created. Dilation of the "neo vagina" was very painful for about six months. This surgery is irreversible. I am no longer able to experience sexual sensation and pleasure and have a life-long sexual dysfunction.

9. In December 2011 I also had my name legally changed to "Teresa" and the gender marker on my birth certificate changed.

10. I transitioned to a female identity at work and had breast augmentation surgery in 2012.

11. I was highly functioning and happy with my transition for a few years.

12. After being on cross-sex hormones and living as a female for twelve years, however, I began to see the irrationality of what I had done. I began to question what I had done and had an internal realization that what I was pretending to be was not real.

13. The internal incongruity grew by the day to the point that I began to become suicidal. I could no longer live what was essentially a lie any longer. I became severely depressed. The only thing that kept me alive was that my granddaughter was living with me.

14. In March 2021 I made the decision to detransition. I re-connected with my male biology, re-established my male identity, and re-established relationships with others as a male.

15. Detransitioning meant that I stopped taking hormones. I removed the breast augmentation and changed my gender marker and name back to male. I did what I could to change my appearance, cut my hair, stopped wearing make-up and women's clothes, but I could not undo the facial surgery or the genital surgery. I could not get back the lost organs, sensations, enjoyment, or functionality.

16. I have no regret detransitioning to my biological sex and wish I had done it sooner. I deeply regret having wasted years of my life, the damage to my body, the permanent loss to my body, the exorbitant cost of these treatments, and the damaged relationships. I think I would dead if I had not detransitioned. The depression was so severe, I think I would have taken my life.

17. VCCAP is necessary and essential because children and adolescents are incapable of making these irreversible decisions. In retrospect, I do not believe I

made a sound decision that I could live with the rest of my life, and I was 50 years old at the time. It is impossible for any adolescent to do so.

18. I am a living example that gender identity is not innate or immutable, like one's sex, race or ethnicity. I had been convinced that I was a "female" born in a male body. I had felt that way since childhood. Based on that consistent and persistent conviction, I fully transitioned in every possible way to live and appear as a woman. Now I realize that it was all a lie, a mental state of mind that was subject to change, and that it didn't solve the internal consternation and deeper emotional problems.

19. VCCAP will help spare my fellow Alabama citizens from similar loss and distress.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 28, 2022.

Ted H Halley

DEFENDANT'S EXHIBIT 38

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Kellie C.*
In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, Kellie C.[1] declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP") provides parents necessary protections against manipulation and coercion on the part of health care providers, ex-spouses and confused children to comply with demands for medical and surgical interventions aimed at "affirming" a child's professed discordant gender identity under threats of alienation or loss of a child to suicide.

3. Because there is no such parent and child-protective law in place in my home state, I have been subjected to alienation from my daughter, coercion, manipulation, and blatant disregard for my parental right to make sound medical and mental health decisions for my child. The VCCAP will prevent parents and children in Alabama from suffering similar harms. It will actually restore the rights of all parents, not just those who agree with demands for "gender-affirming" medical

[1] Declarant is submitting this Declaration using a pseudonym to protect the privacy of her children and other family members.

interventions, to make medical and mental health care decisions for their children in accordance with their natural, healthy development.

4. My daughter, D., became involved in fan fiction at age 11, when she began puberty. By age 13, D. had diagnosed herself with gender dysphoria and began identifying as a 17-year-old male character from Harry Potter. Every year since then, D. has celebrated the birthday of the fictional identity, and is now, at age 17, identifying as a 23-year-old male.

5. D. underwent a psychiatric evaluation which found that she is delusional and incapable of taking care of herself, on the autism spectrum, has OCD and possibly ADHD, but is not psychotic. The evaluation team admits that D. is identifying as a 23-year-old man and is proclaiming that she has Dissociative Identity ("multiple personality") Disorder, but that they do not believe she has DID. Instead, the psychiatric team believes that D. has researched DID and is using it as a maladaptive coping tool for working through the childhood trauma of being sexually assaulted at age 13 or 14, something I just recently learned about.

6. D. is in a residential treatment center. The treatment team has not engaged in therapy with D. to address her underlying issues. Instead, they have embraced her delusion that she is a 23-year-old fictional male character as a transgender identity. The therapists reiterate that they want D. to feel "safe" so they will not address underlying issues, including the sexual assault, unless D. wants to.

7. D. has asked for puberty blockers and testosterone. Despite her myriad co-morbidities and unaddressed sexual trauma, the treatment team say that D. is ready for "gender-affirming" medical interventions. The therapists and D.'s father have told her the only thing standing in the way of her getting those interventions is my refusal to consent.

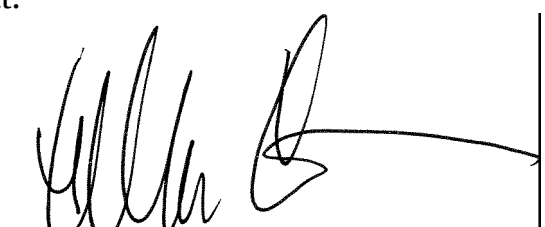
8. The therapists and psychologists have told me that I should do my own research, but if I do not agree with them I "will have a dead daughter instead of a 'live son.'" I am constantly told that I need to "get on board" with what D wants.

9. The VCCAP Act is an important step in preventing harm to vulnerable children. Making these medical interventions unavailable to children will prevent the harms of these interventions on the children and the harms inflicted on parents fighting to protect their mentally disturbed children from irresponsible health care providers.

10. The VCCAP Act prevents coercive manipulation and potential harm against Alabama's vulnerable children and should be upheld for the protection of children and their families.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 28, 2022.



Kellie C. (pseudonym)

DEFENDANT'S EXHIBIT 39

UNITED STATES DISTRICTCOURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER; BRIANNA BOE, individually and on behalf of her minor son, MICHAEL BOE; JAMES ZOE, individually and on behalf of his minor son, ZACHARY ZOE; MEGAN POE, individually and on behalf of her minor daughter, ALLISON POE; KATHY NOE, individually and on behalf of her minor son, CHRISTOPHER NOE; JANE MOE, Ph.D; and RACHEL KOE, M.D.

Plaintiffs,

v.

KAY IVEY, in her official capacity As Governor of the State of Alabama; STEVE MARSHALL, in his official capacity as Attorney General of the State of Alabama; DARYL D. BAILEY, in his official capacity as District Attorney for Montgomery County; C. WILSON BAYLOCK, in his official capacity as District Attorney for Cullman County; JESSICA VENTIERE, in her official capacity as District Attorney for Lee County; TOM ANDERSON in his official capacity as District Attorney for the 12th Judicial Circuit; and DANNY CARR, in his official Capacity as District Attorney for Jefferson County.

Defendants

CIVIL ACTION # 2:22-cv-00184-LCB-SRW

Declaration of Gary Warner In Support of Defendants' Opposition to Plaintiffs' Motion for Preliminary Injunction

I, Gary Warner, declare as follows:

1. I am over the age of 18 years and am not a party to this action. I have actual knowledge of the following facts and if called upon to testify to them could and would do so competently. I am a resident of Alabama and the father of a daughter who committed suicide after being placed on some of the medical interventions that are the subject of Alabama's Vulnerable Child Compassion and Protection Act ("VCCAP"). I am submitting this Declaration in support of Defendants' opposition to Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction.

2. If VCCAP had been in effect in 2013 then my 18-year-old daughter could not have been offered testosterone as a means of "affirming" what she had been led to believe was her "true" identity as a male after suffering horrific sexual abuse. She would have been provided with other options for dealing with her psychological and emotional pain and perhaps gotten the therapy she needed instead of spiraling into despair and suicide.

3. My daughter, K., struggled with health issues, including kidney stones for much of her life. Beginning at age 11 she was the subject of bullying and cyber-bullying at school, much of it of a sexual nature. This increased her anxiety and made her fear for her safety. One of the incidents during high school included threats of dragging her into the boys' bathroom and forcing her to perform sex acts.

4. K. was under the care of professional counselors and psychiatrists for most of her teen years. She was diagnosed with Borderline Personality Disorder and at one point after the bullying incidents was diagnosed with PTSD.

5. Shortly after turning 18, K. was drugged and raped by the older brother of one of her friends while attending a lake party. Because the rapist was a prominent citizen and K was viewed as a troubled teen, there was no criminal prosecution.

6. After the rape, K. began distancing herself from former romantic partners. Her friends insisted that the reason she no longer wanted to be romantically involved was because she really was a man trapped in a woman's body. K. began wearing male clothing and adopted a male name.

7. One of her friends announced that she was transgender at about the same time.

8. K.'s friends who insisted K. was really a man trapped in a woman's body recommended that she see Keith Abrams, a clinical psychologist in Birmingham and avid promoter of gender transition treatments for trans-identifying youth. Abrams recommended that K begin taking testosterone to "help her transition."

9. We attended a session with Abrams. K. wanted him to explain to us why it was advisable for K to move forward with testosterone. He did not provide us with information that would have allowed us or K. to understand the irreversible

nature of these treatments or their long-term effects. He simply told us we needed to "support" our daughter's decision. We did not give informed consent.

10. There was no attempt to deal with the underlying trauma and co-morbidities K was experiencing, but just a push to begin testosterone.

11. K became fixated on the idea that she was born the wrong gender and rejected any counsel or suggestion that did not align with that belief.

12. She did begin testosterone and it exacerbated her anxiety and also transformed her into an angry, threatening person. She threatened to kill her mother to the point that her mother slept with the door locked from fear. Prior to this K. had never been a violent or angry person.

13. Testosterone was not the solution K had been promised. It did nothing to help her emotional pain, which escalated to the point that she took her own life at age 18.

14. The total ban on medical interventions on children age 19 and under enacted under VCCAP is necessary because, like K., I believe most of the young people dealing with gender dysphoria have underlying trauma and/or mental health problems that are not being addressed so long as the medical transitions interventions are available to young people. The availability of these treatments is causing physicians to ignore these underlying causes and empowering young people to deny biological reality to their harm.

15. VCCAP is also especially necessary because the medical community not giving informed consent – they are cheerleading a lifestyle. Rather than giving young people the professional help they need, doctors are acting as activists pushing parents to consent by claiming this is a medically advisable choice, thereby driving the children toward an irreversible life change.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 29, 2022.

Gary Warner (Apr 29, 2022 22:11 MDT)

Gary Warner

DEFENDANT'S EXHIBIT 40

**IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION**

REV. PAUL A. EKNES-TUCKER, *et al.*,	)	
Plaintiffs,	)	
v.	)	Civil Action No. 2:22-cv-184-LCB
KAY IVEY, in her official capacity as Governor of Alabama, *et al.*,	)	
Defendants.	)	

DECLARATION OF EDMUND G. LACOUR JR. IN SUPPORT OF DEFENDANTS' RESPONSE IN OPPOSITION TO PLAINTIFFS' MOTION FOR PRELIMINARY INJUNCTION (DOC. 7)

I, Edmund G. LaCour Jr., hereby declare as follows:

1. I am over 18 years of age and am competent to make this declaration.

2. I am the Solicitor General of the State of Alabama and one of the attorneys for Defendants in the above-captioned matter.

3. Attached to this declaration is a copy of an email exchange from April 15, 2022, between myself and Melody H. Eagan, lead counsel for Plaintiffs in the above-captioned matter.

4. The exhibit is a true and correct copy of what it purports to be.

5. I declare under the penalty of perjury that the foregoing is true and correct.

Executed on May 2, 2022

/s/ Edmund G. LaCour Jr.
Counsel for Defendants

LaCour, Edmund

From: LaCour, Edmund
Sent: Friday, April 15, 2022 4:34 PM
To: Melody H. Eagan
Cc: Jeffrey P. Doss; Amie A. Vague; Bowdre, Barrett; Davis, Jim
Subject: RE: Ladinsky v. Ivey, et al. - addendum to our conversation

Melody,

Thank you for your call earlier and the follow-up email. We will note that both sets of plaintiffs consent to consolidation. Have a great weekend.

Best,
Eddie

Edmund LaCour
Solicitor General
Office of Alabama Attorney General Steve Marshall
Direct: 334-353-2196
Fax: 334-353-8400

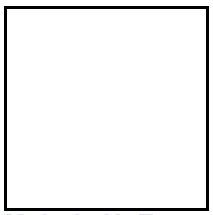
From: Melody H. Eagan <meagan@lightfootlaw.com>
Sent: Friday, April 15, 2022 4:20 PM
To: LaCour, Edmund <Edmund.LaCour@AlabamaAG.gov>
Cc: Jeffrey P. Doss <jdoss@lightfootlaw.com>; Amie A. Vague <avague@lightfootlaw.com>
Subject: Ladinsky v. Ivey, et al. - addendum to our conversation

Eddie,

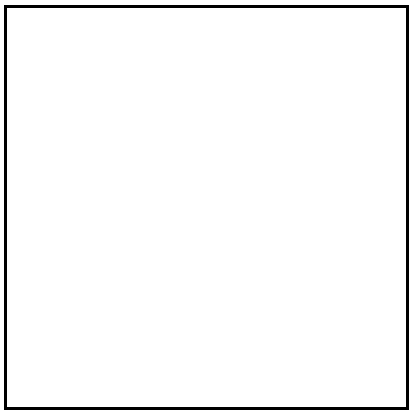
One other thing I should have mentioned. I spoke with counsel for the Walker plaintiffs, and they consent to consolidation. So you probably want to phrase your motion as an unopposed motion, and also put in there that counsel for the Walker plaintiffs also consent to consolidation.

Call me if questions.

Thanks,
Melody



Melody H. Eagan
Attorney



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meagan@lightfootlaw.com

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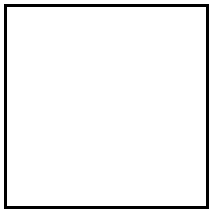
Birmingham, AL 35203



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