

**IN THE 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,

and

UNITED STATES OF AMERICA,

Plaintiff-Intervenor,

v.

STATE OF ALABAMA; 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 BLAYLOCK, 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

Case No.

2:22-cv-184-LCB-SRW

Honorable Liles C. Burke

the 12th Judicial Circuit; and DANNY CARR, in his official capacity as District Attorney for Jefferson County.

Defendants.

PLAINTIFF-INTERVENOR UNITED STATES'
LIST OF PROPOSED EXHIBITS AND EXPECTED WITNESS

Pursuant to the Court's April 22, 2022 Order (Dkt. No. 34), Plaintiff-Intervenor United States of America ("United States"), respectfully submits its list of proposed exhibits and expected witness should it be allowed to participate in the hearing regarding the Motion for a Temporary Restraining Order and a Preliminary Injunction, which begins on May 5, 2022.

PROPOSED EXHIBITS

The United States may present the following exhibits during the hearing on its Motion for a Temporary Restraining Order and a Preliminary Injunction.

Ex. No.	Exhibit
1	American Psychiatric Association, <i>Diagnostic and Statistical Manual of Mental Disorders</i> , Fifth Edition, Text Revision (2022)
2	Jason Rafferty, <i>Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents</i> , American Academy of Pediatrics Policy Statement (Oct. 1, 2018)
3	Wylie Hembree, Peggy Cohen-Kettenis, & Louis Gooren et al., <i>Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline</i> , The Journal of Clinical Endocrinology & Metabolism 3869-3903, Vol. 102, Issue 11 (Nov. 2017)

4	World Professional Association for Transgender Health, <i>Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People</i> , 7th Version (2012)
5	Alabama Psychological Association (aPA), <i>Statement of the Alabama Psychological Association (aPA) Supporting Gender-Affirming Care for Transgender Youth and Urging Opposition to Alabama SB 184/HB 266</i> (2022)
6	American Academy of Pediatrics, <i>American Academy of Pediatrics and Its Alabama Chapter Oppose Bill Threatening Health of Transgender Youth</i> (2022)
7	Declaration of Armand H. Antommara, MD, PhD, FAAP, HEC-C
8	Bibliography of Armand H. Antommara
9	Curriculum Vitae of Armand H. Antommara
10	Food and Drug Administration, <i>Understanding Unapproved Use of Approved Drugs “Off Label”</i>
11	Susan D. Boulware, M.D., <i>Biased Science: The Texas and Alabama Measures Criminalizing Medical Treatment for Transgender Children and Adolescents Rely on Inaccurate and Misleading Scientific Claims</i> (Apr. 28, 2022)
12	Kiara Alfonseca, ABCNews.com, <i>Alabama Governor Signs ‘Don’t Say Gay,’ Trans Care and Bathroom Ban Bills</i> (Apr. 8, 2022)
13	Tony Perkins, <i>Wes Allen Discusses Upcoming Alabama Senate Vote on Vulnerable Child Compassion and Protection Act</i> , YouTube (Feb. 15, 2021), https://www.youtube.com/watch?v=E9Q_b22cUWw
14	Alabama House Judiciary Committee, House Judy Committee – 3/2/2022, 1:34:28 PM, Vimeo (Mar. 2, 2022), https://vimeo.com/683940881/4edaeefda2
15	a House of Representatives, House Part 1 – 4/7/2022, 9:32:05 AM, Vimeo (Apr. 7, 2022), https://vimeo.com/697000650/59a642f5d4

The United States reserves the right to offer into evidence any exhibit or document referenced by Plaintiffs or Defendants in their respective exhibit lists.

EXPECTED WITNESS

The United States expects to call the following witness to testify in person:

- Armand H. Antommaria, MD, PhD, FAAP, HEC-C

The United States reserves the right to question any witness on direct examination or cross-examination who may be called to testify by Plaintiffs or Defendants.

Dated: May 3, 2022

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on May 3, 2022, I electronically filed the foregoing with the Clerk of the Court using the CM/ECF system, which will send notification of such filing to counsel of record.

Respectfully submitted,

s/ Jason R. Cheek

Jason R. Cheek

Assistant U.S. Attorney

Diagnostic & Statistical Manual of Mental Disorders, 5th ed. S2H14

Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition | May 2013 Update

SECTION II. Diagnostic Criteria and Codes

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 (F64.0)

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 concrete, 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) familiarity 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 harassment 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 question. 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 emasculation 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 depressive 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.

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POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System
and/or Improve the Health of all ChildrenAmerican Academy
of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Ensuring Comprehensive Care and
Support for Transgender and Gender-
Diverse Children and AdolescentsJason 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 <i>DSM-5</i> , 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 <i>DSM-IV</i> (changed to "gender dysphoria" in the <i>DSM-5</i>); 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 2008²⁵ (with practice guidelines released in 2015⁸) 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 transgender³² 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 unsuccessful³⁸ 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 visits⁵⁰ 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 metabolism⁶² 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

Health³⁵ and Endocrine Society⁶⁸ 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.

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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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

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).

- 1.4. We recommend against puberty blocking and gender-affirming hormone treatment in pre-pubertal 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

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

Table 1. Definitions of Terms Used in This Guideline

<i>Biological sex, biological male or female:</i> 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.
<i>Cisgender:</i> This means not transgender. An alternative way to describe individuals who are not transgender is “non-transgender people.”
<i>Gender-affirming (hormone) treatment:</i> See “gender reassignment”
<i>Gender dysphoria:</i> 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.
<i>Gender expression:</i> 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.
<i>Gender identity/experienced gender:</i> 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.
<i>Gender identity disorder:</i> 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.”
<i>Gender incongruence:</i> 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.
<i>Gender variance:</i> See “gender incongruence”
<i>Gender reassignment:</i> 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.
<i>Gender-reassignment surgery (gender-confirming/gender-affirming surgery):</i> These terms refer only to the surgical part of gender-confirming/gender-affirming treatment.
<i>Gender role:</i> 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.
<i>Sex designated at birth:</i> This refers to sex assigned at birth, usually based on genital anatomy.
<i>Sex:</i> 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.
<i>Sexual orientation:</i> 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.
<i>Transgender:</i> 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.
<i>Transgender male (also: trans man, female-to-male, transgender male):</i> This refers to individuals assigned female at birth but who identify and live as men.
<i>Transgender woman (also: trans woman, male-to-female, transgender female):</i> This refers to individuals assigned male at birth but who identify and live as women.
<i>Transition:</i> 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.
<i>Transsexual:</i> 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).

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 $\geq$ 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).

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, spermatogenesis 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 $\oplus\oplus\oplus\oplus$)
- 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 $\oplus\oplus\oplus\oplus$)

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

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 ⊕ ⊕ ⊕ ⊕)

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

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 $\mu\text{g/kg/d}$
- 10 $\mu\text{g/kg/d}$
- 15 $\mu\text{g/kg/d}$
- 20 $\mu\text{g/kg/d}$
- 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 $\mu\text{g/24 h}$ (cut 25- μg patch into quarters, then halves)
- 25 $\mu\text{g/24 h}$
- 37.5 $\mu\text{g/24 h}$
- Adult dose = 50–200 $\mu\text{g/24 h}$

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 $\text{mg/m}^2/2 \text{ wk}$ (or alternatively, half this dose weekly, or double the dose every 4 wk)
- 50 $\text{mg/m}^2/2 \text{ wk}$
- 75 $\text{mg/m}^2/2 \text{ wk}$
- 100 $\text{mg/m}^2/2 \text{ wk}$
- 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.

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

Table 11. Hormone Regimens in Transgender Persons

Transgender females ^a	
Estrogen	
Oral	
Estradiol	2.0–6.0 mg/d
Transdermal	
Estradiol transdermal patch	0.025–0.2 mg/d
(New patch placed every 3–5 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.

^aEstrogens used with or without antiandrogens or GnRH agonist.

^bNot available in the United States.

^cOne thousand milligrams initially followed by an injection at 6 wk then at 12-wk intervals.

^dAvoid 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. 5 α -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 17 β -estradiol, or transdermal 17 β -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 anti-androgen 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), Assche-man *et al.* (156), Gooren *et al.* (157), Wierckx *et al.* (158).

^aPrevention and treatment as recommended for biological men.

^bMenorrhagia requires diagnosis and treatment by a gynecologist.

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).

^aComplete removal of male sexual hair requires electrolysis or laser treatment or both.

^bFamilial scalp hair loss may occur if estrogens are stopped.

^cTreatment 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.

^aAdapted 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 ⊕⊕○○)

Evidence

Estrogen therapy can increase the growth of pituitary lactotroph 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.

- 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 pre-treatment 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

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 autologous 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 reinnervation 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

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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WPATH WORLD PROFESSIONAL
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4

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Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People

The World Professional Association for Transgender Health

7th Version

Standards of Care

for the Health of Transsexual, Transgender, and Gender Nonconforming People

The World Professional Association for Transgender Health

7th Version¹ | www.wpath.org

¹ This is the seventh version of the Standards of Care. The original SOC were published in 1979. Previous revisions were in 1980, 1981, 1990, 1998, and 2001.

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Purpose and Use of the Standards of Care

The World Professional Association for Transgender Health (WPATH)¹ is an international, multidisciplinary, professional association whose mission is to promote evidence-based care, education, research, advocacy, public policy, and respect for transgender health. The vision of WPATH is to bring together diverse professionals dedicated to developing best practices and supportive policies worldwide that promote health, research, education, respect, dignity, and equality for transsexual, transgender, and gender nonconforming people in all cultural settings.

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.² 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

1 Formerly the Harry Benjamin International Gender Dysphoria Association

2 *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 for 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 culturally 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 point 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 incidence³ and prevalence⁴ 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

3 **incidence**—the number of new cases arising in a given period (e.g., a year)

4 **prevalence**—the number of individuals having a condition, divided by the number of people in the general population

countries such as Sweden (Wålinder, 1968, 1971), the United Kingdom (Hoenig & Kenna, 1974), 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 1968 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 (for example, 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.



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; The 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 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 experience 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 is 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:

- Offline and online peer support resources, groups, or community organizations that provide avenues for social support and advocacy;
- Offline 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, particular 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.⁵ 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 the 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.

⁵ 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 co-existing 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 autistic 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., in press). 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 co-existing 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 co-existing 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 multi-disciplinary 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 co-existing mental health concerns; and educate clients and their families about therapeutic options, if needed. Acceptance and removal 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.

1. 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.
2. 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.
3. 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 should respond.
4. 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.
5. 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 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 co-existing 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 marrow 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 analog 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 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 co-existing 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); or 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 co-existing 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 co-existing 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 co-existing 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 co-existing 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 (for example, 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 (for example, 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 the 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 co-existing mental health concerns and when working in the context of a multidisciplinary specialty team. The referring health professional provides 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 about the fact 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 (for example, 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 (for example, 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 with 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 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 co-existing 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 fear 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 to work with family members, or to sources of peer support (e.g., online 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. Etherapy, online counseling, or distance counseling

Online or etherapy has been shown to be particularly useful for people who have difficulty accessing competent psychotherapeutic treatment and who may experience isolation and stigma (Derrig-Palumbo & Zeine, 2005; Fenichel et al., 2004; Fraser, 2009b). By extrapolation, etherapy may be a useful modality for psychotherapy with transsexual, transgender, and gender nonconforming people. Etherapy 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 defined (Maheu et al., 2005). Until sufficient evidence-based data on this use of etherapy is available, caution in its use is advised.

Mental health professionals engaging in etherapy 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 etherapy has been published (Fraser, 2009b).

Other Tasks of the Mental Health Professional

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 treatment 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 *Standards of Care* 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 co-existing 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 non-hormonal 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 (see also 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 co-existing 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, increased libido, 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 libido and erections, 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, co-morbidities, 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, & Jaber, 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 ^A	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

^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 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 co-morbidities 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 co-morbid 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. Co-morbid 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.

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 (Catrall & 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, 2011), 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 co-morbid 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 co-morbidities 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 pressure, weight, pulse, and skin; and heart and lung exams (Feldman & Safer, 2009). Laboratory monitoring should be based on the risks of hormone therapy described above, a patient's individual co-morbidities 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 economic 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 those 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 gonadotropin 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 III et al., 1986). There are concerns regarding potential adverse effects of progestins, including depression, weight gain, and lipid changes (Meyer III 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 undecenoate, available outside the United States, results in lower serum testosterone levels than non-oral 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 undecenoate (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 III, & 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 make 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.



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; Vancouver Coastal Health, Vancouver, British Columbia, Canada).

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; Vancouver Coastal Health, Vancouver, British Columbia, Canada). Targets of treatment typically include pitch, intonation, loudness and stress patterns, voice quality, resonance, articulation, speech rate and phrasing, language, and non-verbal 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 non-pitch 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 of course 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, are competent in the assessment and treatment of gender dysphoria, because the surgeon is relying heavily on 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 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 irreversible, 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. Non-genital, non-breast 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/ovariectomy, 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. Non-genital, non-breast 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 pre-requisite.

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 ovariectomy 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 the patient has a medical contraindication or is otherwise unable or unwilling to take hormones).

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 the patient has a medical contraindication or is otherwise unable or unwilling to take hormones).
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 Persons 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. 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, ovariectomy (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, Hildebrand, & 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 co-existing 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, & LWPE1/ESPE2 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 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, in press). 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, in press). 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, in press).

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.

Crossdressing (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 male or female 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).

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 "the other" gender role; for others this means finding a gender role and expression that is 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 is variable and individualized.

Transphobia, internalized: Discomfort with one's own transgender feelings or identity as a result of internalizing society's normative gender expectations.

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 feminizing 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 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 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.

- 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 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 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 pre-requisite.

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)

Hysterectomy and ovariectomy in FtM patients and 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 the patient has a medical contraindication or is otherwise unable or unwilling to take hormones).

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 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 the patient has a medical contraindication or is otherwise unable or unwilling to take hormones);
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 – 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.

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 underwent 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 III, 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 was not recorded. Study participants who were taking testosterone had typically been 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).

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 2000 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, a *Standards of Care* 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 revision. 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.

The plans are to disseminate this version of the SOC and invite feedback for further revisions. The WPATH Board of Directors decides the timing of any revision of the SOC.

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.

Members of the Standards of Care Revision Committee¹

Eli Coleman, PhD (USA)* - Committee chair	Arlene Istar Lev, LCSW (USA)
Richard Adler, PhD (USA)	Gal Mayer, MD (USA)
Walter Bockting, PhD (USA)*	Walter Meyer, MD (USA)*
Marsha Botzer, MA (USA)*	Heino Meyer-Bahlburg, Dr. rer.nat. (USA)
George Brown, MD (USA)	Stan Monstrey, MD, PhD (Belgium)*
Peggy Cohen-Kettenis, PhD (Netherlands)*	Blaine Paxton Hall, MHS-CL, PA-C (USA)
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Randall Ehrbar, PsyD (USA)	Bean Robinson, PhD (USA)
Randi Ettner, PhD (USA)	Loren Schechter, MD (USA)
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Jamie Feldman, MD, PhD (USA)*	Mick van Trotsenburg, MD (Netherlands)
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Jamison Green, PhD, MFA (USA)*	Stephen Whittle, OBE (UK)
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Aaron Devor, PhD (Canada)	Blaine Paxton Hall, MHS-CL, PA-C (USA)
Randall Ehrbar, PsyD (USA)	

¹ * Writing Group member

All members of the *Standards of Care, Version 7 Revision Committee* donated their time to work on this revision.

International Advisory Group

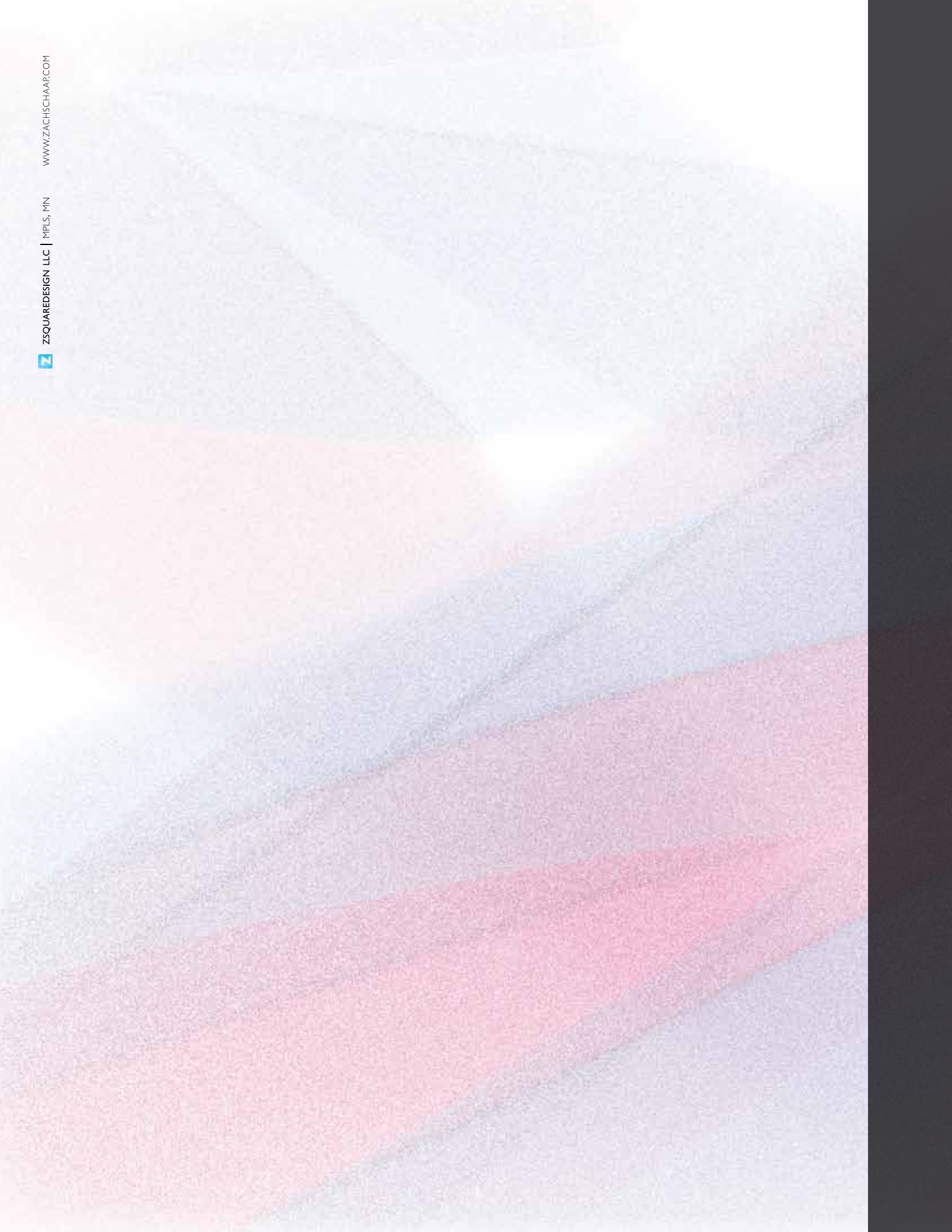
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Craig Andrews, FTM Australia (Australia)
Christine Burns, MBE, Plain Sense Ltd (UK)
Naomi Fontanos, Society for Transsexual Women's Rights in the Phillipines (Phillipines)
Tone Marie Hansen, Harry Benjamin Resource Center (Norway)
Rupert Raj, Shelburne Health Center (Canada)
Masae Torai, FTM Japan (Japan)
Kelley Winters, GID Reform Advocates (USA)

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Statement of the Alabama Psychological Association (aPA) Supporting Gender-Affirming Care for Transgender Youth and Urging Opposition to Alabama SB184/HB266

Alabama SB184/HB266, known as the Alabama Vulnerable Child Compassion and Protection Act, is without scientific merit and is harmful to transgender individuals, impacting their ability to seek and receive gender-affirming care.

The proposed legislation would prevent transgender youth and their families from:

- **Accessing standard medical care** which has been available and practiced for over 25 years throughout our country, is backed by science, and is endorsed by the American Academy of Pediatrics, the American Psychological Association, the Endocrine Society, and the American Medical Association
- **Making joint decisions with medical providers** relative to their individual needs.

The proposed legislation would:

- **Criminalize medical providers**, by making it a Class C Felony, with a prison sentence up to 10 years and fines up to \$15,000 to provide standard medical care to transgender youth and families
- **Force nurses, counselors, teachers, principals, or other administrative officials at public or private schools to break trusted confidential relationships with children and gender diverse adolescents** by sharing this sensitive information with parents.

Gender-affirming care saves lives, and access to this care results in better mental health and psychosocial outcomes. Scientific evidence has shown unequivocally that gender affirming care has the potential to reduce mental health difficulties, suicide rates, as well as other negative psychosocial and health outcomes (1). **Gender-affirming care is provided by the medical team in alignment with ethical guidelines and standards of care** (e.g., World Professional Association for Transgender Health). Gender-affirming care is individualized and assists patient and families in defining, exploring, and actualizing their gender identity. **Patients and families lead the way, and the medical team shifts to adapt with the family if there is a change in gender identity.** The care can include psychoeducation about gender and sexuality (appropriate for the individual's age and developmental level), parental and family support, psychosocial interventions and gender affirming medical interventions. **Surgery is not part of gender affirming care for minors in Alabama.** Use of hormones for pubertal suppression is completely reversible and simply pauses puberty to provide the individual with time for their gender identity to develop further. **Gender affirming hormone therapy, which involves the use of masculinizing or feminizing hormones to allow the body to develop physical changes that align with a person's gender identity, is discussed thoroughly with the patient and family, and requires both patient and parent consent prior to treatment.**

Asking licensed professionals to disregard their medical knowledge and scientific evidence and thereby violate their professional ethics (e.g., the Hippocratic Oath) would codify in law a new low point in healthcare in Alabama. In addition, while the proposed legislation appears protective in aim and name (Alabama Vulnerable Child Compassion and Protection Act), it actually harms gender diverse youth by criminalizing all appropriate care and undermining flexibility that is critical for each individual patient to

receive the best possible care for their individual circumstances **Proper treatment saves lives**, by reducing anxiety, depression, and suicide in transgender youth, and with the unified support of their caregivers, families, providers and community, transgender youth can not only survive but thrive.

The proposed legislation would place undue burden on an already taxed mental health care system in Alabama. Increased rates of behavioral concerns, anxiety, depression, and suicide rates were a major concern for adolescents and young adults prior to the pandemic. Suicide is now the second leading cause of death in adolescents ages 15-19 (2). With the onset of the pandemic, rates of mental health disorders increased, symptoms of depression and anxiety doubled (3), and emergency room visits in the U.S. for suspected suicide doubled for adolescent girls compared to the same period in early 2019 (4). Moreover, **Alabama currently ranks 46th in the U.S. regarding access to mental health care for those in need and 51st (last) in mental health workforce availability, with only one mental health provider for every 1,100 people in need (5).** Our transgender youth are more vulnerable than their peers to depression, anxiety, shame, isolation, and various forms of self-harm including substance use and suicidal behaviors. **Removing access to affirming medical care by taking away treatments transgender youth and families are already receiving puts them for at risk for increased mental health concerns and is a civil rights violation.** This legislation could also impact federal funding from the Health and Human Services (HHS), reducing access to needed medical and mental health care for everyone who lives and may seek care in the state of Alabama (6).

The Alabama Psychological Association stands in solidarity with transgender youth and their families in Alabama and across the United States. We support and stand with our LGBTQ+ colleagues, consumers, families, neighbors, and friends. We will continue to fight for your rights, utilizing our clinical and scientific knowledge to advocate for the right to appropriate healthcare for all persons in Alabama and beyond, without political interference, utilizing policies that advance and protect the rights of everyone, including the LGBTQ+ community.

We strongly oppose Alabama HB266/SB184 and urge all our legislators and Governor Ivey to demonstrate their true compassion for and desire to protect vulnerable youth in our state by opposing this bill as well.

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News Release

American Academy of Pediatrics and Its Alabama Chapter Oppose Bill Threatening Health of Transgender Youth**For Release:**

4/7/2022

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Alabama's efforts to criminalize gender-affirming care violate pediatric recommendations and doctor-family relationship, harm transgender patients

MONTGOMERY, AL AND WASHINGTON, DC – The American Academy of Pediatrics (AAP) and the Alabama Chapter of AAP (AL-AAP) strongly oppose SB 184, a bill that endangers the health and well-being of transgender and gender-diverse youth.

On April 7, the Alabama House passed SB 184, which bans all forms of evidence-based gender-affirming medical care, requires educators and school staff to disclose gender-questioning students' identities to their parents, and classifies providing gender-affirming care as a Class C felony, punishable by up to 10 years in prison. The bill passed both chambers of the state legislature with limited debate and awaits the governor's signature.

"Pediatricians are dedicated to the well-being of all children. Laws like these directly interfere with their ability to keep their patients healthy and provide evidence-based care," said **AAP CEO/Executive Vice President Mark Del Monte, JD**. "This legislation targets vulnerable young people and puts them at great risk of physical and mental harm. Pediatricians are committed to caring for all children. Criminalizing evidence-based, medically necessary services is dangerous to their patients and profession."

The AAP has long supported gender-affirming care for transgender youth, which includes the use of puberty-suppressing medications when appropriate, as outlined in its own [policy statement](#), urging that youth who identify as transgender have access to comprehensive, gender-affirming, and developmentally appropriate health care that is provided in a safe and inclusive clinical space in close consultation with parents.

The Academy has repeatedly [opposed](#) bills that discriminate against transgender youth and their right to receive medical care, and [advocated against](#) restrictions to their rights in other states. The Alabama Chapter of AAP has [consistently advocated against](#) prohibitions on gender-affirming care in Alabama.

For young people who identify as transgender, [studies show](#) that gender-affirming care can reduce emotional distress, improve their sense of well-being and reduce the risk of suicide.

"The Alabama Chapter of AAP strongly opposes this bill, which criminalizes evidence-based care, endangers the safety of vulnerable youth at home, and interferes with the fundamental physician-patient-family relationship. Pediatricians in our state care for transgender patients the way we care for all of our patients, by providing science-based, high-quality care to those who need it. We know our patients best, and physicians, not politicians, should be the ones determining how to best do our job. We urge Governor Ivey to veto this bill and instead pursue policies that prioritize children's health and safety," said **Alabama Chapter-AAP Vice President Nola Ernest, MD, FAAP**.

About the American Academy of Pediatrics

The American Academy of Pediatrics is an organization of 67,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents and young adults. For more information, visit www.aap.org and follow us on Twitter @AmerAcadPeds.

About the Alabama Chapter of the American Academy of Pediatrics

A 501 (c) 3 organization, the Alabama Chapter of the AAP is the only statewide member organization of pediatricians, with more than 850 members across the state, representing both academic and community pediatrics in both urban and rural areas. With a mission to obtain optimal health and well-being for all children in Alabama, and to provide educational and practice support for its membership so the highest quality of medical care can be achieved, the organization has an active voice on almost every state collaborative effort that serves the health interests of children.

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF ALABAMA
NORTHERN DIVISION

REV. PAUL A. EKNES-TUCKER, et
al.,

Plaintiffs,

and

UNITED STATES OF AMERICA,

Plaintiff-Intervenor,

v.

KAY IVEY, in her official capacity as
Governor of Alabama, et al.

Defendants.

Case No. 2:22-cv-184-LCB-SRW

**EXPERT DECLARATION OF ARMAND H. ANTOMMARIA,
MD, PhD, FAAP, HEC-C**

1. Counsel for the United States have retained me as an expert in connection with the above-captioned litigation.

2. 2022 Alabama Senate Bill 184 (SB 184) singles out for anomalous treatment certain medical interventions when these interventions are used for the purpose of gender transition, which I will refer to as gender-affirming medical care, criminalizing healthcare professionals who provide minors gender-affirming medical care or who refer minors for such care.

3. The legislative findings in SB 184 do not provide a sound medical or ethical basis for criminalizing the provision of gender-affirming medical care to minors with gender dysphoria nor could they because a sound medical or ethical basis for criminalizing such care does not exist.

4. I have actual knowledge of the matters stated in this declaration. In preparing this declaration, I reviewed the materials listed in the attached Bibliography (Exhibit A), as well as SB 184. I may rely on those documents as additional support for my opinions. I have also relied on my years of research and relevant experience, as set out in my curriculum vitae (Exhibit B), and on the materials listed therein. The materials I have relied upon in preparing this declaration are the same types of materials that experts in medicine and bioethics regularly rely upon when forming opinions on the subject. I may wish to supplement these opinions or the bases for them as a result of new scientific research or publications, or in response to statements and issues that may arise in my area of expertise.

BACKGROUND AND QUALIFICATIONS

5. I hold the following positions at Cincinnati Children's Hospital Medical Center: Director of the Ethics Center, Lee Ault Carter Chair of Pediatric Ethics, and Attending Physician in the Division of Hospital Medicine. I am also a

Professor in the Departments of Pediatrics and Surgery at the University of Cincinnati College of Medicine.

6. In 2000, I received both my medical degree from Washington University School of Medicine in St. Louis, Missouri and my PhD in Religious Ethics from The University of Chicago Divinity School. I completed my Pediatrics residency at the University of Utah in 2003.

7. I have been licensed to practice medicine since 2001 and am currently licensed to practice medicine in Ohio. I have been Board Certified in General Pediatrics since 2004 and in Pediatric Hospital Medicine since the inception of this certification in 2019. I have been certified as a Healthcare Ethics Consultant since the inception of this certification in 2019.

8. I have extensive experience as a practicing pediatrician. I have been in clinical practice since 2003 and approximately 30 percent of my current work is dedicated to caring for hospitalized patients.

9. I also have extensive experience as a bioethicist. Bioethicists examine the ethical issues that arise in medicine and the life sciences. I was Chair of the Ethics Committee at Primary Children's Medical Center in Salt Lake City, Utah from 2005 to 2012 and have been Director of the Ethics Center at Cincinnati Children's Hospital Medical Center since 2012. I consult on patients in the Transgender Health Clinic at Cincinnati Children's Hospital Medical Center whose

care presents unique ethical issues and participate in the Clinic's monthly multidisciplinary team meetings. I remain current with the medical and bioethics literature regarding the treatment of minors with gender dysphoria. I am also part of Cincinnati Children's Hospital Medical Center team that cares for patients born with intersex traits, also known as differences or disorders of sex development (DSD). I am also the Chair of Cincinnati Children's Hospital Medical Center Fetal Care Center's Oversight Committee, which provides the Center with recommendations regarding innovation and research.

10. I am a member of the American Academy of Pediatrics (AAP), the American Society for Bioethics and Humanities (ASBH), the Association of Bioethics Program Directors, and the Society for Pediatric Research. I was a member of the AAP's Committee on Bioethics from 2005 to 2011. I served as a member of the ASBH's Clinical Ethics Consultation Affairs Committee from 2009 to 2014 and currently serve on its Healthcare Ethics Consultant Certification Commission.

11. I am the author of 38 peer-reviewed journal articles, 11 non-peer-reviewed journal articles, 6 book chapters, and 26 commentaries. My peer-reviewed journal articles have been published in high-impact journals, including the *Journal of the American Medical Association* and *Annals of Internal Medicine*. I am also an

author of 17 policy statements and technical reports, including 4 as lead author, by the AAP.

12. I am a member of the Executive Editorial Board and the Associate Editor for Ethics Rounds of *Pediatrics*. *Pediatrics* is the AAP's flagship journal and Ethics Rounds is a type of article in which commentators analyze cases that raise ethical issues. I am an active peer reviewer for many medical journals, including the *American Journal of Bioethics* and the *Journal of Pediatrics*. I also review abstracts for meetings of professional organizations, including the Pediatric Academic Societies and ABSH. I was previously a member of the editorial boards of the *Journal of Clinical Ethics* and the *Journal of Medical Humanities*.

13. I have prepared declarations as an expert witness in the following cases involving the provision of gender-affirming medical care to adolescents with gender dysphoria: *Brant v. Rutledge*, Case No. 4:21CV450-JM (E.D. Ark.), *Doe v. Abbott*, No. D-1-GN-22-000977, 2022 WL 628912 (Tex. Dist. 353rd Judicial District, March 2, 2022), and *Walker v. Marshall*, No. 2:22-cv-167-ECM-SMD (M.D. Ala.). In *Doe v. Abbott*, I testified in court as an expert witness. I am being compensated at an hourly rate of \$250 per hour for preparation of expert declarations and reports, and \$400 per hour for time spent preparing for or giving deposition or trial testimony. My compensation does not depend on the outcome of this litigation, the opinions I express, or the testimony I provide.

GENDER-AFFIRMING MEDICAL CARE IS CLINICAL CARE

14. The SB 184 legislative findings claim that the use of gonadotrophin releasing hormone (GnRH) agonists, colloquially known as puberty blockers, to treat gender dysphoria¹ are experimental and not approved by the U.S. Food and Drug Administration (FDA). These claims are inaccurate and irrelevant, respectively.

15. Clinical practice and research are distinguished by their goals and methods. The goal of clinical practice is to benefit individual patients, and its method is individualized decision-making. The goal of research is to contribute to generalizable knowledge, and its method uses formal protocols that describe the research study's objectives and procedures. *See* National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. The Commission; 1978.

16. The clinical use of puberty blockers to treat gender dysphoria is not research or experimentation. The same is true for gender-affirming hormone treatment and mastectomies on transgender males (individuals assigned female at birth who identify as male) referred to at chest surgery. When administering these

¹ Gender dysphoria is “a marked incongruence between one’s experienced/expressed gender and their assigned gender” which is “associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.” American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. American Psychiatric Publishing; 2013.

treatments, clinicians seek to benefit individual patients and adjust the treatment based on individual patients' responses.

17. To the extent the legislative findings use the term "experimental" to convey an absence of evidence for gender affirming medical care, that suggestion is baseless. Gender affirming medical care is supported by clinical studies, evidence comparable to many other treatments in pediatrics, as detailed below.

18. SB 184 not only criminalizes gender-affirming medical care as clinical care, but also criminalizes the provision of these interventions as research. Such research is necessary, as it is in every area of medicine, to continue to advance treatment.

19. The suggestion that because puberty blockers and gender-affirming hormone treatment are not approved by the FDA for the treatment of gender dysphoria they are therefore experimental or unsafe is misleading. Off-label use of FDA-approved medications is legal, common, and often evidence-based.

20. FDA approval is not required for all uses of a medication. Once the FDA has approved a medication for one indication,² thereby agreeing that it is safe

² According to the FDA, an indication includes a number of factors: the particular disease or condition or the manifestation or symptoms of the disease or condition for which the drug is approved; whether the drug is approved for treatment, prevention, mitigation, cure, or diagnosis; and the population, including age group, for which the drug is safe and effective. Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research, Food and Drug Administration,

(*i.e.*, its benefits outweigh its potential risks) and effective for this intended use, as is the case with the medications at issue here, prescribers are generally free to prescribe it for other indications. U.S. Food & Drug Administration. Understanding unapproved use of approved drugs “off label.” February 5, 2018. Accessed March 23, 2022. <https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label>. The American Academy of Pediatrics (AAP) Committee on Drugs states, “[i]t is important to note that the term ‘off-label’ does not imply an improper, illegal, contraindicated, or investigational use” and “[t]he administration of an approved drug for a use that is not approved by the FDA is not considered research and does not warrant special consent or review if it is deemed to be in the individual patient’s best interest.”

21. The AAP Committee on Drugs further states “in no way does a lack of labeling signify that therapy is unsupported by clinical experience or data in children.” Frattarelli DA, Galinkin JL, Green TP, et al. Off-label use of drugs in

U.S. Department of Health and Human Services. Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products—Content and Format: Guidance for Industry. July 2018. Accessed April 29, 2022. Available at <https://www.fda.gov/files/drugs/published/Indications-and-Usage-Section-of-Labeling-for-Human-Prescription-Drug-and-Biological-Products-%E2%80%94-Content-and-Format-Guidance-for-Industry.pdf>. A medication approved for the treatment of asthma in adults would, for example, be prescribed off label if used to treat a different disease, like pneumonia, or a different age group, like children.

children. *Pediatrics*. 2014;133(3):563-567. Among the reasons for this is that, even if there is substantial evidence of safety and efficacy for a new indication, a sponsor may not seek FDA approval for it because doing so is not economically beneficial. Wittich CM, Burkle CM, Lanier WL. Ten common questions (and their answers) about off-label drug use. *Mayo Clin Proc*. 2012;87(10):982-990.

22. “Off-label” use of drugs is common in many areas of medicine, including pediatrics. For example, nafcillin, an antibiotic commonly used to treat children with invasive staphylococcal infections, such as lung or joint infections, lacks FDA approval in individuals under 18 years of age. *See* Nafcillin Injection, USP. February 2007. Accessed April 5, 2022. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/050655s017lbl.pdf. A recent study of children’s hospitals found that in 28.1% of encounters, at least one off-label drug was prescribed. *See* Yackey K, Stukus K, Cohen D, Kline D, Zhao S, Stanley R. Off-label medication prescribing patterns in pediatrics: An update. *Hosp Pediatr*. 2019;9(3):186-193. Examples of medications used off-label in this study included: albuterol, which is used to treat asthma; morphine, which is used to treat pain; and lansoprazole (Prevacid®), which is used to treat gastrointestinal reflux. The rate of off-label use may be significantly higher in certain age groups, categories of drugs, and clinical settings.

THE SAFETY AND EFFICACY OF GENDER-AFFIRMING MEDICAL CARE IS SUPPORTED BY EVIDENCE

23. The SB 184 legislative findings also incorrectly characterize gender-affirming medical treatment as new, unproven, and poorly studied. Gender-affirming medical care is not new. Hormone treatment for gender dysphoria began soon after estrogen and testosterone became commercially available in the 1930's. Stryker S. *Transgender History*. 2nd ed. Seal Press; 2017. The use of puberty blockers to treat gender dysphoria in adolescents, while more recent, is not new. The first reference to this treatment in the medical literature was in 1998, over twenty years ago. Cohen-Kettenis PT, van Goozen SH. Pubertal delay as an aid in diagnosis and treatment of a transsexual adolescent. *Eur Child Adolesc Psychiatry*. 1998;7(4):246-248. Prospective observational trials of puberty blockers began recruiting participants in 2000. de Vries AL, Steensma TD, Doreleijers TA, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *J Sex Med*. 2011;8(8):2276-2283

24. Gender-affirming medical care of adolescents with gender dysphoria is also neither poorly studied nor unproven. The major categories of studies used to evaluate innovative treatments are observational studies, which include cross-sectional and longitudinal studies, and randomized trials. In cross-sectional studies, investigators collect data at a single point in time. Cross-sectional design permits investigators to examine potential associations between factors, but it cannot prove

one factor caused the other. In longitudinal studies, researchers follow individuals over time, making continuous or repeated measures. In a randomized trial, participants are randomly assigned to a treatment or a comparison group. Neither the investigators nor the participants know to which group the participant is assigned. The major benefit of a randomized trial is that it decreases the likelihood that any differences in the outcomes between the groups is the result of baseline differences between the groups rather than the result of the intervention. Guyatt G, Rennie D, Meade MO, et al., eds. *Users' Guide to the Medical Literature: A Manual for Evidence-Based Clinical Practice*. 3rd ed. McGraw Hill Education; 2015; Perry-Parrish C, Dodge R. Research and statistics: Validity hierarchy for study design and study type. *Pediatr Rev*. 2010;31(1):27-29.

25. While randomized controlled trials are described in the medical literature as “high quality” evidence and observational studies as “low quality” evidence, randomized controlled trials may not be feasible or ethical, may have intrinsic methodological limitations, or may be unavailable in some contexts. “Low quality” evidence can be sufficient to justify treatment recommendations. See Swiglo BA, Murad MH, Schunemann HJ, et al. A case for clarity, consistency, and helpfulness: State-of-the-art clinical practice guidelines in endocrinology using the Grading of Recommendations, Assessment, Development, and Evaluation System. *J Clin Endocrinol Metab*. 2008;93(3):666-673. For example, the Endocrine Society

recommends that “clinicians prescribe and support the reduction of inactivity and also a minimum of 20 minutes of moderate to vigorous physical activity daily, with a goal of 60 minutes, all in the context of a calorie-controlled diet” to treat obesity. This recommendation is based on “low quality” evidence. Styne DM, Arslanian SA, Connor EL, et al. Pediatric obesity-assessment, treatment, and prevention: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2017;102(3):709-757.

26. It may, at times, be unethical to conduct randomized trials. For randomized trials to be ethical, clinical equipoise must exist; that is, there must be uncertainty about whether the efficacy of the intervention or the control is greater. It would be unethical to knowingly expose some trial participants to an inferior intervention. Trials must also be feasible. It would be unethical to expose individuals to the risks of trial participation without the benefit of the trial generating generalizable knowledge. A randomized trial that is unlikely to find enough people to participate because they believe they might be randomized to an inferior intervention would be unethical because it could not generate generalizable knowledge due to an inadequate sample size. *See Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? JAMA.* 2000;283(20):2701-2711.

27. The use of puberty blockers to treat gender dysphoria is supported by prospective observational trials including: Delemarre-van de Waal HA, Cohen-

Kettenis PT. Clinical management of gender identity disorder in adolescents: A protocol on psychological and pediatric endocrinology aspects. *Eur J Endocrinol*. 2006;155(suppl 1):S131–S137; de Vries AL, Steensma TD, Doreleijers TA, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *J Sex Med*. 2011;8(8):2276-2283; and de Vries AL, McGuire JK, Steensma TD, Wagenaar EC, Doreleijers TA, Cohen-Kettenis PT. Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics*. 2014;134(4):696-704.

28. Gender-affirming hormone therapy to treat gender dysphoria is also supported by prospective observational trials. These trials include de Vries AL, McGuire JK, Steensma TD, Wagenaar EC, Doreleijers TA, Cohen-Kettenis PT. Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics*. 2014;134(4):696-704.

29. There are also ongoing federally funded prospective observational trials of gender-affirming healthcare for adolescents with gender dysphoria in the U.S., trials that SB 184 would criminalize in Alabama. See National Institutes of Health RePORTER, The impact of early medical treatment in transgender youth. Accessed January 21, 2022.

<https://reporter.nih.gov/search/lGJnh68uokiic97N2X00kA/project->

[details/8965408](https://reporter.nih.gov/search/lGJnh68uokiic97N2X00kA/project-details/8965408); Olson-Kennedy J, Chan YM, Garofalo R, et al. Impact of early

medical treatment for transgender youth: Protocol for the longitudinal, observational trans youth care study. *JMIR Res Protoc*. 2019;8(7):e14434.

30. Under the applicable ethical standards, randomized, placebo-controlled trials (trials that compare pharmacological treatment to no pharmacological treatment) in gender dysphoria are currently unethical. Potential investigators do not have equipoise between pharmacological treatment and no pharmacological treatment; they believe that pharmacological treatment is superior. It is also highly unlikely that enough participants would enroll in randomized controlled trials for them to be informative. See Chew D, Anderson J, Williams K, May T, Pang K. Hormonal treatment in young people with gender dysphoria: A systematic review. *Pediatrics*. 2018;141(4):e20173742; Reisner SL, Deutsch MB, Bhasin S, et al. Advancing methods for US transgender health research. *Curr Opin Endocrinol Diabetes Obes*. 2016;23(2):198-207.

31. Even if randomized, placebo-controlled trials of gender-affirming health care were ethical, they would provide a lower quality of evidence because of intrinsic limitations in their design. For example, it would be impossible to “blind” the investigators or the participants to whether the participants were receiving the active treatment or a placebo. They would know if they were in the intervention or control arm of the study due to the physical changes in their bodies, or the lack thereof, over time. This might bias their perception of the outcomes. Atkins D, Best

D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ*. 2004;328(7454):1490.

32. In the field of pediatrics, parents and their children often must make decisions about medical care without the benefit of randomized trials. Clinical research focusing on children is less likely to use randomized trials than is clinical research for adults. Reasons for this disparity include the low prevalence of childhood disease or conditions, small market share for therapeutic agents in children, low level of National Institutes of Health funding, and difficulty enrolling children in research. *See* Martinez-Castaldi C, Silverstein M, Baucher H. Child versus adult research: The gap in high-quality study design. *Pediatrics*. 2008;122(1):52-57.

33. One directly relevant example of a widely accepted treatment based on prospective observational trials is the use of puberty blockers to treat central precocious puberty. Central precocious puberty is the premature initiation of puberty, before age 8 in people assigned female at birth and before age 9 in people assigned male, by the central nervous system. Its negative effects include impairment of final adult height as well as antisocial behavior and lower academic achievement. There are no randomized trials evaluating the adult height of treated and untreated individuals. Most studies are observational and compare pretreatment predicted and actual final height. These studies have additional limitations including

small sample sizes. This “low quality” evidence is nonetheless sufficiently strong to support the use of GnRH agonists as the standard of care for treatment of central precocious puberty. *See* Mul D, Hughes IA. The use of GnRH agonists in precocious puberty. *Eur J Endocrinol*. 2008;159(Suppl 1):S3-8.

34. Professional medical organizations develop evidence-based clinical practice guidelines to provide clinicians with helpful, evidence-based recommendations and improve patient care and outcomes. Organizations develop guidelines using systematic processes to select and review scientific evidence. Guidelines typically rate the quality of the evidence and grade the strength of recommendations. American Academy of Pediatrics Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. *Pediatrics*. 2004;114(3):874-877; Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations, *BMJ*. 2004;328(7454):1490.

35. The Endocrine Society, an international medical organization of over 18,000 endocrinology researchers and clinicians, has published a clinical practice guideline for the treatment of gender-dysphoric (GD)/gender-incongruent persons, which may include pubertal suppression, gender-affirming hormone therapy, and gender-affirming surgery. The guideline both rates the quality of the supporting evidence and grades the strength of its recommendations. It recommends both the

use of puberty blockers and gender-affirming hormone therapy to treat gender dysphoria in adolescents based on the best available evidence. The guideline recommends delaying gender-affirming genital surgery that removes the testicles, ovaries, and/or uterus until adulthood. *See* Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2017;102(11):3869-3903; *see also* World Professional Organization for Transgender Health. *Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People*, Version 7. World Professional Association for Transgender Health (WPATH); 2012.

36. Recommendations for pediatric care made by professional associations in guidelines are seldom based on well-designed and conducted randomized controlled trials due to their rarity and are frequently based on observational studies or, if such studies are unavailable, expert opinion. The medical use of the term “expert opinion” in this context differs from what I understand to be the use of this term in legal contexts. It refers to the consensus of experts in the field when studies are not available.

37. For example, none of the Endocrine Society’s 84 recommendations in two of its other guidelines that focus on the pediatric population—guidelines on pediatric obesity and congenital adrenal hyperplasia—is based on “high quality”

evidence. Twenty-four (29%) of the recommendations are based on “moderate,” and 49 (58%) on “low” or “very low quality” evidence. The remaining recommendations (11, 13%) are Ungraded Good Practice Statements. Table 1 (Exhibit C). See Speiser PW, Arlt W, Auchus RJ, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2018;103(11):4043-88; Styne DM, Arslanian SA, Connor EL, et al. Pediatric obesity-assessment, treatment, and prevention: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2017;102(3):709-757.

38. Guidelines issued by other professional associations concerning pediatric medical care are similar. For example, of the 130 recommendations in the American Heart Association’s guideline for Pediatric Basic and Advanced Life Support, only 1 (1%) is based on “high-quality evidence from more than 1 [randomized clinical trial]” and 3 (3%) on “moderate-quality evidence from 1 or more [randomized clinical trials].” The remainder of the recommendations were based on lower quality evidence. Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation.* 2020;142(16_suppl_2):S469-S523. As reflected in medical professional associations’ guidelines, medical treatment in pediatrics is infrequently

based on “high” quality evidence and commonly based on lower quality evidence, including observational studies.

PARENTS AND LEGAL GUARDIANS ARE CAPABLE OF PROVIDING INFORMED CONSENT FOR GENDER-AFFIRMING MEDICAL CARE

39. SB 184 also incorrectly asserts that minors and their parents are unable to comprehend and fully appreciate the risks and life implications of gender-affirming health care.

40. First and foremost, parents or legal guardians generally must provide informed consent for medical treatment for minors, including gender-affirming medical care. There is no evidence cited in support of the assertion that parents of adolescents with gender dysphoria are unable to comprehend and fully appreciate the implications of gender-affirming medical care. Parents or legal guardians are frequently asked to consent to medical treatments for minors with comparable risks, uncertainty, or levels of evidence. Limitations in adults’ ability to predict what will contribute to satisfaction in the future, called affective forecasting, is not unique to decisions regarding gender-affirming medical care. And there are approaches healthcare providers use to improve affective forecasting. Wilson TD, Gilbert DT. Affective forecasting: Knowing what to want. *Curr Dir Psychol Sci*. 2005;14(3):131-134; Halpern J, Arnold RM. Affective forecasting: An unrecognized challenge in making serious health decisions. *J Gen Intern Med*. 2008;23(10):1708-1712.

41. Adolescents generally possess comparable medical decision-making capacity to adults. Louis A. Weithorn and Susan B. Campbell, for example, found that 14-year-olds performed similarly to adults with respect to their ability to understand and reason about treatment information. Weithorn LA, Campbell SB. The competency of children and adolescents to make informed treatment decisions. *Child Dev.* 1982;53(6):1589-1598. There is evidence that most adolescents with gender dysphoria have sufficient medical decision-making capacity to make decisions regarding puberty blockers. Vrouenraets L, de Vries ALC, de Vries MC, van der Miesen AIR, Hein IM. Assessing medical decision-making competence in transgender youth. *Pediatrics.* 2021;148(6): e2020049643. Similar to the aforementioned approaches to improve adult's affective forecasting, there are steps that healthcare providers take to promote adolescents' decision-making capacity. Katz AL, Webb SA, Committee on Bioethics. Informed consent in decision-making in pediatric practice. *Pediatrics.* 2016;138(2):e20161485.

42. The current standard of care for treating gender dysphoria in minors is consistent with general ethical principles instantiated in the practices of informed consent and shared decision-making. The Endocrine Society clinical practice guideline extensively discusses the potential benefits, risks, and alternatives to gender-affirming medical care, and its recommendations regarding the timing of interventions are based in part on the treatment's potential risks and the adolescent's

decision-making capacity. The guideline recommends that informed consent for pubertal blockers and gender-affirming hormones include a discussion of the implications for fertility and options for fertility preservation. The Endocrine Society clinical guideline also advises delaying gender-affirming hormone treatment, which results in partly irreversible physical changes until an adolescent has developed sufficient medical decision-making capacity. The guideline states clinicians should individualize decision-making for breast or chest surgery in transgender males and that chest surgery may be considered in individuals under 18 years old. *See* Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2017;102(11):3869-3903.

SB 184 SINGLES OUT GENDER-AFFIRMING MEDICAL CARE FOR ANOMALOUS TREATMENT

43. SB 184's legislative findings do not provide a sufficient basis for criminalizing and singling out for anomalous treatment the provision of gender-affirming healthcare to adolescents with gender dysphoria. For example, as previously mentioned, SB 184 permits the use of puberty blockers to treat central precocious puberty, but criminalizes the use of puberty blockers to treat gender dysphoria, even though using puberty blockers in connection with both conditions has comparable risks and is supported by comparable types of evidence.

44. Additionally, while SB 184 would prohibit chest surgery on transgender males, minors are permitted to undergo many comparable surgeries, such as those for gynecomastia, pectus excavatum or carinatum, and breast reconstruction. Gynecomastia is the proliferation of ductal or glandular breast tissue, as opposed to adipose tissue or fat, in individuals whose sex assigned at birth is male. Pectus excavatum and carinatum are chest wall anomalies in which the sternum is depressed or protrudes, respectively. While surgeries to treat these conditions, as well as breast reduction and augmentation for individuals whose sex assigned at birth and gender identity are female, may at times be performed to lessen physical symptoms, such as pain or exercise intolerance, they are commonly performed to reduce psychosocial distress. Gynecomastia and breast augmentation surgery affirm patients' gender identity, that is, to respectively help someone assigned male at birth feel more typically masculine and someone assigned female at birth feel more typically feminine. Risks of these procedures include bleeding, infection, scarring and poor cosmetic outcome, loss of sensation, and impaired breast/chest feeding. Some surgeries have unique risks such as catastrophic perforations of the heart or lungs in some forms of pectus repair, or capsule formation around a breast implant causing hardening and pain. *See Buziashvili D, Gopman JM, Weissler H, et al. An evidence-based approach to management of pectus excavatum and carinatum. Ann Plast Surg. 2019;82(3):352-358; Nordt CA,*

DiVasta AD. Gynecomastia in adolescents. *Curr Opin Pediatr*. 2008;20(4):375-382; Zuckerman D, Abraham A. Teenagers and cosmetic surgery: Focus on breast augmentation and liposuction. *J Adolesc Health*. 2008;43(4):318-324.

45. As these examples of chest surgeries in adolescents illustrate, surgeries for minors can require weighing short- and long-term effects, benefits, and risks in the face of uncertainty. Individual needs shape these evaluations and, therefore, the adolescents' participation is essential. There is nothing unique about chest surgery for gender dysphoria that justifies singling out this and other medical treatments for gender dysphoria for a criminal prohibition based on a concern for adolescents' inability to assent or parents or guardians' inability to consent. As with other medical decisions for adolescents, medical decisions regarding treatment for gender dysphoria should continue to be left to the discretion of transgender adolescents, their parents or guardians, and their healthcare providers.

46. Ironically, while SB 184 criminalizes gender-affirming medical care for youth with gender dysphoria in the name of protecting vulnerable children, the statute expressly allows doctors to perform irreversible surgeries on infants and children with intersex conditions or differences or disorders of sex development (DSD) at ages when they are unable to meaningfully participate in medical decision making. Such surgeries are highly controversial when performed at such an early age and can result in life-long complications and side effects. See Frader J, Alderson

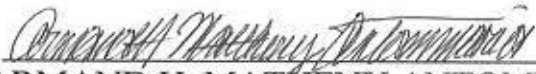
P, Asch A, et al. Health care professionals and intersex conditions, *Arch Pediatr Adolesc Med.* 2004;158(5):426-428.

CONCLUSIONS

47. The Endocrine Society's recommendations for treating adolescents with gender dysphoria with pubertal suppression, gender-affirming hormones, and chest surgery are well within the range of other decisions that adolescents and their parents or guardians in Alabama have the discretion to make. Based on my research and experience as a pediatrician and bioethicist, there is no sound medical or ethical basis to criminalize this care. Doing so puts clinicians in the untenable position of having to either follow state law and knowingly harm their patients, or face penalties including imprisonment and loss of their medical licenses.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed: April 29, 2022


ARMAND H. MATHENY ANTOMMARIA, MD, PhD

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Understanding Unapproved Use of Approved Drugs "Off Label"



Has your healthcare provider ever talked to you about using an FDA-approved drug for an unapproved use (sometimes called an “off-label” use) to treat your disease or medical condition?

It is important to know that before a drug can be approved, a company must submit clinical data and other information to FDA for review. The company must show that the drug is safe and effective for its intended uses. “Safe” does not mean that the drug has no side effects. Instead, it means the FDA has determined the benefits of using the drug for a particular use outweigh the potential risks.

When you are prescribed a drug for its approved use, you can be sure:

- That FDA has conducted a careful evaluation of its benefits and risks for that use.
- The decision to use the drug is supported by strong scientific data.
- There is approved drug labeling for healthcare providers on how to use the drug safely and effectively for that use.

The approved drug labeling for healthcare providers gives key information about the drug that includes:

- The specific diseases and conditions that the drug is approved to treat.
- How to use the drug to treat those specific diseases and conditions.
- Information about the risks of the drug.
- Information that healthcare providers should discuss with patients before they take a drug.

Some drugs may also have labeling information for patients such as Medication Guides, Patient Package Inserts and Instructions for Use.

Why might an approved drug be used for an unapproved use?

From the FDA perspective, once the FDA approves a drug, healthcare providers generally may prescribe the drug for an unapproved use when they judge that it is medically appropriate for their patient.

You may be asking yourself why your healthcare provider would want to prescribe a drug to treat a disease or medical condition that the drug is not approved for. One reason is that there might not be an approved drug to treat your disease or medical condition. Another is that you may have tried all approved treatments without seeing any benefits. In situations like these, you and your healthcare provider may talk about using an approved drug for an unapproved use to treat your disease or medical condition.

What are examples of unapproved uses of approved drugs?

Unapproved use of an approved drug is often called “off-label” use. This term can mean that the drug is:

- Used for a disease or medical condition that it is not approved to treat, such as when a chemotherapy is approved to treat one type of cancer, but healthcare providers use it to treat a different type of cancer.
- Given in a different way, such as when a drug is approved as a capsule, but it is given instead in an oral solution.
- Given in a different dose, such as when a drug is approved at a dose of one tablet every day, but a patient is told by their healthcare provider to take two tablets every day.

If you and your healthcare provider decide to use an approved drug for an unapproved use to treat your disease or medical condition, remember that FDA has not determined that the drug is safe and effective for the unapproved use.

Questions you may want to consider

If your healthcare provider is thinking about using an approved drug for an unapproved use, you may want to ask your healthcare provider questions like these:

- What is the drug approved for?
- Are there other drugs or therapies that are approved to treat my disease or medical condition?
- What scientific studies are available to support the use of this drug to treat my disease or medical condition?
- Is it likely that this drug will work better to treat my disease or medical condition than using an approved treatment?
- What are the potential benefits and risks of treating my disease or medical condition with this drug?
- Will my health insurance cover treatment of my disease or medical condition with this drug?
- Are there any clinical trials studying the use of this drug for my disease or medical condition that I could enroll in?

Resources For You

- [FDA Approved Medication Guides \(/drugs/drug-safety-and-availability/medication-guides\)](#)
- [Drugs@FDA Database \(http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm\)](http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm)
- [DailyMed \(https://dailymed.nlm.nih.gov/dailymed/index.cfm\)](https://dailymed.nlm.nih.gov/dailymed/index.cfm)

Curriculum Vitae

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PERSONAL DATA

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Birth Place: Pittsburgh, Pennsylvania

Citizenship: United States of America

CONTACT INFORMATION

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EDUCATION

1983-1987	BSEE	Valparaiso University, with High Distinction Valparaiso, IN
1983-1987	BS	Valparaiso University (Chemistry), with High Distinction Valparaiso, IN
1987-1989	MD	Washington University School of Medicine Saint Louis, MO
1989-2000	PhD	The University of Chicago Divinity School (Religious Ethics) Chicago, IL
2000-2003	Resident	University of Utah (Pediatrics) Salt Lake City, UT
2005-2006	Certificate	Conflict Resolution Certificate Program, University of Utah Salt Lake City, UT

BOARD CERTIFICATION

2019	Pediatric Hospital Medicine, American Board of Pediatrics
2019	Healthcare Ethics Consultant-Certified, Healthcare Ethics Consultation Certification Commission
2004	General Pediatrics, American Board of Pediatrics

PROFESSIONAL LICENSES

2012-Present	Doctor of Medicine, Ohio
2006-2010	Alternative Dispute Resolution Provider—Mediator, Utah
2001-2014	Physician and Surgeon, Utah
2001-2014	Physician and Surgeon Controlled Substance, Utah

PROFESSIONAL EXPERIENCE**Full Time Positions**

2019-Present	<i>Professor</i> Cincinnati Children's Hospital Medical Center, Cincinnati, OH Department of Surgery
2019-Present	<i>Professor of Clinical-Affiliated</i> University of Cincinnati, Cincinnati, OH Department of Surgery
2017-Present	<i>Professor</i> Cincinnati Children's Hospital Medical Center, Cincinnati, OH

2017-Present Division of Pediatric Hospital Medicine
Professor of Clinical-Affiliated
 University of Cincinnati, Cincinnati, OH
 Department of Pediatrics

2016-2017 *Associate Professor of Clinical-Affiliated*
 University of Cincinnati, Cincinnati, OH
 Department of Pediatrics

2012-2017 *Associate Professor*
 Cincinnati Children's Hospital Medical Center, Cincinnati, OH
 Division of Pediatric Hospital Medicine

2012-Present *Lee Ault Carter Chair in Pediatric Ethics*
 Cincinnati Children's Hospital Medical Center

2012-2016 *Associate Professor-Affiliated*
 University of Cincinnati, Cincinnati, OH
 Department of Pediatrics

2010-2012 *Associate Professor of Pediatrics (with Tenure)*
 University of Utah School of Medicine, Salt Lake City, UT
 Divisions of Inpatient Medicine and Medical Ethics

2010-2012 *Adjunct Associate Professor of Medicine*
 University of Utah School of Medicine, Salt Lake City, UT
 Division of Medical Ethics and Humanities

2004-2010 *Assistant Professor of Pediatrics (Tenure Track)*
 University of Utah School of Medicine, Salt Lake City, UT
 Divisions of Inpatient Medicine and Medical Ethics

2004-2010 *Adjunct Assistant Professor of Medicine*
 University of Utah School of Medicine, Salt Lake City, UT
 Division of Medical Ethics and Humanities

2003-2004 *Instructor of Pediatrics (Clinical Track)*
 University of Utah School of Medicine, Salt Lake City, UT
 Divisions of Inpatient Medicine and Medical Ethics

2003-2004 *Adjunct Instructor of Medicine*
 University of Utah School of Medicine, Salt Lake City, UT
 Division of Medical Ethics

Part Time Positions

2021 *Consultant*
 Proctor & Gamble, Cincinnati, OH

2019 *Consultant*
 Sanofi Genzyme, Cambridge, MA

2018-Present *Consultant*
 Center for Conflict Resolution in Healthcare, Memphis, TN

2017-2020 *Consultant*
 Amicus Therapeutics, Cranbury, NJ

- 2017 *Expert Witness*
Robert J. Klickovich, MD, PLLC v. Tristate Arthritis & Rheumatology, PSC, *et al.*,
Commonwealth of Kentucky, Boone Circuit Court, Division III, Civil Action No. 16-CI-
01690
- 2017 *Consultant*
Sarepta Therapeutics, Cambridge, MA
- 2014 *Consultant*
Genzyme, A Sanofi Company, Cambridge, MA

Editorial Experience

Editorial Board

- 2020-Present *Pediatrics*, Associate Editor for Ethics Rounds and Member of the Executive Editorial
Board
- 2015-2020 *Journal of Clinical Ethics*
- 2009-2020 *Journal of Medical Humanities*

Guest Academic Editor

- 2017 *PLOS ONE*

Ad Hoc Reviewer: *Academic Medicine, Academic Pediatrics, AJOB Primary Research, American Journal of Bioethics, American Journal of Law & Medicine, American Journal of Medical Genetics, American Journal of Transplantation, BMC Medical Ethics, BMJ Open, Canadian Journal of Bioethics, CHEST, Clinical Transplantation, European Journal of Human Genetics, Frontiers in Genetics, Hospital Medicine, International Journal of Health Policy and Management, International Journal of Nursing Studies, Journal of Adolescent and Young Adult Oncology, Journal of Clinical Ethics, Journal of Empirical Research on Human Research Ethics, Journal of General Internal Medicine, Journal of Healthcare Leadership, Journal of Hospital Medicine, Journal of the Kennedy Institute of Ethics, Journal of Law, Medicine & Ethics, Journal of Medical Ethics, Journal of Medical Humanities, Journal of Medicine and Life, Journal of Palliative Care, Journal of Pediatrics, Journal of Pediatric Surgery, Mayo Clinic Proceedings, Medicine, Healthcare and Philosophy, Molecular Diagnosis & Therapy, New England Journal of Medicine, Patient Preference and Adherence, Pediatrics, Pediatrics in Review, Personalized Medicine, PLOS ONE, Risk Management and Healthcare Policy, Saudi Medical Journal, SSM - Qualitative Research in Health, and Theoretical Medicine and Bioethics*

SCHOLASTIC AND PROFESSIONAL HONORS

- 2021 *Hidden Gem Award*, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- 2019-2021 *Presidential Citation*, American Society for Bioethics and Humanities, Chicago, IL
- 2016 *Laura Mirkinson, MD, FAAP Lecturer*, Section on Hospital Medicine, American Academy of Pediatrics, Elk Grove Village, IL
- 2016, 2018 *Certificate of Excellence*, American Society for Bioethics and Humanities, Glenview, IL
- 2013, 2016 *Senior Resident Division Teaching Award*, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- 2012 *Role Model*, Quality Review Committee, Primary Children's Medical Center, Salt Lake City, UT
- 2011 *Member*, Society for Pediatric Research, The Woodlands, TX
- 2011 *Presidential Citation*, American Society for Bioethics and Humanities, Glenview, IL
- 2009 *Role Model*, Quality Review Committee, Primary Children's Medical Center, Salt Lake City, UT
- 2008 *Nominee*, Physician of the Year, Primary Children's Medical Center, Salt Lake City, UT
- 2005-2006 *Fellow*, Medical Scholars Program, University of Utah School of Medicine, Salt Lake City, UT

- 1995-1997 *Doctoral Scholar*, Crossroads, A Program of Evangelicals for Social Action, Philadelphia PA
- 1989-1992 *Fellow*, The Pew Program in Medicine, Arts, and the Social Sciences, University of Chicago, Chicago, IL

ADMINISTRATIVE EXPERIENCE

Administrative Duties

- 2019-Present *Chair*, Oversight Committee, Cincinnati Fetal Center, Cincinnati, OH
- 2014-Present *Chair*, Ethics Committee, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- 2012-Present *Director*, Ethics Center, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- 2012-Present *Chair*, Ethics Consultation Subcommittee, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- 2010 *Co-Chair*, Ethics Subcommittee, Work Group for Emergency Mass Critical Care in Pediatrics, Centers for Disease Control and Prevention, Atlanta, GA
- 2009 *Chair*, Ethics Working Group, H1N1 and Winter Surge, Primary Children's Medical Center, Salt Lake City, UT
- 2005-2012 *Chair*, Ethics Committee, Primary Children's Medical Center, Salt Lake City, UT
- 2005-2012 *Chair*, Ethics Consultation Subcommittee, Primary Children's Medical Center, Salt Lake City, UT
- 2003-4 *Chair*, Clinical Pertinence Committee, Primary Children's Medical Center, Salt Lake City, UT

Professional & Scientific Committees

Committees

- 2021 *Member*, EMCO Capacity Collaboration, Ohio Hospital Association, Columbus, OH
- 2020-2021 *Member*, Allocation of Scarce Resources Work Group, Ohio Hospital Association, Columbus, OH
- 2020-Present *Member*, Literature Selection Technical Review Committee, National Library of Medicine, Bethesda, MD
- 2020 *Member*, Crisis Standards of Care Workgroup, The Health Collaborative, Cincinnati, OH
- 2019-Present *Member*, Healthcare Ethics Consultant Certification Commission, Oak Park, IL
- 2019 *Member*, Expert Panel, Pediatric Oncology End-of-Life Care Quality Markers, Institute for Cancer Outcomes & Survivorship, University of Alabama at Birmingham, Birmingham, AL
- 2018 *Member*, Resource Planning and Allocation Team Implementation Task Force, Ohio Department of Health, Columbus, OH
- 2012-Present *Member*, Gaucher Initiative Medical Expert Committee, Project HOPE, Millwood, VA
- 2009-2014 *Member*, Clinical Ethics Consultation Affairs Committee, American Society for Bioethics and Humanities, Glenview, IL
- 2005-2011 *Member*, Committee on Bioethics, American Academy of Pediatrics, Oak Park, IL

Data Safety and Monitoring Boards

- 2019-Present *Member*, Data and Safety Monitoring Board, Sickle Cell Domestic Trials, National Heart, Lung, and Blood Institute, Bethesda, MD
- 2018-2019 *Member*, Standing Safety Committee for P-188-NF (Carmeseal-MD™) in Duchenne Muscular Dystrophy, Phrixus Pharmaceuticals, Inc., Ann Arbor, MI
- 2017-Present *Member*, Observational Study Monitoring Board, Sickle Cell Disease Observational Monitoring Board, National Heart, Lung, and Blood Institute, Bethesda, MD
- 2016-2018 *Member*, Observational Study Monitoring Board, Long Term Effects of Hydroxyurea in Children with Sickle Cell Anemia, National Heart, Lung, and Blood Institute, Bethesda, MD

Reviewer

2020-Present *Abstract Reviewer*, American Society for Bioethics and Humanities Annual Meeting
 2020 *Grant Reviewer*, The Croatian Science Foundation, Hrvatska zaklada za znanost (HRZZ)
 2018 *Book Proposal Reviewer*, Elsevier
 2018-2019 *Category Leader*, Religion, Culture, and Social Sciences, American Society for Bioethics and Humanities Annual Meeting
 2017 *Timekeeper*, American Society for Bioethics and Humanities Annual Meeting
 2017-Present *Abstract Reviewer*, Pediatric Academic Societies Annual Meeting
 2016-2021 *Workshop Reviewer*, Pediatric Academic Societies Annual Meeting
 2016 *Grant Reviewer*, Innovation Research Incentives Scheme, The Netherlands Organisation for Health Research and Development
 2016-2017 *Abstract Reviewer*, American Society for Bioethics and Humanities Annual Meeting
 2014, 2016 *External Peer Reviewer*, PSI Foundation, Toronto, Ontario, Canada
 2014 *Member*, Scientific Committee, International Conference on Clinical Ethics and Consultation
 2013 *Abstract Reviewer*, American Society for Bioethics and Humanities Annual Meeting
 2013 *Reviewer*, Open Research Area Plus, Agence Nationale de la Recherche, Deutsche Forschungsgemeinschaft, Economic and Social Research Council, National Science Foundation, and Organization for Scientific Research
 2011-2012 *Abstract Reviewer*, Pediatric Academic Societies Annual Meeting
 2011-2013 *Workshop Reviewer*, Pediatric Academic Societies Annual Meeting
 2011-2014 *Abstract Reviewer*, Pediatric Hospital Medicine Annual Meeting
 2011-2012 *Religious Studies Subcommittee Leader*, Program Committee, American Society for Bioethics and Humanities Annual Meeting
 2010 *Abstract Reviewer*, American Society for Bioethics and Humanities Annual Meeting

Other

2021 *Timekeeper*, American Society for Bioethics and Humanities Annual Meeting
 2021 *Mentor*, Early Career Advisor Professional Development Track, American Society for Bioethics and Humanities.
 2021 *Mentor*, Early Career Advisor Paper or Project Track, American Society for Bioethics and Humanities.
 2109 *Mentor*, Early Career Advising Program, American Society for Bioethics and Humanities
 2018 *Passing Point Determination*, Healthcare Ethics Consultant-Certified Examination, Healthcare Ethics Consultant Certification Commission
 2018 *Member*, Examination Committee, Healthcare Ethics Consultant-Certified Examination, Healthcare Ethics Consultant Certification Commission
 2018 *Item Writer*, Healthcare Ethics Consultant-Certified Examination, Healthcare Ethics Consultant Certification Commission

UNIVERSITY COMMUNITY ACTIVITIES

Cincinnati Children's Hospital Medical Center

2020-Present *Member*, Faculty Diversity and Inclusion Steering Committee
 2020-Present *Member*, Medical Management of COVID-19 Committee
 2020-2021 *Member*, Caregiver Refusal Team
 2020-2021 *Member*, COVID-19 Vaccine Allocation Committee
 2020 *Member*, Personal Protective Equipment Subcommittee of the COVID-19 Steering Committee
 2018-2019 *Member*, Planning Committee, Center for Clinical & Translational Science & Training Research Ethics Conference
 2017-Present *Member*, Donor Selection Committee
 2017-2020 *Member*, Employee Emergency Fund Review Committee
 2017 *Member*, Root Cause Analysis Team
 2016-2017 *Member*, Planning Committee, Center for Clinical & Translational Science & Training Research Ethics Conference
 2015-2019 *Member*, Destination Excellence Medical Advisory Committee
 2015-Present *Member*, Disorders of Sexual Development Case Review Committee
 2015-2019 *Member*, Destination Excellence Case Review Committee
 2014-2018 *Member*, Genomics Review Group, Institutional Review Board
 2014-2017 *Member*, Center for Pediatric Genomics Leadership Committee
 2013-2017 *Member*, Genetic Testing Subcommittee, Health Network
 2013-2016 *Member*, Schwartz Center Rounds Planning Committee
 2013-2014 *Member*, Genomics Ad Hoc Subcommittee, Board of Directors
 2012-Present *Member*, Cincinnati Fetal Center Oversight Committee
 2012-Present *Member*, Ethics Committee
 2012-Present *Member*, G-23
 2012-2016 *Member*, Integrated Solid Organ Transplant Steering Committee

University of Utah

2009-2012 *Member*, Consolidated Hearing Committee

University of Utah School of Medicine

2010-2012 *Member*, Medical Ethics, Humanities, and Cultural Competence Thread Committee
 2008-2010 *Member*, Fourth Year Curriculum Committee

University of Utah Department of Pediatrics

2010-2011 *Member*, Planning Committee, 25th Annual Biological Basis of Children's Health Conference, "Sex, Gender, and Sexuality"
 2009-2012 *Member*, Medical Executive Committee
 2005-2012 *Member*, Retention, Promotion, and Tenure Committee
 2004-2012 *Interviewer*, Residency Program
 2003-2012 *Member*, Education Committee

Intermountain Healthcare

2009-2012 *Member*, System-Wide Bioethics Resource Service
 2009-2012 *Member*, Pediatric Guidance Council

Primary Children's Medical Center

2012-2012 *Member, Shared Accountability Organization Steering Committee*
 2009 *Member, H1N1 and Winter Surge Executive Planning Team*
 2005-2010 *Member, Continuing Medical Education Committee*
 2005-2010 *Member, Grand Rounds Planning Committee*
 2003-2012 *Member, Ethics Committee*

ACTIVE MEMBERSHIPS IN PROFESSIONAL SOCIETIES

2012-Present Association of Bioethics Program Directors
 2011-Present Society for Pediatric Research
 2000-Present American Academy of Pediatrics
 1999-Present American Society of Bioethics and Humanities

FUNDING

Past Grants

2015-2019 "Better Outcomes for Children: Promoting Excellence in Healthcare Genomics to Inform Policy."
 Percent Effort: 9%
 National Human Genome Research Institute
 Grant Number: 1U01 HG008666-01
 Role: Investigator

2015-2016 "Ethics of Informed Consent for Youth in Foster Care"
 Direct Costs: \$10,000
 Ethics Grant, Center for Clinical and Translational Science and Training
 University of Cincinnati Academic Health Center
 Role: Co-Investigator

2014-2015 "Extreme Personal Exposure Biomarker Levels: Engaging Community Physicians and Ethicists for Guidance"
 Direct Costs: \$11,640
 Center for Environmental Genetics
 University of Cincinnati College of Medicine
 Role: Investigator

2014-2015 "Child, Adolescent, and Parent Opinions on Disclosure Policies for Incidental Findings in Clinical Whole Exome Sequencing"
 Direct Costs: \$4,434
 Ethics Grant, Center for Clinical and Translational Science and Training, University of Cincinnati Academic Health Center
 Role: Principal Investigator

2013-2014 "Better Outcomes for Children: GWAS & PheWAS in eMERGEII
 Percent Effort: 5%
 National Human Genome Research Institute
 Grant Number: 3U01HG006828-0251
 Role: Investigator

2004-2005 "Potential Patients' Knowledge, Attitudes, and Beliefs Regarding Participating in Medical Education: Can They be Interpreted in Terms of Presumed Consent?"
 Direct Costs: \$8,000

Interdisciplinary Research in Applied Ethics and Human Values, University Research Committee, University of Utah
 Role: Principal Investigator

TEACHING RESPONSIBILITIES/ASSIGNMENTS

Course and Curriculum Development

2003-2012 Medical Ethics, Internal Medicine 7560, University of Utah School of Medicine, Taught 1 time per year, Taken by medical students, Enrollment 100

Course Lectures

2018, 2021 Introduction to Biotechnology, “Ethics and Biotechnology” and “Clinical Ethics,” BIOL 3027, University of Cincinnati, Taught 1 time per year, Taken by undergraduate students, Enrollment 25.

2018-Present Biomedical Ethics, “Conscientious Objection in Healthcare” and “Ethical Issues in the Care of Transgender Adolescents,” MEDS 4035 & MEDS 4036, University of Cincinnati College of Medicine, Taught 1 time per year, Taken by senior undergraduate students, Enrollment 52.

2016 Foundations of Healthcare Ethics and Law, “Clinical Ethics,” HESA 390, Xavier University.

2014-Present Physicians and Society, “Transfusion and the Jehovah’s Witness Faith,” “Obesity Management: Ethics, Policy, and Physician Implicit Bias,” “Embryos and Ethics: The Ethics of Designer Babies,” “Ethics and Genetic Testing,” and “Ethics and Direct to Consumer Genetic Testing,” 26950112 and 26950116, University of Cincinnati School of Medicine, Taken by first and second year medical students, Enrollment 100.

2014-Present Ethical Issues in Health Care, “Ethical Issues in Managing Drug Shortages: The Macro, Meso, and Micro Levels,” HESA 583, College of Social Sciences, Health, and Education Health Services Administration, Xavier University, Taken by health services administration students, Enrollment 25.

2009 Physical Diagnosis II, Internal Medicine 7160, University of Utah School of Medicine, Taught 1 time per year, Taken by medical students, Enrollment 100

2003-2012 Medical Ethics, Internal Medicine 7560, University of Utah School of Medicine, Taught 1 time per year, Taken by fourth year medical students, Enrollment 100

Small Group Teaching

2018-Present Ethics in Research, GNTD 7003-001, University of Cincinnati School of Medicine, Taught 1 time per year, Taken by fellows, MS, and PhD students, Enrollment 110.

2007 Physical Diagnosis I, Internal Medicine 7150, University of Utah School of Medicine, Taught 1 time per year, Taken by medical students, Enrollment 100

2003-2012 Medical Ethics, Internal Medicine 7560, University of Utah School of Medicine, Taught 1 time per year, Taken by fourth medical students, Enrollment 100

2003 Pediatric Organ System, Pediatrics 7020, University of Utah School of Medicine, Taught 1 time per year, Taken by medical students, Enrollment 100

Graduate Student Committees

2018-Present *Chair*, Scholarship Oversight Committee, William Sveen, Pediatric Critical Care Fellowship, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

2018-2020 *Member*, Scholarship Oversight Committee, Anne Heueman, Genetic Counseling, University of Cincinnati, Cincinnati, OH

2017-2019 *Chair*, Scholarship Oversight Committee, Bryana Rivers, Genetic Counseling, University of Cincinnati, Cincinnati, OH

- 2013-2015 *Mentor*, Sophia Hufnagel, Combined Pediatrics/Genetics Residency, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- 2013-2015 *Co-Chair*, Scholarship Oversight Committee, Andrea Murad, Genetic Counseling, University of Cincinnati, Cincinnati, OH
- 2013-2014 *Member*, Scholarship Oversight Committee, Grace Tran, Genetic Counseling, University of Cincinnati, Cincinnati, OH
- 2011-2012 *Chair*, Scholarship Oversight Committee, Kevin E. Nelson, MD, PhD, Pediatric Inpatient Medicine Fellowship, University of Utah, Salt Lake City, UT

Continuing Education Lectures

- 2008 *Choosing Healthplans All Together (CHAT) Exercise Facilitator*, 18th Annual Intermountain Medical Ethics Conference, "Setting Priorities for Healthcare in Utah: What Choices are We Ready to Make?," Salt Lake City, Utah, October 3.
- 2007 *Speaker*, Infant Medical Surgical Unit, Primary Children's Medical Center, "Withholding and Withdrawing Artificial Nutrition and Hydration: Can It Be Consistent With Care?," Salt Lake City, Utah, September 6.
- 2007 *Faculty Scholar-in Residence*, Summer Seminar, "The Role of Religion in Bioethics," Utah Valley State College, Orem, Utah, May 1.
- 2006 *Workshop Leader*, Faculty Education Retreat, "Publications and Publishing in Medical Education," University of Utah School of Medicine, Salt Lake City, Utah, September 15.
- 2006 *Breakout Session*, 16th Annual Intermountain Medical Ethics Conference, "Donation after Cardiac Death: Evolution of a Policy," Salt Lake City, Utah, March 28.

Other Educational Activities

- 2008 *Instructor*, Contemporary Ethical Issues in Medicine and Medical Research, Osher Lifelong Learning Institute, University of Utah, "Religion and Bioethics: Religiously Based Demands for and Refusals of Treatment," Salt Lake City, Utah, February 7.
- 2007 *Speaker*, Biology Seminar, Utah Valley State College, "Is He Dead?: Criteria of the Determination of Death and Their Implications for Withdrawing Treatment and Recovering Organs for Transplant," Orem, Utah, September 21.

PEER-REVIEWED JOURNAL ARTICLES

1. Anne C Heuerman, Danielle Bessett, Armand H. Matheny Antommaria, Leandra. K. Tolusso, Nicki Smith, Alison H. Norris and Michelle L. McGowan (2021). "Experiences of reproductive genetic counselors with abortion regulations in Ohio." *Journal of Genetic Counseling*. Online ahead of print. PMID: 34755409.
2. Armand H. Matheny Antommaria and Ndidi I. Unaka. (2021) "Counterpoint: Prioritizing Health Care Workers for Scarce Critical Care Resources is Impractical and Unjust." *Journal of Hospital Medicine*. 16: 182-3. PMID 33617445.
3. Gregory A. Grabowski, Armand H. Matheny Antommaria, Edwin H. Kolodny, and Pramod K. Mistry. (2021) "Gaucher Disease: Basic and Translational Science Needs for More Complete Therapy and Management." *Molecular Genetics and Metabolism*. 132: 59-75. PMID: 33419694.
4. Armand H. Matheny Antommaria, Laura Monhollen, and Joshua K. Schaffzin. (2021) "An Ethical Analysis of Hospital Visitor Restrictions and Masking Requirements During the COVID-19." *Journal of Clinical Ethics*. 32(1): 35-44. PMID 33416516.
5. Armand H. Matheny Antommaria (2020) "The Pediatric Hospital Medicine Core Competencies: 4.05 Ethics." *Journal of Hospital Medicine*. 15(S1): 120-121.
6. Armand H. Matheny Antommaria, Tyler S. Gibb, Amy L. McGuire, Paul Root Wolpe, Matthew K. Wynia, Megan K. Applewhite, Arthur Caplan, Douglas S. Diekema, D. Micah Hester, Lisa Soleymani Lehmann, Renee McLeod-Sordjan, Tamar Schiff, Holly K. Tabor, Sarah E. Wieten, and Jason T. Eberl for a Task Force of the Association of Bioethics Program Directors (2020) "Ventilator

- Triage Policies During the COVID-19 Pandemic at U.S. Hospitals Associated With Members of the Association of Bioethics Program Directors.” *Annals of Internal Medicine*. 173(3): 188-194. PMID: 32330224.
7. Armand H. Matheny Antommara (2020) “Conflicting Duties and Reciprocal Obligations During a Pandemic.” *Journal of Hospital Medicine*. 5:284-286. PMID: 32379030.
 8. Mary V. Greiner, Sarah J. Beal, and Armand H. Matheny Antommara (2020) “Perspectives on Informed Consent Practices for Minimal-Risk Research Involving Foster Youth.” *Pediatrics*. 45:e20192845. PMID: 32156772.
 9. Jennifer deSante-Bertkau, Michelle McGowan, and Armand H. Matheny Antommara (2018) “Systematic Review of Typologies Used to Characterize Clinical Ethics Consultations.” *Journal of Clinical Ethics*. 29:291-304. PMID: 30605439.
 10. Andrew J. Redmann, Melissa Schopper, Armand H. Matheny Antommara, Judith Ragsdale, Alessandro de Alarcon, Michael J. Jutter, Catherine K. Hart, and Charles M. Myer. (2018) “To Transfuse or Not to Transfuse? Jehovah’s Witnesses and PostOperative Hemorrhage in Pediatric Otolaryngology.” *International Journal of Pediatric Otorhinolaryngology*. 115:188-192. PMID: 30368384.
 11. Armand H. Matheny Antommara, Kyle B. Brothers, John A. Myers, Yana B Feygin, Sharon A. Aufox, Murray H. Brilliant, Pat Conway, Stephanie M. Fullerton, Nanibaa’ A. Garrison, Carol R. Horowitz, Gail P. Jarvik, Rongling Li, Evette J. Ludman, Catherine A. McCarty, Jennifer B. McCormick, Nathaniel D. Mercaldo, Melanie F. Myers, Saskia C. Sanderson, Martha J. Shrubsole, Jonathan S. Schildcrout, Janet L. Williams, Maureen E. Smith, Ellen Wright Clayton, Ingrid A. Holm. (2018) “Parents’ Attitudes toward Consent and Data Sharing in Biobanks: A Multi-Site Experimental Survey.” *AJOB Empirical Research*. 21:1-15. PMID: 30240342.
 12. Armand H. Matheny Antommara and Cynthia A. Prows. (2018) “Content Analysis of Requests for Religious Exemptions from a Mandatory Influenza Vaccination Program for Healthcare Personnel” *Journal of Medical Ethics*. 44: 389-391. PMID: 29463693.
 13. Armand H. Matheny Antommara (2017) “May Medical Centers Give Nonresident Patients Priority in Scheduling Outpatient Follow-Up Appointments?” *Journal of Clinical Ethics*. 28: 217-221. PMID: 28930708.
 14. Andrea M. Murad, Melanie F. Myers, Susan D. Thompson, Rachel Fisher, and Armand H. Matheny Antommara (2017) “A Qualitative Study of Adolescents’ Understanding of Biobanks and Their Attitudes Toward Participation, Re-contact, and Data Sharing.” *American Journal of Medical Genetics: Part A*. 173: 930-937. PMID: 28328120.
 15. Saskia Sanderson, Kyle Borthers, Nathaniel Mercaldo, Ellen Wright Clayton, Armand Antommara, Sharon Aufox, Murray Brilliant, Diego Campos, David Carrell, John Connolly, Pat Conway, Stephanie Fullerton, Nanibaa Garrison, Carol Horowitz, Gail Jarvik, David Kaufman, Terrie Kitchner, Rongling Li, Evette Ludman, Catherine McCarty, Jennifer McCormick, Valerie McManus, Melanie Myers, Aaron Scrol, Janet Williams, Martha Shrubsole, Jonathan Schildcrout, Maureen Smith, and Ingrid Holm (2017) “Public Attitudes Towards Consent and Data Sharing in Biobank Research: A Large Multisite Experimental Survey in the US.” *The American Journal of Human Genetics*. 100: 414-427. PMID: 28190457.
 16. Maureen E. Smith, Saskia C Sanderson, Kyle B Brothers, Melanie F Myers, Jennifer McCormick, Sharon A Aufox, Martha J Shrubsole, Nanibaa' A Garrison, Nathaniel D Mercaldo, Jonathan S Schildcrout, Ellen Wright Clayton, Armand H. Matheny Antommara, Melissa Basford, Murray Brilliant, John J Connolly, Stephanie M Fullerton, Carol R Horowitz, Gail P Jarvik, Dave Kaufman, Terrie Kitchner, Rongling Li, Evette J Ludman, Catherine McCarty, Valerie McManus, Sarah C Stallings, Janet L Williams, and Ingrid A Holm (2016) “Conducting a Large, Multi-Site Survey about Patients' Views on Broad Consent: Challenges and Solutions.” *BMC Medical Research Methodology*. 16: 162. PMID: 27881091.
 17. Angela Lorts, Thomas D. Ryan, Armand H. Matheny Antommara, Michael Lake, and John Bucuvalas (2016) “Obtaining Consensus Regarding International Transplantation Continues to be

- Difficult for Pediatric Centers in the United States.” *Pediatric Transplant*. 20: 774-777. PMID: 27477950.
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Newspaper Articles

1. W. Bradley Poss and Armand H. Matheny Antommara (2010) “Mass casualty planning must incorporate needs of children.” *AAP News* 31 (July): 38.
2. Robert Murray and Armand H. Matheny Antommara (2010) “Pediatricians should work with school nurses to develop action plans for children with DNAR orders.” *AAP News* 31 (May): 30..
3. Armand H. Matheny Antommara (2009) “Addressing physicians’ conscientious objections in health care.” *AAP News* 30 (December): 32.

UNPUBLISHED POSTER PRESENTATIONS

1. Armand H. Matheny Antommara. (2018) “Ethical Issues in the Care of International Patients: A Case Study.” International Conference on Clinical Ethics and Consultation, Oxford, United Kingdom.
1. Jill S Sweney, Brad Poss, Colin Grissom, Brent Wallace, and Armand H Matheny Antommara, (2010) “Development of a Statewide Pediatric Pandemic Triage Plan in Utah.” Pediatric Academic Societies Annual Meeting, Vancouver, Canada. E-PAS20103713.147.
2. Christopher G. Maloney, Armand H. Matheny Antommara, James F. Bale, Thomas Greene, Jian Ying, Gena Fletcher, and Rajendu Srivastava (2010) “Why Do Pediatric Interns Violate the 30 Hour Work Rule?” Pediatric Academic Societies Annual Meeting, Vancouver, Canada. E-PAS20101500.596
3. Armand H. Matheny Antommara and Edward B. Clark (2007) “Resolving Conflict through Bioethics Mediation.” 3rd International Conference on Ethics Consultation and Clinical Ethics, Toronto, Canada.
4. Elizabeth Tyson, Tracy Hill, Armand Antommara, Gena Fletcher, and Flory Nkoy (2007) “Physician Practice Patterns Regarding Nasogastric Feeding Supplementation and Intravenous Fluids in Bronchiolitis Patients.” Pediatrics Academic Societies Annual Meeting, Toronto, Canada. E-PAS2007:61300.

ORAL PRESENTATIONS**Keynote/Plenary Lectures****International**

1. 2021, *Panelist*, Partnership for Quality Medical Donations, Charitable Access Programming for Rare Diseases, “Ethical Issues,” Webinar, April 6.
2. 2017, *Invited Speaker*, Spina Bifida Fetoscopic Repair Study Group and Consortium, “Ethics of Innovation and Research in Fetal Surgery,” Cincinnati, Ohio, October 26.
3. 2014, *Invited Speaker*, CIC 2013 CCI: Canadian Immunization Conference, “Condition-of-Service Influenza Prevention in Health Care Settings,” Ottawa, Canada, December 2.
4. 2014, *Invited Speaker*, National Conference of the Chinese Pediatric Society, “A Brief Introduction to Pediatric Research and Clinical Ethics,” Chongqing, China, September 12.

National

1. 2020, *Panelist*, Children’s Mercy Bioethics Center, “Ethical Issues in the COVID Pandemic at Children’s Hospitals,” Webinar, March 2.
2. 2019, *Invited Speaker*, North American Fetal Therapy Network (NAFTnet), “Ethics of Innovation,” Chicago, Illinois, October 12.
3. 2019, *Panelist*, National Society of Genetic Counselors Prenatal Special Interest Group, “Fetal Intervention Ethics,” Webinar, September 12.
4. 2017, *Invited Participant*, American College of Epidemiology Annual Meeting, Preconference Workshop, “Extreme Personal Exposure Biomarker Levels: Guidance for Study Investigators,” New Orleans, Louisiana, September 24.
5. 2016, *Invited Speaker*, American Academy of Pediatrics National Conference & Exhibition, Joint Program: Section on Hospital Medicine and Section on Bioethics, “Resource Allocation: Do We Spend Money to Save One Patient with Ebola or Over a 1,000?” San Francisco, California, October 23.
6. 2016, *Invited Speaker*, 26th Annual Specialist Education in Extracorporeal Membrane Oxygenation (SEECHMO) Conference, “Ethical Issues in ECMO: The Bridge to Nowhere,” Cincinnati, Ohio, June 5.
7. 2015, *Invited Speaker*, Extracorporeal Life Support Organization (ELSO) 26th Annual Conference, “ECMO-Supported Donation after Circulatory Death: An Ethical Analysis,” Atlanta, Georgia, September 20.
8. 2014, *Invited Speaker*, Pediatric Evidence-Based Practice 2014 Conference: Evidence Implementation for Changing Models of Pediatric Health Care, “Ethical Issues in Evidence-Based Practice,” Cincinnati, Ohio, September 19.
9. 2014, *Invited Speaker*, 6th Annual David Kline Symposium on Public Philosophy: Exploring the Synergy Between Pediatric Bioethics and Child Rights, “Does Predictive Genetic Testing for Adult Onset Conditions that Are Not Medically Actionable in Childhood Violate Children’s Rights?” Jacksonville, Florida, March 6.
10. 2010, *Invited Speaker*, Quest for Research Excellence: The Intersection of Standards, Culture and Ethics in Childhood Obesity, “Research Integrity and Religious Issues in Childhood Obesity Research,” Denver, Colorado, April 21.
11. 2010, *Invited Speaker*, Symposium on the Future of Rights of Conscience in Health Care: Legal and Ethical Perspectives, J. Reuben Clark Law School at Brigham Young University and the Ave Maria School of Law, “Conscientious Objection in Clinical Practice: Disclosure, Consent, Referral, and Emergency Treatment,” Provo, Utah, February 26.
12. 2009, *Invited Speaker*, Pediatric Organ Donation Summit, “Research Findings Regarding Variations in Pediatric Hospital Donation after Cardiac Death Policies,” Chicago, Illinois, August 18.
13. 2008, *Meet-the-Experts*, American Academy of Pediatrics National Conference & Exhibition, “Physician Refusal to Provide Treatment: What are the ethical issues?” Boston, Massachusetts, October 11.

14. 2008, *Invited Conference Faulty*, Conscience and Clinical Practice: Medical Ethics in the Face of Moral Controversy, The MacLean Center for Clinical Medical Ethics at the University of Chicago, “Defending Positions or Identifying Interests: The Uses of Ethical Argumentation in the Debate over Conscience in Clinical Practice,” Chicago, IL, March 18.
15. 2007, *Symposium Speaker*, Alternative Dispute Resolution Strategies in End-of-Life Decisions, The Ohio State University Mortiz College of Law, “The Representation of Children in Disputes at the End-of-Life,” Columbus, Ohio, January 18.
16. 2005, *Keynote Speaker*, Decisions and Families, *Journal of Law and Family Studies* and The University of Utah S.J. Quinney College of Law, “Jehovah’s Witnesses, Roman Catholicism, and Calvinism: Religion and State Intervention in Parental, Medical Decision-Making,” Salt Lake City, Utah, September 23.

Regional/Local

1. 2021, *Panelist*, Pediatric Residency Noon Conference, University of Tennessee Health Science Center, “Bioethics Rounds—Ethical Issues in the Care of Transgender Adolescents,” Memphis, Tennessee, September 21.
2. 2020, *Keynote Speaker*, 53rd Annual Clinical Advances in Pediatrics, “Referral to a Fetal Care Center: How You Can Help Patients’ Mothers Address the Ethical Issues,” Kansas City, Kansas, September 16.
3. 2019, *Speaker*, Patient and Family Support Services, Primary Children’s Hospital, “Ethical Issues in the Care of Trans Adolescents,” Salt Lake City, Utah, December 5.
4. 2019, *Speaker*, Evening Ethics, Program in Medical Ethics and Humanities, University of Utah School of Medicine, “Patients, Parents, and Professionals: Ethical Issues in the Treatment of Trans Adolescents,” Salt Lake City, Utah, December 4.
5. 2019, *Speaker*, Pediatric Hospital Medicine Board Review Course, “Ethics, Legal Issues, and Human Rights including Ethics in Research,” Cincinnati, Ohio, September 8.
6. 2019, *Speaker*, Advances in Fetology, “Evolving Attitudes Toward the Treatment of Children with Trisomies,” Cincinnati, Ohio, September 6.
7. 2019, *Speaker*, Half-Day Ethics Training: Ethics Consultation & Ethics Committees, “Navigating the Rapids of Clinical Ethics Consultation: Intake, Recommendations, and Documentation,” Salt Lake City, Utah, June 1.
8. 2019, *Speaker*, Scientific and Ethical Underpinnings of Gene Transfer/Therapy in Vulnerable Populations: Considerations Supporting Novel Treatments, BioNJ, “What Next? An Ethical analysis of Prioritizing Conditions and Populations for Developing Novel Therapies,” Cranbury, New Jersey, March 7.
9. 2018, *Panelist*, Periviability, 17th Annual Regional Perinatal Summit, Cincinnati, Ohio, October 12.
10. 2018, *Speaker*, Regional Advance Practice Registered Nurse (APRN) Conference, “Adults are Not Large Children: Ethical Issues in Caring for Adults in Children’s Hospitals,” Cincinnati, Ohio, April 26.
11. 2018, *Speaker*, Southern Ohio/Northern Kentucky Sigma Theta Tau International Annual Conference, “Between Hope and Hype: Ethical Issues in Precision Medicine,” Sharonville, Ohio, March 2.
12. 2017, *Speaker*, Advances in Fetology 2017, “Ethics of Innovation and Research: Special Considerations in Fetal Therapy Centers,” Cincinnati, Ohio, October 27.
13. 2016, *Speaker*, End-of-Life Pediatric Palliative Care Regional Conference, “Ethical/Legal Issues in Pediatric Palliative Care,” Cincinnati, Ohio, September 15.
14. 2016, *Speaker*, 26th Annual Bioethics Network of Ohio (BENO) Conference, “When Does Parental Refusal of Medical Treatment for Religious Reasons Constitute Neglect?” Dublin, Ohio, May 29.
15. 2014, *Speaker*, Cincinnati Comprehensive Sickle Cell Center Symposium: Research Ethics of Hydroxyurea Therapy for Sickle Cell Disease During Pregnancy and Lactation, “Ethical Issues in Research with Pregnant and Lactating Women,” Cincinnati, Ohio, October 30.

16. 2014, *Speaker*, Advances in Fetology 2014, "The 'Miracle Baby' and Other Cases for Discussion," Cincinnati, Ohio, September 26.
17. 2014, *Speaker*, Advances in Fetology 2014, "'Can you tell me ...?': Achieving Informed Consent Given the Prevalence of Low Health Literacy," Cincinnati, Ohio, September 26.
18. 2014, *Panelist*, Center for Clinical & Translational Science & Training, Secrets of the Dead: The Ethics of Sharing their Data, Cincinnati, Ohio, August 28.
19. 2014, *Speaker*, Office for Human Research Protections Research Community Forum: Clinical Research ... and All That Regulatory Jazz, "Research Results and Incidental Findings: Do Investigators Have a Duty to Return Results to Participants," Cincinnati, Ohio, May 21.
20. 2013, *Opening Presentation*, Empirical Bioethics: Emerging Trends for the 21st Century, University of Cincinnati Center for Clinical & Translational Science & Training, "Empirical vs. Normative Ethics: A Comparison of Methods," Cincinnati, Ohio, February 21.
21. 2012, *Videoconference*, New York State Task Force on Life and the Law, "Pediatric Critical Care Triage," New York, New York, March 1.
22. 2011, *Presenter*, Fall Faculty Development Workshop, College of Social Work, University of Utah, "Teaching Ethics to Students in the Professions," Salt Lake City, Utah, November 14.
23. 2011, *Speaker*, 15th Annual Conference, Utah Chapter of the National Association of Pediatric Nurse Practitioners, "Ethical Issues in Pediatric Practice," Salt Lake City, Utah, September 22.
24. 2011, *Speaker*, Code Silver! Active Shooter in the Hospital, Utah Hospitals & Health Systems Association, Salt Lake City, Utah, March 21.
25. 2009, *Speaker*, Medical Staff Leadership Conference, Intermountain Healthcare, "The Ethics of Leadership," Park City, Utah, October 30.
26. 2008, *Speaker*, The Art and Medicine of Caring: Supporting Hope for Children and Families, Primary Children's Medical Center, "Medically Provided Hydration and Nutrition: Ethical Considerations," Salt Lake City, Utah, February 25.
27. 2005, *Speaker*, Utah NAPNAP (National Association of Pediatric Nurse Practitioners) Chapter Pharmacology and Pediatric Conference, "Immunization Update," Salt Lake City, Utah, August 18.
28. 2005, *Keynote Speaker*, 17th Annual Conference, Utah Society for Social Work Leadership in Health Care, "Brain Death: Accommodation and Consultation," Salt Lake City, March 18.
29. 2004, *Continuing Education Presentation*, Utah NAPNAP (National Association of Pediatric Nurse Practitioners), "Febrile Seizures," Salt Lake City, Utah, April 22.
30. 2004, *Speaker*, Advocacy Workshop for Primary Care Providers, "Ethics of Advocacy," Park City, Utah, April 3.
31. 2002, *Speaker*, 16th Annual Biologic Basis of Pediatric Practice Symposium, "Stem Cells: Religious Perspectives," Deer Valley, Utah, September 14.

Meeting Presentations

International

1. 2018, *Speaker*, International Conference on Clinical Ethics and Consultation, "A Systematic Review of Typologies Used to Characterize Clinical Ethics Consultations," Oxford, United Kingdom, June 21.

National

1. 2021, *Panelist*, Pediatric Endocrine Society Annual Meeting, Difference of Sex Development Special Interest Group, Virtual Conference, April 29.
2. 2020, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “Is This Child Dead? Controversies Regarding the Neurological Criteria for Death,” Virtual Conference, October 17.
3. 2020, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “Contemporary Ethical Controversy in Fetal Therapy: Innovation, Research, Access, and Justice,” Virtual Conference, October 15.
4. 2020, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “K-12 Schools and Mandatory Public Health Programs During the COVID-19 Pandemic,” Virtual Conference, October 15.
5. 2019, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “Ethical Issues in Translating Gene Transfer Studies Involving Children with Neurodegenerative Disorders,” Pittsburgh, Pennsylvania, October 26.
6. 2019, *Moderator*, Pediatric Academic Societies Annual Meeting, Clinical Bioethics, Baltimore, Maryland, April 28.
7. 2018, *Presenter*, American Society for Bioethics and Humanities Annual Meeting, “Looking to the Past, Understanding the Present, and Imaging the Future of Bioethics and Medical Humanities’ Engagement with Transgender Health,” Anaheim, California, October 19.
8. 2018, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “Should Vaccination Be a Prerequisite for Solid Organ Transplantation?” Anaheim, California, October 18.
9. 2018, Lindsey Douglas, Armand H. Matheny Antommaria, Derek Williams. *Workshop Presenter*, Pediatric Hospital Medicine Annual Meeting, “IRB Approved! Tips and Tricks to Smooth Sailing through the Institutional Review Board (IRB).” Atlanta, Georgia, July 20.
10. 2018, Alan Schroeder, Armand H. Matheny Antommaria, Hannah Bassett, Kevin Chi, Shawn Ralston, Rebecca Blankenburg. *Workshop Speaker*, Pediatric Hospital Medicine Annual Meeting, “When You Don’t Agree with the Plan: Balancing Diplomacy, Value, and Moral Distress,” Atlanta, Georgia, July 20.
11. 2018, Alan Schroeder, Hannah Bassett, Rebecca Blankenburg, Kevin Chi, Shawn Ralston, Armand H. Matheny Antommaria. *Workshop Speaker*, Pediatric Academic Societies Annual Meeting, “When You Don’t Agree with the Plan: Balancing Diplomacy, Value, and Moral Distress,” Toronto, Ontario, Canada, May 7.
12. 2017, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “Tensions in Informed Consent for Gender Affirming Hormone Therapy and Fertility Preservation in Transgender Adolescents,” Kansas City, Missouri, October 19.
13. Lindsey Douglas, Armand H. Matheny Antommaria, and Derek Williams. 2017, *Workshop Leader*, PHM[Pediatric Hospital Medicine]2017, “IRB Approved! Tips and Tricks to Smooth Sailing through the Institutional Review Board (IRB) Process,” Nashville, Tennessee, July 21.
14. 2016, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “Ethical Challenges in the Care of International Patients: Organization, Justice, and Cultural Considerations,” Washington, DC, October 9.
15. 2015, *Coauthor*, The American Society of Human Genetics Annual Meeting, “Adolescents’ Opinions on Disclosure of Non-Actionable Secondary Findings in Whole Exome Sequencing,” Baltimore, Maryland, October 9.
16. 2012, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “A Public Health Ethics Analysis of the Mandatory Immunization of Healthcare Personnel: Minimizing Burdens and Increasing Fairness,” Washington, DC, October 21.
17. Armand H. Matheny Antommaria, Valerie Gutmann Koch, Susie A. Han, Carrie S. Zoubul. 2012, *Moderator*, American Society for Bioethics and Humanities Annual Meeting, “Representing the

Underrepresented in Allocating Scarce Resources in a Public Health Emergency: Ethical and Legal Considerations,” Washington, DC, October 21.

18. 2012, *Platform Presentation*, Pediatric Academic Societies Annual Meeting, “Qualitative Analysis of International Variation in Donation after Circulatory Death Policies and Rates,” Boston, Massachusetts, April 30. Publication 3150.4.
19. 2011, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “The Intersection of Policy, Medicine, and Ethics during a Public Health Disaster: Special Considerations for Children and Families,” Minneapolis, Minnesota, October 13.
20. Armand H. Matheny Antommara and Joel Frader. 2010, *Workshop Leader*, Pediatric Academic Societies Annual Meeting, “Conscientious Objection in Health Care: Respecting Conscience and Providing Access,” Vancouver, British Columbia, Canada. May 1. Session 1710.
21. 2009, *Workshop Leader*, American Society for Bioethics and Humanities Annual Meeting, “Advanced Clinical Ethics Consultation Skills Workshop: Process and Interpersonal Skills,” Washington, DC, October 15.
22. 2009, *Platform Presentation*, Pediatric Academic Societies Annual Meeting, “Qualitative Analysis of Donation after Cardiac Death Policies at Children’s Hospitals,” Baltimore, Maryland, May 2. Publication 2120.6.
23. 2008, *Speaker*, American Society for Bioethics and Humanities Annual Meeting, “Qualitative Analysis of Donation After Cardiac Death (DCD) Policies at Children’s Hospitals,” Cleveland, Ohio, October 26.
24. 2007, *Participant*, Hamline University School of Law Biennial Symposium on Advanced Issues in Dispute Resolution, “An Intentional Conversation About Conflict Resolution in Health Care,” Saint Paul, Minnesota, November 8-10.
25. 2007, *Speaker*, American Society of Bioethics and Humanities Annual Meeting, “Bioethics Consultation and Alternative Dispute Resolution: Opportunities for Collaboration,” Washington, DC, October 21.
26. 2007, *Speaker*, American Society of Bioethics and Humanities Annual Meeting, “DNAR Orders in Schools: Collaborations Beyond the Hospital,” Washington, DC, October 18.
27. Armand H. Matheny Antommara and Jeannie DePaulis. 2007, *Speaker*, National Association of Children’s Hospitals and Related Institutions Annual Meeting, “Using Mediation to Address Conflict and Form Stronger Therapeutic Alliances,” San Antonio, Texas, October 9.
28. 2006, *Speaker*, American Society of Bioethics and Humanities Annual Meeting, “Bioethics Mediation: A Critique,” Denver, Colorado, October 28.
29. 2005, *Panelist*, American Society of Bioethics and Humanities Annual Meeting, “How I See This Case: ‘He Is Not His Brain,’” Washington, DC, October 20.
30. 2005, *Paper Presentation*, Pediatric Ethics: Setting an Agenda for the Future, The Cleveland Clinic, “‘He Is Not His Brain:’ Accommodating Objections to ‘Brain Death,’” Cleveland, Ohio, September 9.
31. 2004, *Speaker*, American Society for Bioethics and Humanities Spring Meeting, “Verification and Balance: Reporting Within the Constraints of Patient Confidentiality,” San Antonio, Texas, March 13.
32. 2002, *Panelist*, American Society for Bioethics and Humanities Annual Meeting, “‘Who Should Survive?:’ Mental Retardation and the History of Bioethics,” Baltimore, Maryland, October 24.

Invited/Visiting Professor Presentations

1. 2013, Visiting Professor, “How to Listen, Speak and Think Ethically: A Multidisciplinary Approach,” Norton Suburban Hospital and Kosair Children’s Hospital, Louisville, Kentucky, May 22.
2. 2010, Visiting Professor, Program in Bioethics and Humanities and Department of Pediatrics, “What to Do When Parents Want Everything Done: ‘Futility’ and Ethics Facilitation,” University of Iowa Carver College of Medicine, Iowa City, Iowa, September 10.

Grand Round Presentations

1. 2019, David Green Lectureship, “Establishing Goals of Care and Ethically Limiting Treatment,” Primary Children’s Hospital, Salt Lake City, Utah, December 5.
2. 2018, “The Ethics of Medical Intervention for Transgender Youth,” El Rio Health, Tucson, Arizona, September 29.
3. 2018, Pediatrics, “Patient Selection, Justice, and Cultural Difference: Ethical Issues in the Care of International Patients,” Cleveland Clinic, Cleveland, Ohio, April 10.
4. 2018, Bioethics, “Reversibility, Fertility, and Conflict: Ethical Issues in the Care of Transgender and Gender Nonconforming Children and Adolescents,” Cleveland Clinic, Cleveland, Ohio, April 9.
5. 2017, Heart Institute, “‘Have you ever thought about what you would want—if god forbid—you became sicker?’: Talking with adult patients about advance directives,” Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, October 16.
6. 2017, Pediatrics, “Respectful, Effective Treatment of Jehovah’s Witnesses,” with Judith R. Ragsdale, PhD, MDiv and David Morales, MD, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, March 14.
7. 2017, Pediatrics, “Ethical Dilemmas about Discharging Patients When There Are Disagreements Concerning Safety,” Seattle Children’s Hospital, Seattle, Washington, January 19.
8. 2015, Pediatrics, “‘Nonbeneficial’ Treatment: What must providers offer and what can they withhold?,” Greenville Health System, Greenville, South Carolina, May 10.
9. 2014, Advance Practice Providers, “Common Ethical Issues,” Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, August 13.
10. 2014, Respiratory Therapy, “Do-Not-Resuscitate (DNR) Orders,” Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, July 15.
11. 2013, Heart Institute, “No Not Months. Twenty-Two *Years*-Old: Transiting Patients to an Adult Model of Care,” Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, October 21.
12. 2013, Division of Neonatology, “This Premature Infant Has a *BRCA1* Mutation!?: Ethical Issues in Clinical Whole Exome Sequencing for Neonatologists,” Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, October 11.
13. 2013, Department of Pediatrics, “Adults are Not Large Children: Ethical Issues in Caring for Adults in Children’s Hospitals,” Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, February 26.
14. 2012, “Mandate or Moratorium?: Persisting Ethical Controversies in Donation after Circulatory Death,” Cedars-Sinai Medical Center, Los Angeles, California, May 16.
15. 2011, Division of Pediatric Neurology Friday Lecture Series, “Inducing or Treating ‘Seizures’ with Placebos: Is It Ever Ethical?,” University of Utah, Salt Lake City, Utah, October 7.
16. 2011, Department of Surgery, “DNR Orders in the OR and other Ethical Issues in Pediatric Surgery: Case Discussions,” Primary Children’s Medical Center, Salt Lake City, Utah, October 3.
17. 2009, Department of Pediatrics, “What to Do When Parents Want Everything Done: ‘Futility’ and Bioethical Mediation,” Primary Children’s Medical Center, Salt Lake City, Utah, September 17.
18. 2008, Division of Pulmonology and Critical Care, “Futility: May Clinicians Ever Unilaterally Withhold or Withdraw Medical Treatment?” Utah Valley Regional Medical Center, Provo, Utah, April 17.
19. 2007, Division of Otolaryngology-Head and Neck Surgery, “Advance Directives, Durable Powers of Attorney for Healthcare, and Do Not Attempt Resuscitation Orders: Oh My!,” University of Utah School of Medicine, Salt Lake City, Utah, June 20.

Outreach Presentations

1. 2019, *Panelist*, Cincinnati Edition, WVXU, “The Ethics of Human Gene Editing,” Cincinnati, Ohio, June 13.
2. 2019, *Speaker*, Adult Forum, Indian Hill Church, “Medical Ethics,” Indian Hill, Ohio, March 24.

3. 2016, *Speaker*, Conversations in Bioethics: The Intersection of Biology, Technology, and Faith, Mt. Washington Presbyterian Church, “Genetic Testing,” Cincinnati, Ohio, October 12.
4. 2008, *Speaker*, Science in Society, Co-sponsored by KCPW and the City Library, “Death—Choices,” Salt Lake City, Utah, November 20.
5. 2003, *Panelist*, Utah Symposium in Science and Literature, “The Goodness Switch: What Happens to Ethics if Behavior is All in Our Brains?” Salt Lake City, Utah, October 10.
6. 2002, *Respondent*, H. Tristram Englehardt, Jr. “The Culture Wars in Bioethics,” Salt Lake Community College, Salt Lake City, Utah, March 29.

Podcasts

1. 2021, “Ethics of COVID Vaccines in Kids,” PHM from Pittsburgh, August 12.
2. 2020, COVID Quandaries: Episode 1, “Is Getting Sick Just Part of the Job?” Hard Call, October 6.

April 28, 2022

Biased Science: The Texas and Alabama Measures Criminalizing Medical Treatment for Transgender Children and Adolescents Rely on Inaccurate and Misleading Scientific Claims

Susan D. Boulware, M.D., Associate Professor of Clinical Pediatrics (Endocrinology), Yale School of Medicine; Director Clinical Operations, Section of Pediatric Endocrinology; Medical Director, Yale Pediatric Gender Program

Rebecca Kamody, PhD (Clinical Psychology), Assistant Professor, Yale School of Medicine: Child Study Center, Pediatrics, and Psychiatry

Laura Kuper PhD (Psychology), ABPP, Assistant Professor in Psychiatry, University of Texas Southwestern; Child & Adolescent Psychologist, Children's Medical Center Dallas

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Introduction and Summary

On February 18, 2022, Texas Attorney General Ken Paxton issued an interpretation of Texas state law (the “AG Opinion”), taking the position that certain medical procedures constitute child abuse as defined in the Texas Family Code.¹ Texas Governor Greg Abbott cited the AG Opinion as authority for his February 22, 2022 directive requiring the Texas Department of Family and Protective Services to “conduct a prompt and thorough investigation of any reported instances of these abusive procedures” (the “Governor’s Directive”).²

* We would like to thank Dr. Sundes Kazmir, M.D., FAAP, who provided helpful information on medical research on child abuse investigations. Calleigh Higgins, Christina Lepore, and Henry Robinson provided excellent research assistance.

¹ Tex. Op. Att’y. Gen. No. KP-0401 (Feb. 18, 2022) (hereinafter, “AG Opinion”).

² Letter from Greg Abbott, Governor of Texas, to Jaime Masters, Commissioner, Texas Department of Family and Protective Services, Feb. 22, 2022, at <https://gov.texas.gov/uploads/files/press/O-MastersJaime202202221358.pdf>

On April 7, 2022, Governor Kay Ivey of Alabama signed S.B. 184 (the “Alabama Law”), which imposes felony penalties on anyone providing certain medical care to any child, adolescent, or young adult under age 19.³

We are a group of six scientists and one law professor. Among the scientists, three of us are M.D.s., three are PhD’s, and all treat transgender children and adolescents in daily clinical practice. We all hold academic appointments at major medical schools, including the University of Texas Southwestern and Yale University. In this report, we examine in depth the scientific claims made in the AG Opinion and the text of the Alabama Law about medical care for transgender children and adolescents. Note that, although we reject the AG’s assertion that gender-affirming care constitutes child abuse and we oppose the Alabama Law’s criminalization of such care, we do not address, in this report, the legal validity of either.⁴ In accordance with our expertise, our focus is on the science.

After examining the AG Opinion and the findings of “fact” in the Alabama Law in detail, we conclude that their medical claims are not grounded in reputable science and are full of errors of omission and inclusion. These errors, taken together, thoroughly discredit the AG Opinion’s claim that standard medical care for transgender children and adolescents constitutes child abuse. The Alabama Law contains similar assertions of scientific fact, and these too are riddled with errors, calling into question the scientific foundations of the law.

In this report, we focus closely on the AG Opinion, because it contains a full explanation of its reasoning, while the Alabama law presents a list of purported scientific findings without argument or citation. We note, throughout, when the purported findings in the Alabama law echo the claims made in the AG Opinion.

The Texas Attorney General either misunderstands or deliberately misstates medical protocols and scientific evidence. The AG Opinion and the Alabama Law make exaggerated and unsupported claims about the course of treatment for gender dysphoria, specifically claiming that standard medical care for pediatric patients includes surgery on genitals and reproductive organs. In fact, the authoritative protocols for medical care for transgender children and adolescents, which define what we term “gender-affirming care,” specifically state that individuals must be over the age of majority before they can undergo such surgery. The AG Opinion and the Alabama Law also ignore the mainstream scientific evidence showing the significant benefits of gender-affirming care and exaggerate potential risks.

These are not close calls or areas of reasonable disagreement. The AG Opinion and the Alabama Law’s findings ignore established medical authorities and repeat discredited, outdated, and poor-quality information. The AG Opinion also mischaracterizes reputable sources and repeatedly cites a fringe group whose listed advisors have limited (or no) scientific and medical credentials and include well-known anti-trans activists.

³ Vulnerable Child Compassion and Protection Act, 2022 Ala. Laws 289 (hereinafter, “Alabama Law”).

⁴ For legal analysis, see Plaintiffs’ Original Petition and Application for Temporary Restraining Order, Temporary Injunction, Permanent Injunction, and Request for Declaratory Relief, Doe v. Abbott, March 1, 2022, at <https://www.aclu.org/legal-document/doe-v-abbott-petition>.

The AG Opinion falsely implies that puberty blockers and hormones are administered to prepubertal children, when, in fact, the standard medical protocols recommend drug treatments only for adolescents (and not prepubertal children). For purposes of this report, we use the term “adolescent” to refer to a child under the age of majority in whom pubertal development has begun.

The AG Opinion also omits mention of the extensive safeguards established by the standard protocols to ensure that medication is needed and that adolescents and their parents give informed assent and consent, respectively, to treatment when it is determined to be essential care. There is no rush to treatment: the course of gender-affirming care is tailored to each individual, and standard protocols mandate a process of consultation involving an interdisciplinary team including mental health professionals, medical providers, and parents.

By omitting the evidence demonstrating the substantial benefits of treatment for gender dysphoria, and by focusing on invented and exaggerated harms, the AG Opinion and the Alabama Law portray a warped picture of the scientific evidence. Contrary to their claims, a solid body of reputable evidence shows that gender-affirming care can be lifesaving and significantly improves mental health and reduces suicide attempts. The standard medical protocols were crafted by bodies of international experts based on a solid scientific foundation and have been in use for decades. Thus, treating gender dysphoria is considered not only ethical but also the clinically and medically recommended standard of care. Indeed, it would be considered unethical to *withhold* medical care from patients with gender dysphoria, just as it would be unethical to withhold potentially lifesaving care for patients with any other serious medical condition.

The repeated errors and omissions in the AG Opinion are so consistent and so extensive that it is difficult to believe that the opinion represents a good-faith effort to draw legal conclusions based on the best scientific evidence. It seems apparent that the AG Opinion is, rather, motivated by bias and crafted to achieve a preordained goal: to deny gender-affirming care to transgender youth. The same is true of the scientific claims made in the Alabama Law.

Many reputable scientific and professional organizations have issued statements opposing the Texas action,⁵ but to our knowledge, none have conducted the in-depth, point-by-point review that we provide here.

⁵ See APA President Condemns Texas Governor’s Directive to Report Parents of Transgender Minors [Internet]. Washington, D.C.: American Psychological Association; 2022 Feb 24 [cited 2022 Apr 15]. Available from: <https://www.apa.org/news/press/releases/2022/02/report-parents-transgender-children>; American Academy of Pediatrics, AAP, Texas Pediatric Society Oppose Actions in Texas Threatening Health of Transgender Youth [Internet]. Itasca (IL): American Academy of Pediatrics; 2022 Feb 24 [cited 2022 Apr 15]. Available from: <https://www.aap.org/en/news-room/news-releases/aap/2022/aap-texas-pediatric-society-oppose-actions-in-texas-threatening-health-of-transgender-youth/>; AACAP Statement Opposing Actions in Texas Threatening the Health, Mental Health and Well-Being of Transgender and Gender Diverse Youth and Their Families [Internet]. Washington, D.C.: American Academy of Child & Adolescent Psychiatry; 2022 March 1 [cited 2022 Apr 22]. Available from: https://www.aacap.org/AACAP/zLatest_News/AACAP_Statement_Opposing_Actions_in_Texas.aspx. See also Letter from James L. Madara, CEO and Executive Vice President of the American Medical Association, to Bill McBride, Executive Director of the National Governors Association, April 26, 2021 (opposing legislation in

Throughout this report, we use the highest-quality scientific evidence available. In this context, large-scale, randomized controlled trials would be inappropriate for ethical reasons: when medical care has been shown (by other methods) to reduce gender dysphoria and improve mental health, as is the case for gender-affirming care for individuals with gender dysphoria, it would be unethical to deny that care to a control group of patients. This is true in many areas of medicine. In such cases, physicians instead rely on studies using other scientific methods, and they judge the relative quality of evidence based on several factors, including whether the study is peer-reviewed, published in a high-impact journal, up to date, and conducted by reputable investigators.

In this report, we cite studies that are peer-reviewed, up to date, conducted by respected investigators, and published in high-impact journals that are widely read. This represents the highest-quality evidence available to physicians making treatment decisions in this context. By contrast, the AG Opinion relies on very poor-quality evidence. Only two of its sources are peer-reviewed scientific studies. Of these, one is badly out-of-date, and the other is cited for a proposition that is irrelevant to the treatment of transgender children and adolescents.⁶

To summarize, we find that:

1. The AG Opinion and the Alabama Law falsely claim that current medical standards authorize the surgical sterilization of transgender children and adolescents. In fact, present medical standards state that individuals must be the age of majority or older before undergoing surgery on genitals or reproductive organs.

Current medical protocols do not allow for either surgery or drug therapy for prepubertal children and specifically state that genital surgery should not be carried out before patients reach the legal age of majority. The standards of care do permit the careful use of drug therapies for adolescents (but not prepubertal children) and caution that drug therapies should be undertaken only after a careful, staged process of psychological and medical counseling. The AG Opinion's and Alabama Law's lists of "sex change procedures" and the claims that doctors are routinely sterilizing children and teenagers do not reflect current medical practice.

Arkansas and other states that would deny gender-affirming care), at <https://www.ama-assn.org/press-center/press-releases/ama-states-stop-interfering-health-care-transgender-children>; Clarke M, Farnan A, Barba A, Giovanni K, Brymer M, Julian J. Gender-Affirming Care Is Trauma-Informed Care [Internet]. Los Angeles (CA) and Durham (NC): National Child Traumatic Stress Network; 2022 [cited 2022 Apr 15]. Available from: <https://www.nctsn.org/sites/default/files/resources/fact-sheet/gender-affirming-care-is-trauma-informed-care.pdf>.

⁶ One study is Dhejne C, Lichtenstein P, Boman M, Johansson AL, Langstrom N, Landen M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PLoS One* 2011 Feb 22;6(2):e16885. We discuss in Section 2 why Dhejne et al. is out of date and unsupportive of the AG's claims. The AG Opinion also cites one study for the proposition that "hysterectomy, oophorectomy, and orchiectomy result in permanent sterility." The cited study is Cheng PJ, Pastuszak AW, Myers JB, Goodwin IA, Hotaling JM. Fertility concerns of the transgender patient. *Transl Androl Urol*. 2019 Jun;8(3):209-218. As we explain in Section 1, current medical protocols do not authorize surgery on genitals or reproductive organs for anyone under the age of majority, and so the reference is irrelevant to the treatment of minors.

2. The AG Opinion and the Alabama Law ignore the substantial benefits of medical care for transgender children and adolescents, care which has consistently been shown to reduce gender dysphoria and improve mental health. The best scientific evidence shows that gender dysphoria is real, that untreated gender dysphoria leads predictably to serious, negative medical consequences, and that gender-affirming care significantly improves mental health outcomes, including reducing rates of suicide.

The AG Opinion and the Alabama Law omit any discussion of the demonstrated benefits of gender-affirming care as recognized by established medical science. The AG Opinion and the Alabama Law also greatly exaggerate the percentage of adolescents whose diagnosed gender dysphoria dissipates without gender-affirming care. And the AG Opinion repeats discredited evidence claiming that there is a wave of so-called “rapid-onset” gender dysphoria among U.S. adolescents.

3. The AG Opinion and the Alabama Law greatly exaggerate the risks of gender-affirming drug therapy.

The AG Opinion exhibits a poor understanding of medicine and consistently misstates medical protocols and scientific evidence. Contrary to the AG Opinion’s statements, gender-affirming drug therapy (including puberty blockers and hormonal treatments) is safe and effective and has been approved by the major medical authorities. Puberty blockers are fully reversible; when discontinued, puberty begins, and fertility develops normally.

Gender-affirming hormone treatments can reduce fertility to some degree while ongoing, but the evidence suggests that these effects are reversible when hormone therapy is discontinued. Standard medical protocols manage these risks in the way any medical risks should be managed: by weighing the benefits of treatment against potential harms and by a careful and individualized process of consultation and consent. Indeed, the informed consent procedures for gender-affirming drug treatment are at least as rigorous as the consent required for any other drug treatment.

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Section 1. The AG Opinion and the Alabama Law falsely claim that current medical standards authorize the surgical sterilization of transgender children and adolescents. In fact, present medical standards state that individuals must be the age of majority or older before undergoing surgery on genitals or reproductive organs.

The AG Opinion asserts that the medical treatments for transgender children include a list of surgical procedures including “sterilization through castration, vasectomy, hysterectomy, oophorectomy, metoidioplasty, orchiectomy, penectomy, phalloplasty, and vaginoplasty.”⁷ The AG Opinion also claims that physicians dispense “drugs to children that induce transient or permanent infertility,” including “(1) puberty-suppression or puberty-blocking drugs, (2) supraphysiologic doses of testosterone to females; and (3) supraphysiologic doses of estrogen to males.”⁸ The AG Opinion asserts that “[t]he novel trend of providing these elective sex changes to minors often has the effect of permanently sterilizing those minor children.”⁹ The Alabama Law contains similar statements.¹⁰

These statements are incorrect. Current medical protocols state that genital surgery should not be carried out before patients reach the legal age of majority. To make the distinction clear, we refer to the AG Opinion’s list of procedures as the “AG Opinion claims.” We refer to the standard medical protocols issued by the World Professional Association for Transgender Health (“WPATH”) and the Endocrine Society as “gender-affirming care.”¹¹

The AG Opinion fails to engage with the WPATH and Endocrine Society guidelines (or any other recognized set of medical guidelines), even though these are well-known, widely viewed as authoritative, and readily available to the public.¹² These standards are explicitly

⁷ AG Opinion, p. 1. The AG Opinion also includes “(2) mastectomies; and (3) removing from children otherwise healthy or non-diseased body part or tissue.” These procedures do not affect fertility, which is the opinion’s stated concern, and they are common among cisgender adolescents (e.g., rhinoplasty and breast reduction). We do not address these procedures in this report.

⁸ AG Opinion, p. 1.

⁹ AG Opinion, pp. 2-3.

¹⁰ Alabama Law, Section 2(6).

¹¹ See 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, Pfafflin F, Rachlin K, Robinson B, Schechter LS, Tangpricha V, van Trotsenburg M, Vitale A, Winter S, Whittle S, Wylie KR, Zucker K. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th version [Internet]. East Dundee (IL): World Professional Association for Transgender Health; 2012 [cited 2022 Apr 17]. Available from: <https://www.wpath.org/publications/soc> (hereinafter, “WPATH (2012)”); Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T’Sjoen GG. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Sept 13;102(11):3869-3903 (hereinafter, “Endocrine Society (2017)”).

¹² The AG Opinion quotes the WPATH standards once, but the opinion mischaracterizes the source material and persists in its repeated claims that gender-affirming care involves genital surgery on children. At page 4, the AG Opinion quotes WPATH (2012) to the effect that genital surgery should not be carried out before patients reach the age of majority. See AG Opinion, p. 4. The AG Opinion misleadingly uses the WPATH quotation as evidence that there is no benefit from gender-affirming care; in fact, WPATH (2012), pp. 10-21, acknowledges the benefits of psychotherapy and, in the case of adolescents, puberty blockers and hormone therapy. Apart from the isolated and misleading citation to WPATH (2012) at p. 4, the AG Opinion does not otherwise discuss the WPATH standards or correct its repeated assertion that children and adolescents are undergoing “sex change” procedures.

followed by major gender clinics in the United States.¹³ We address the AG Opinion's misstatements in turn.

a. The medical standards of care for transgender children specifically state that individuals must be the age of majority or older before undergoing surgery on genitals or reproductive organs.

Gender dysphoria is a recognized medical condition¹⁴ that merits medical treatment, and the evidence shows that treatment improves mental health outcomes, including reducing rates of suicidal ideation and suicide attempts. (See Section 2 of this report.)

Individuals with gender dysphoria seek care at a wide variety of ages, which depends on sociocultural and environmental factors, including parental support, socioeconomic status, and access to care. In the early phases of treatment, gender-affirming care consists of using the individual's preferred pronouns, psychosocial support, and education about the next stages of transition if desired. Medical professionals draw an important distinction between hormonal treatment and gender-affirming surgery. Hormonal transition is an established practice in older adolescents experiencing gender dysphoria, but current standards for gender-affirming care set the age of majority as the threshold for considering surgery on genitals and reproductive organs.

Two of the leading guidelines for the medical treatment of transgender children and adolescents are those published by WPATH and by the Endocrine Society. WPATH is a leading international organization of scientists, which has issued standards of care for transgender adults and children since 1979.¹⁵ Several revisions have been made as scientific evidence drives changes in standards. The current version, WPATH Standards of Care, version 7, is viewed as authoritative in the medical community and is widely consulted by physicians and other clinicians. The WPATH standards explicitly state that genital surgery should not be carried out until the patient reaches the age of majority. Further, WPATH advises that "the age threshold should be seen as a minimum criterion and not an indication in and of itself for active intervention."¹⁶

The Endocrine Society is the leading international organization of endocrinologists, i.e., physicians specializing in the study and treatment of the human endocrine system, including hormonal treatment.¹⁷ In 2017, the Endocrine Society issued clinical practice guidelines for the

¹³ See Kuper LE, Stewart S, Preston S, Lau M, Lopez X. Body Dissatisfaction and Mental Health Outcomes of Youth on Gender-Affirming Hormone Therapy. *Pediatrics* 2020 Apr;145(4):e20193006. doi: 10.1542/peds.2019-3006 (stating that Endocrine Society guidelines are followed). The same is true of the Greenwich Center for Gender & Sexuality. The Yale Pediatric Gender Clinic generally follows WPATH standards.

¹⁴ American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, Fifth edition. 2013.

¹⁵ The current version is WPATH (2012). According to WPATH, the first six versions were published in 1979, 1980, 1981, 1990, 1998, and 2001.

¹⁶ WPATH (2012), at p. 21: "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."

¹⁷ Who We Are [Internet]. Washington, D.C.: The Endocrine Society; c2022 [cited 2022 Apr 15]. Available from: <https://www.endocrine.org/about-us>.

treatment of gender dysphoria.¹⁸ Like WPATH, the Endocrine Society does not authorize surgery on the genitals or reproductive organs of transgender children or adolescents.¹⁹

Both WPATH and Endocrine Society guidelines are based on reviews of the best available science conducted by panels of experts across medical disciplines. These guidelines are updated periodically to ensure that they reflect a current understanding of scientific knowledge and clinical practice. The statements in this report refer to current WPATH and Endocrine Society standards, i.e., those in force as of the date of publication of this report.

b. The standards of care do not recommend drug treatments (puberty blockers or hormones) for prepubertal children.

The AG Opinion wrongly conflates treatments available to adolescents with those offered to children.²⁰ In fact, current medical protocols for gender-affirming care do not recommend either surgery or drug treatments (puberty blockers and hormones) for prepubertal children.

The WPATH standards state clearly that physical interventions, including drug therapy, are recommended only for adolescents and only after an in-depth process of mental health and medical counseling, described below. The WPATH standards state that social transition, which is entirely reversible, may be considered by the parents of prepubertal children.²¹ (Social transition consists of, e.g., wearing clothes and using a name that are consistent with the child's gender identity.) The Endocrine Society also "recommend[s] against puberty blocking and gender-affirming hormone treatment in prepubertal children."²² (There is, of course, no need for such medication in children who have not reached puberty.)

c. Present standards of care recommend drug treatments for adolescents (youth who have developed pubertal changes) only for those with puberty-induced worsening gender dysphoria and only after a careful protocol that begins with psychological and medical counseling to ensure valid consent.

The AG Opinion claims that "[c]hildren and adolescents are promised relief and asked to 'consent' to life-altering, irreversible treatment—and to do so in the midst of reported psychological distress, when they cannot weigh long-term risks the way adults do."²³ The Alabama Law contains a similar statement.²⁴

This statement misdescribes both medical practice and the consent procedures used for the treatment of adolescents. Legally, a parent or guardian must consent to the medical treatment of a minor, and so the AG Opinion is incorrect in implying that medical treatment depends on a

¹⁸ Endocrine Society (2017).

¹⁹ Id. (Guideline 5.5).

²⁰ AG Opinion, p. 2 (claiming that there is a "novel trend of providing these elective sex changes to minors," with "sex changes" previously defined to include surgery and drug therapies).

²¹ WPATH (2012), p. 17.

²² Endocrine Society (2017) (Guideline 1.4).

²³ AG Opinion, p. 4.

²⁴ Alabama Law, Section 2(15).

child or teenager's consent alone.²⁵ As noted above, medical protocols do not recommend drug therapy for prepubertal children, and so consent by young children is never an issue. For adolescents, the standard medical protocols provide for gender-affirming drug therapy only when medically necessary and after a comprehensive process that includes specialist medical consultation and assessment, parent consent and youth assent, and mental health evaluation.

A key feature of both the WPATH Standards of Care and the Endocrine Society Clinical Practice Guidelines is the central role of mental health professionals in assessing gender dysphoria and appropriate modes of medical treatment. The Endocrine Society notes, for example, that, "because of the psychological vulnerability of many individuals with [gender dysphoria], it is important that mental health care is available before, during, and sometimes also after transitioning."²⁶ Both WPATH and the Endocrine Society provide extensive guidance on how to provide psychosocial support to youth experiencing gender dysphoria, as well as a definition of what constitutes a properly trained mental health professional.

Contrary to the AG Opinion's implication, there is no medical rush to prescribe drug treatments to transgender adolescents. The current WPATH and Endocrine Society standards recommend a staged process for physical interventions, one that takes into account the presentation of gender dysphoria in each individual, along with their medical history and psychological functioning. Social transition, puberty blockers, and hormonal treatment may be used in stages, but not all adolescents with gender dysphoria undergo each treatment.²⁷ As always in medicine, the priority is to treat the patient as an individual and to address their physical and mental health needs holistically. WPATH, for example, expressly states that, "[b]efore any physical interventions are considered for adolescents, extensive exploration of psychological, family, and social issues should be undertaken The duration of this exploration may vary considerably depending on the complexity of the situation."²⁸

WPATH and Endocrine Society standards recommend puberty-suppressing medications (GnRH agonist treatment), only for adolescents and only with guardrails to ensure that medication is medically necessary and that adolescents and their parents give informed consent to treatment. These safeguards are worth summarizing in some detail, because they contradict the AG Opinion's claim that gender-affirming care, including drug therapy, is being casually administered.²⁹

For puberty-suppressing medications, the standards require the participation of a qualified mental health practitioner, who confirms that the adolescent has demonstrated a long-lasting and intense pattern of gender dysphoria, that gender dysphoria worsened with the onset of

²⁵ While the law usually grants parents the final decision, bioethicists have found that adolescents can be meaningful participants in the consent process. Clark BA, Virani A. "This Wasn't a Split-Second Decision": An Empirical Ethical Analysis of Transgender Youth Capacity, Rights, and Authority to Consent to Hormone Therapy. *J Bioeth Inq.* 2021 Mar;18(1):151-64; Vrouenraets LJ, de Vries ALC, de Vries MC, van der Miesen AIR, Hein IM. Assessing Medical Decision-Making Competence in Transgender Youth. *Pediatrics* 2021 Dec 1;148(6):e2020049643.

²⁶ Endocrine Society (2017).

²⁷ WPATH (2012), p. 18; Endocrine Society (2017) (Guidelines 2.1 and 2.2).

²⁸ WPATH (2012), p. 16.

²⁹ We quote the Endocrine Society phrasing, but the two protocols are substantively the same.

puberty, and that any coexisting psychological, medical, or social problems that could interfere with treatment have been addressed, so that the adolescent's situation and functioning are stable enough to start treatment. The guidelines also require informed assent by adolescents and (if under the age of majority) informed consent by their parents, and they require the involvement of a pediatric endocrinologist (or another physician versed in gender-affirming treatment) to ensure that puberty-blocking medication is warranted, that puberty has begun in the adolescent patient, and that there are no medical contraindications to puberty-blocking medication.³⁰

For those adolescents for whom progression to hormone therapy is medically indicated, WPATH and the Endocrine Society require additional counseling regarding the possible fertility effects of hormone therapy. In addition to parental consent, the guidelines require that a mental health practitioner confirm that the adolescent has "sufficient mental capacity (which most adolescents have by age 16 years)" to evaluate the benefits and risks of treatment.³¹

Section 2. The AG Opinion and the Alabama Law ignore the substantial benefits of medical care for transgender children and adolescents, care which has consistently been shown to reduce gender dysphoria and improve mental health. The best scientific evidence shows that gender dysphoria is real, that untreated gender dysphoria leads predictably to serious, negative medical consequences, and that gender-affirming care significantly improves mental health outcomes, including reducing rates of suicide.

The AG Opinion omits any discussion of the documented benefits of gender-affirming care and vastly overstates potential risks by relying on misrepresented or unreliable studies. The AG Opinion also misstates scientific evidence on the percentage of children and adolescents whose gender dysphoria resolves without treatment (sometimes termed "desistance"), and the opinion repeats discredited evidence on a purported novel trend of so-called rapid-onset gender dysphoria. The Alabama Law contains similar errors.³²

The AG Opinion falsely states that "The medical evidence does not demonstrate that children and adolescents benefit from engaging in these irreversible sterilization procedures."³³ Contrary to the AG Opinion's statements, scientific studies have demonstrated that gender dysphoria is a well-documented condition for which medical care is essential treatment. The established scientific evidence shows that treatment improves mental health outcomes, including reducing rates of suicidal ideation and suicide attempts.

In this Section, we review the scientific evidence on gender dysphoria and the benefits of gender-affirming treatment, and we correct the AG Opinion's and Alabama Law's erroneous claims.

a. Gender dysphoria is real, and untreated gender dysphoria is harmful.

The American Psychiatric Association explains that

³⁰ Endocrine Society (2017) (Table 5), citing WPATH (2012), p. 16.

³¹ Endocrine Society (2017) (Table 5).

³² Alabama Law, Section 2 and Section 2(4).

³³ AG Opinion, at 3.

[T]he term “transgender” refers to a person whose sex assigned at birth (i.e., the sex assigned by a physician at birth, usually based on external genitalia) does not match their gender identity (i.e., one’s psychological sense of their gender). Some people who are transgender will experience “gender dysphoria,” which refers to psychological distress that results from an incongruence between one’s sex assigned at birth and one’s gender identity. Though gender dysphoria often begins in childhood, some people may not experience it until after puberty or much later.³⁴

In 2013, the American Psychiatric Association released the fifth edition of the DSM-5, the standard reference for the diagnosis of mental health conditions. The DSM-5 recognizes gender dysphoria and sets forth criteria for diagnosis. These criteria include “a marked incongruence between one’s experienced/expressed gender and primary and/or secondary sex characteristics” and “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).” To meet diagnostic criteria, an individual must exhibit “clinically significant distress or impairment in social, occupational, or other important areas of functioning.”³⁵

In other words, individuals who live in a manner that is physically and socially incongruent to their gender identity can experience gender dysphoria – a clinically significant psychological distress that can lead to depressed mood.³⁶ Suicidal ideation and attempts have been found to be significantly higher among transgender adolescents who cannot obtain or do not receive gender-affirming care than among their cisgender peers. The harm of not providing gender-affirming care is well documented: 40% of trans individuals who do not receive hormones will attempt or complete suicide in their lifetime.³⁷ Untreated gender dysphoria can also lead to disordered eating. Patients may engage in unsafe eating behaviors (e.g., food restriction or purging) as a body-affirming tool and an effort to align their bodies with their gender identity. These behaviors can impair physical health and development.³⁸

³⁴ What is Gender Dysphoria? [Internet]. Washington, D.C.: American Psychiatric Association; 2020 Nov [cited 2022 Apr 15]. Available from: <https://www.psychiatry.org/patients-families/gender-dysphoria/what-is-gender-dysphoria>.

³⁵ American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, D.C.: American Psychiatric Association; 2013.

³⁶ Sorbara JC, Chiniara LN, Thompson S, Palmert MR. Mental health and timing of gender-affirming care. *Pediatrics* 2020 Oct 1;146(4):e20193600 (hereinafter, “Sorbara et al. 2020”).

³⁷ Herman JL, Brown TNT, Haas AP. Suicide Thoughts and Attempts Among Transgender Adults [Internet]. Los Angeles (CA): The Williams Institute, UCLA School of Law; 2019 Sept [cited 2022 Apr 1]. Available from: <https://williamsinstitute.law.ucla.edu/publications/suicidality-transgender-adults/>. So-called “conversion” therapy (an extreme form of denying gender-affirming care, which attempts to change a person’s gender identity to match the sex assigned at birth) has been shown to create psychological distress and prompt suicide. Turban JL, Beckwith N, Reisner SL, Keuroghlian AS. Association Between Recalled Exposure to Gender Identity Conversion Efforts and Psychological Distress and Suicide Attempts Among Transgender Adults. *JAMA Psychiatry* 2019 Sept 11;77(1):68-76.

³⁸ Coelho JS, Suen J, Clark BA, Marshall SK, Geller J, Lam PY. Eating Disorder Diagnoses and Symptom Presentation in Transgender Youth: a Scoping Review. *Curr Psychiatry Rep*. 2019 Oct 15;21(11):107; Kamody RC, Yonkers K, Pluhar EI, Olezski CL. Disordered Eating Among Trans-Masculine Youth: Considerations Through a Developmental Lens. *LGBT Health*. 2020 May/Jun;7(4):170-73; Legroux I, Cortet B. Factors influencing bone loss in anorexia nervosa: assessment and therapeutic options. *RMD Open*. 2019 Nov 13;5(2):e001009.

For all these reasons, the American Academy of Pediatrics, the American Psychological Association, and the American Academy of Child and Adolescent Psychiatry – the three major professional associations of pediatricians, psychologists, and child and adolescent psychiatrists – have endorsed gender-affirming care and condemned efforts to deny medical care to transgender people, as have the Texas Medical Society and the Alabama Psychological Association.³⁹ These organizations have also condemned so-called “conversion therapy” as ineffective, unethical, and dangerous.⁴⁰

The scientific consensus is clear: denying gender-affirming care harms transgender people and puts their lives at risk.⁴¹

b. Gender-affirming care has measurable and significant benefits.

The AG Opinion incorrectly states that “There is no evidence that long-term mental health outcomes are improved or that rates of suicide are reduced by hormonal or surgical intervention.”⁴² The AG’s statement that gender-affirming care is not beneficial is contradicted by a significant body of recent scientific evidence.⁴³

³⁹ Rafferty J, Committee on Psychosocial Aspects of Child and Family Health; Committee on Adolescence; Section on Lesbian, Gay, Bisexual, and Transgender Health and Wellness, Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents. *Pediatrics*. 2018 Oct;142(4):e20182162; American Psychological Association. Guidelines for psychological practice with transgender and gender nonconforming people. *American Psychologist* 2015 Dec;70(9):832-64 (hereinafter, “American Psychological Association (2015)”); AAP Continues to Support Care of Transgender Youth as More States Push Restrictions [Internet]. Itasca (IL): American Academy of Pediatrics; 2022 Jan 6 [cited 2022 Mar 31]. Available from: <https://publications.aap.org/aapnews/news/19021/AAP-continues-to-support-care-of-transgender>; Criminalizing Gender Affirmative Care with Minors [Internet]. Washington, D.C.: American Psychological Association; [cited 2022 Mar 30]. Available from: <https://www.apa.org/pi/lgbt/resources/policy/issues/gender-affirmative-care>; AACAP Statement Opposing Actions in Texas Threatening the Health, Mental Health and Well-Being of Transgender and Gender Diverse Youth and Their Families, Washington, D.C.: American Academy of Child & Adolescent Psychiatry; 2022 March 1 [cited 2022 Apr 22=]. Available from: https://www.aacap.org/AACAP/zLatest_News/AACAP_Statement_Opposing_Actions_in_Texas.aspx; Statement of the Alabama Psychological Association (aPA) Supporting Gender-Affirming Care for Transgender Youth and Urging Opposition to Alabama SB184/HB266 [internet]. Alabama Psychological Association 2022. Available at https://cdn.ymaws.com/www.alapsych.org/resource/resmgr/2022/sb184-hb266_apa_statement_3-.pdf; Sorrel AL, TMA Supports Evidence-Based Gender-Affirming Care in Lawsuit [internet]. Texas Medical Association. March 14, 2022. Available from <https://www.texmed.org/TexasMedicineDetail.aspx?id=59040>.

⁴⁰ APA Resolution on Gender Identity Change Efforts [Internet]. Washington, D.C.: American Psychological Association; 2021 Feb [cited 2022 Mar 31]. Available from: <https://www.apa.org/about/policy/resolution-gender-identity-change-efforts.pdf>.

⁴¹ Abreu RL, Sostre JP, Gonzalez KA, Lockett GM, Matsuno E. “I am afraid for those kids who might find death preferable”: Parental figures’ reactions and coping strategies to bans on gender-affirming care for transgender and gender diverse youth. *Psychology of Sexual Orientation and Gender Diversity* [Internet]. 2021 Jul 29 [cited 2022 Mar 31]; advance online publication. Available from: <https://psycnet.apa.org/record/2021-67997-001>; Hughes LD, Kidd KM, Gamarel KE, Operario D, Dowshen N. (2021). “These Laws Will Be Devastating”: Provider Perspectives on Legislation Banning Gender-Affirming Care for Transgender Adolescents. *Journal of Adolescent Health* 2021 Dec;69(6):976-82; Kidd KM, Sequeira GM, Paglisotti T, Katz-Wise SL, Kazmerski TM, Hillier A, Miller E, Dowshen N. “This could mean death for my child”: Parent perspectives on laws banning gender-affirming care for transgender adolescents. *Journal of Adolescent Health* 2021 Jun;68(6):1082-88.

⁴² AG Opinion, p. 4.

⁴³ De Vries AL, Steensma TD, Doreleijers TA, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *The Journal of Sexual Medicine* 2011 Aug;8(8):2276-83; De Vries

As explained in Section 1 of this report, social transition is an important first step for adolescents (and is the only medically accepted form of gender-affirming care for prepubertal children). The scientific evidence shows that social transition, including using a child or adolescent's chosen name, reduces depression and suicide risk.⁴⁴

A solid body of reliable research has shown that the potential next steps in gender-affirming care for adolescents with gender dysphoria – puberty-blocking medications and hormone therapy – have major mental-health benefits, including higher levels of general well-being and significantly decreased levels of suicidality.⁴⁵ Puberty blockers have been shown to

AL, McGuire JK, Steensma TD, Wagenaar EC, Doreleijers TA, Cohen-Kettenis PT. Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics* 2014 Oct;134(4):696-704; Costa R, Dunsford M, Skagerberg E, Holt V, Carmichael P, Colizzi M. Psychological Support, Puberty Suppression, and Psychosocial Functioning in Adolescents with Gender Dysphoria. *The Journal of Sexual Medicine* 2015 Nov;12(11):2206-14 (hereinafter, "Costa et al. 2015"); Allen LR, Watson LB, Egan AM, Moser CN. Well-being and suicidality among transgender youth after gender-affirming hormones. *Clinical Practice in Pediatric Psychology* 2019 Sept;7(3):302-11 (hereinafter, "Allen et al 2019"); Kaltiala R, Heino E, Tyolajarvi M, Suomalainen L. Adolescent development and psychosocial functioning after starting cross-sex hormones for gender dysphoria. *Nordic Journal of Psychiatry* 2020 Apr;74(3):213-19; de Lara DL, Rodriguez OP, Flores IC, Masa JLP, Campos-Munoz L, Hernandez MC, Amador JTR. Psychosocial assessment in transgender adolescents. *Anales de Pediatria (English Edition)* 2020 Jul;93(1):41-48; van der Miesen AI, Steensma TD, de Vries AL, Bos H, Popma A. Psychological Functioning in Transgender Adolescents Before and After Gender-Affirmative Care Compared with Cisgender General Population Peers. *Journal of Adolescent Health* 2020 Jun;66(6):699-704; Achille C, Taggart T, Eaton NR, Osipoff J, Tafuri K, Lane A, Wilson TA. 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;2020:8; Kuper LE, Stewart S, Preston S, Lau M, Lopez X. Body Dissatisfaction and Mental Health Outcomes of Youth on Gender-Affirming Hormone Therapy. *Pediatrics* 2020 Apr;145(4):e20193006; Turban JL, King D, Carswell JM, Keuroghlian AS. Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation. *Pediatrics* 2020 Feb;145(2):e20191725; Carmichael P, Butler G, Masic U, Cole TJ, De Stavola BL, Davidson S, Skageberg EM, Khadr S, Viner RM. Short-term outcomes of pubertal suppression in a selected cohort of 12 to 15 year old young people with persistent gender dysphoria in the UK. *PLoS One* 2021 Feb 2;16(2):e0243894; Grannis C, Leibowitz SF, Gahn S, Nahata L, Morningstar M, Mattson WI, Chen D, Strang JF, Nelson EE. Testosterone treatment, internalizing symptoms, and body image dissatisfaction in transgender boys. *Psychoneuroendocrinology* 2021 Oct;132:105358; Hisle-Gorman E, Schvey NA, Adirim TA, Rayne AK, Susi A, Roberts TA, Klein DA. Mental Healthcare Utilization of Transgender Youth Before and After Affirming Treatment. *The Journal of Sexual Medicine* 2021 Aug;18(8):1444-54; Green AE, DeChants JP, Price MN, Davis CK. Association of Gender-Affirming Hormone Therapy with Depression, Thoughts of Suicide, and Attempted Suicide Among Transgender and Nonbinary Youth. *Journal of Adolescent Health* 2022 Apr;70(4):643-49 (hereinafter, "Green et al. 2022"); Turban JL, King D, Kobe J, Reisner SL, Keuroghlian AS. Access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults. *PLoS One* 2022 Jan 12;17(1):e0261039 (hereinafter, "Turban et al. 2022"); Tordoff DM, Wanta JW, Collin A, Stephney C, Inwards-Breland DJ, Ahrens K. Mental Health Outcomes in Transgender and Nonbinary Youths Receiving Gender-Affirming Care. *JAMA Network Open* 2022 Feb 1;5(2):e220978 (hereinafter, "Tordoff et al. (2022)").

⁴⁴ Russell ST, Pollitt AM, Li G, Grossman AH. Chosen name use is linked to reduced depressive symptoms, suicidal ideation, and suicidal behavior among transgender youth. *Journal of Adolescent Health* 2018 Oct;63(4):503-05; Durwood L, McLaughlin KA, Olson KR. Mental health and self-worth in socially transitioned transgender youth. *Journal of the American Academy of Child & Adolescent Psychiatry* 2017 Feb;56(2):116-23.

⁴⁵ Allen et al. 2019, cited in note 43; Green et al. (2022), cited in note 43; Connolly MD, Zervos MJ, Barone II CJ, Johnson CC, Joseph CL. The Mental Health of Transgender Youth: Advances in Understanding. *Journal of Adolescent Health* 2016 Nov;59(5):489-95; Turban et al. 2022, cited in note 43; Costa et al. (2015), cited in note 43; See also Witcomb GL, Bouman WP, Claes L, Brewin N, Crawford JR, Arcelus J. 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* 2018 Aug 1; 235:308-15.

decrease suicidality in adulthood and to improve affect and psychosocial functioning as well as social life.⁴⁶ Hormone therapy has been shown to reduce suicidality in transgender adolescents when compared to peers with gender dysphoria who did not receive it.⁴⁷ Notably, none of the studies has found a worsening of these mental health measures among recipients of gender-affirming care.

Among children and adolescents, patients who present for gender-affirming care at later pubertal stages are more likely to require psychoactive medications and are more likely to have considered or attempted suicide than patients who received gender-affirming care at earlier stages of pubertal development.⁴⁸

As evidence for the proposition that “[t]here is no evidence that long-term mental health outcomes are improved or that rates of suicide are reduced by hormonal or surgical intervention,” the AG Opinion cites a 2011 Swedish study by Dhejne et al. that, the AG Opinion claims, “monitored transitioned individuals for 30 years [and] found high rates of post-transition suicide and significantly elevated all-cause mortality, including increased death rates from cardiovascular disease and cancer, although causality could not be established.”⁴⁹ In fact, the 2011 study by Dhejne is badly out-of-date and does not support the AG Opinion’s claim.

The Dhejne study compared post-gender-affirmation transgender individuals with cisgender individuals from the general population, as opposed to transgender individuals who did not receive gender-affirming care. Therefore, as the study’s author explicitly cautions in the body of the text, *it is impossible to conclude from this data* that gender-affirming procedures were a causative factor in suicidality among transgender individuals.⁵⁰ Rather, the study shows only that transgender adults were more likely to experience suicidal ideation/attempts and risky behavior when compared to the general population in Sweden between 1973 and 2003. Further, the Dhejne study is not generalizable to a modern American population or to adolescents. During the study period, Swedish law required that individuals seeking gender-affirming surgery be

⁴⁶ Rew L, Young CC, Monge M, Bogucka R. Review: Puberty blockers for transgender and gender diverse youth – a critical review of the literature. *Child and Adolescent Mental Health* 2021 Feb;26(1):3-14; de Vries AL, Steensma TD, Doreleijers TA, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. *J Sex Med.* 2011 Aug;8(8):2276-83. Epub 2010 Jul 14 (hereinafter, “de Vries et al. (2011)”).

⁴⁷ Tordoff et al (2022), cited in note 43; Sorbara et. al. (2020), cited in note 36.

⁴⁸ Sorbara JC et. al. (2020), cited in note 36. Studies of adults confirm that gender-affirming treatment has been associated with marked improvement in mental health outcomes in transgender patients. See Almazan AN, Keuroghlian AS. Association Between Gender-Affirming Surgeries and Mental Health Outcomes. *JAMA Surgery* 2021 Jul 1;156(7):611-18; Marano AA, Louis MR, Coon D. Gender-Affirming Surgeries and Improved Psychosocial Health Outcomes. *JAMA Surgery* 2021 Jul 1;156(7):685-87; Swan J, Phillips TM, Sanders T, Mullens AB, Debattista J and Bromdal A. Mental health and quality of life outcomes of gender-affirming surgery: A systematic literature review, *Journal of Gay & Lesbian Mental Health*, 2022.

⁴⁹ AG Opinion, at 4, citing Dhejne C, Lichtenstein P, Boman M, Johansson AL, Langstrom N, Landen M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PLoS One* 2011 Feb 22;6(2):e16885 (hereinafter, “Dhejne (2011)”).

⁵⁰ “It is therefore important to note that the current study is only informative with respect to [transgender] persons’ health after sex reassignment; *no inferences can be drawn as to the effectiveness of sex reassignment as a treatment for transsexualism*. In other words, the results should not be interpreted such as sex reassignment per se increases morbidity and mortality. Things might have been even worse without sex reassignment.” Dhejne (2011) at 7 (emphasis added).

sterilized. The presence of this law alone might account for the higher risk of suicide attempts and risky behavior in the transgender population compared to the cisgender population at the time.⁵¹

The AG Opinion also mischaracterizes an important governmental decision, claiming incorrectly that the Centers for Medicare and Medicaid Services (“CMS”) found that gender-affirming care has no benefits. The AG Opinion claims that “there is no scientific consensus that [medical care] even serve[s] to benefit minor children dealing with gender dysphoria,” and that “[t]he lack of evidence in this field is why the CMS rejected a nationwide coverage mandate for adult gender transition surgeries during the Obama Administration.”⁵² Although the CMS did issue a 2016 Decision Memo denying blanket, automatic coverage for gender-affirming surgery, the decision specifically *authorizes* Medicare and Medicaid providers to cover such surgery on a case-by-case basis.⁵³ Thus, contrary to AG Opinion’s claim, the CMS decision memo expressly *permits* state and local decision-makers to authorize coverage for gender-affirming surgery.⁵⁴ The federal directive simply declines to authorize automatic coverage in every case. And, in fact, the 2016 CMS decision marks an expansion of the permissibility of gender-affirming treatment: the Decision Memo followed the 2014 revocation of the CMS’s 1989 decision to deny nationwide coverage.⁵⁵

Further, the CMS did not reach any negative conclusion on the benefits of gender-affirming care for children and adolescents. The CMS reviewed only studies on the outcomes of surgery (not hormone treatment) for an adult population that is overwhelmingly elderly (over age 65) and has a high prevalence of preexisting medical conditions that can make surgery risky, regardless of its purpose.⁵⁶

⁵¹ Nelson R. Transgender People in Sweden No Longer Face Forced Sterilization. Time [Internet]. 2013 Jan 14 [cited 2022 Apr 1]; Available from: <https://newsfeed/time.com/2013/01/14/transgender-people-in-sweden-no-longer-face-forced-sterilization/>. The presence of this law alone might account for the higher risk of suicide attempts and risky behavior in the transgender population at the time.

⁵² AG Opinion, at 3-4, citing Jensen TS, Chin J, Rollins J, Koller E, Gousis L. Decision Memo for Gender Dysphoria and Gender Reassignment Surgery (CAG-00446N). Baltimore (MD): Centers for Medicare and Medicaid Services; 2016 Aug 30 [cited 2022 Feb 18]. Available from: <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&NCAId=282>.

⁵³ Id.

⁵⁴ Id. (“We acknowledge that [gender reassignment surgery] 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 [national coverage decision] that identifies the precise patient population for whom the service would be reasonable and necessary.”)

⁵⁵ Id.

⁵⁶ The CMS Decision Memo notes that “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.” Id.

c. The AG Opinion repeats discredited and unreliable evidence on “desistance” and “rapid-onset gender dysphoria.”

The AG Opinion greatly exaggerates the extent to which adolescent gender dysphoria abates without treatment, and it repeats discredited claims that there is a novel wave of rapid-onset dysphoria among today’s teens.

“Desistance.” The AG Opinion asserts that “[c]hildhood-onset gender dysphoria has been shown to have a high rate of natural resolution, with 61-98% of children reidentifying with their biological sex during puberty.”⁵⁷ The Alabama law makes a parallel statement.⁵⁸ The assertion is incorrect.

As authority for the claimed 61-98% figure, the AG Opinion does not cite reputable scientific evidence. Instead, it cites a biased source – the website of the so-called Society for Evidence-Based Gender Medicine (“SEGM”). SEGM is not a recognized scientific organization, and in Appendix A we document the bias that infuses its medical claims. The SEGM website badly mischaracterizes the underlying source that it cites for the 61-98% figure.

The study SEGM cites is Steensma et al. (2013).⁵⁹ But the Steensma study was not designed to (and the lead author has acknowledged) does not provide a basis for calculating what percentage of prepubertal children diagnosed with gender dysphoria persist with that diagnosis into adolescence. Rather, the Steensma study was designed only to study the characteristics of those who persisted.⁶⁰ Among other limitations, in Steensma (2013), former patients who opted to not participate in the study (either refused to participate or did not respond to an offer to participate) were categorized as “desisters,” i.e., patients whose gender dysphoria resolved without transition or treatment. Patients can fail to respond to a study request for many reasons, including having moved away, receiving treatment elsewhere, or being uninterested in participating in a study. Thus, SEGM misuses the Steensma data by counting nonresponding patients as having “desisted” in experiencing gender dysphoria.⁶¹ Indeed, in published correspondence, Steensma emphasizes that the 2013 study should *not* be used to calculate the percentages of “persisters” and “desisters.”⁶² The misrepresentation of Steensma on the SEGM website constitutes a major violation of the scientific method and the accepted conventions of research.

⁵⁷ AG Opinion, at 4.

⁵⁸ Alabama Law, Section 2(4).

⁵⁹ Steensma TD, McGuire JK, Kreukels BP, Beekman AJ, Cohen-Kettenis PT. Factors associated with desistance and persistence of childhood gender dysphoria: a quantitative follow-up study. *J Am Acad Child Adolesc Psychiatry*. 2013 Jun;52(6):582-90.

⁶⁰ Steensma TD, Cohen-Kettenis PT. A critical commentary on follow-up studies and “desistance” theories about transgender and gender non-conforming children. *Int J Transgend*. 2018 May; 19(2):225-30.

⁶¹ See American Psychological Association (2015), p. 842 (noting that several studies categorized youth who did not return to the clinic after initial assessment as “desisters” who no longer identified with a gender different than sex assigned at birth; “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”).

⁶² *Id.*

Actual scientific evidence on the course of gender dysphoria emphasizes the importance of distinguishing between prepubertal children and adolescents. The evidence suggests that the course of dysphoria is more diverse for prepubertal children, and so it is critical to recognize them as a distinct population from adolescents. By referring to “children,” the AG Opinion creates the misimpression that most or all children *and* teens diagnosed with dysphoria will cease identifying with the gender not assigned at birth. This is false.

The evidence suggests that the vast majority of adolescents who are diagnosed with gender dysphoria will persist in their gender identity and will benefit from gender-affirming medical care.⁶³ In a Dutch study, among 70 adolescents diagnosed with gender dysphoria and treated with puberty-suppressing hormones, 100% opted to continue with gender-affirming treatment.⁶⁴ A recent U.S. study found a consistent pattern. Following a large cohort of U.S. young people who reported some evidence of gender dysphoria but had not yet been formally diagnosed, the study found that adolescents were far more likely than prepubertal children to go on to a formal diagnosis of gender dysphoria and to receive gender-affirming treatment.⁶⁵

The course of gender dysphoria is different in pre-pubertal children. For this group, the percentage of those whose dysphoria resolves without treatment is higher than for adolescents but likely lower than the AG Opinion’s claimed 61-98% figure. When prepubertal children experience gender dysphoria, some will find that their dysphoria resolves before adolescence. That is, many of these children will not, as adolescents, identify as transgender or proceed with gender-affirming medical care. Importantly, as we have emphasized, standard medical protocols do not treat prepubertal children with drug therapy or genital surgery, and so there is zero risk that a prepubertal child with dysphoria will have received physical interventions.

Further, the AG Opinion’s claim of 98% “desistance” is overstated even for prepubertal children. The Endocrine Society reports that, “[c]ombining all outcome studies to date, the [gender dysphoria]/gender incongruence of a minority of prepubertal children appears to persist

⁶³ American Psychological Association (2015), p. 843; WPATH (2012), p. 11; Endocrine Society (2017). See also Turban JL, DeVries ALC, Zucker K. Gender Incongruence & Gender Dysphoria. In Martin A, Bloch MH, Volkmar FR (editors): *Lewis’s Child and Adolescent Psychiatry: A Comprehensive Textbook*, Fifth Edition. Philadelphia: Wolters Kluwer 2018, pp. 20-21 (“we must recognize that [the existing studies of persistence] have been quite limited in power and generalizability and should not be misused to create barriers for TGD youth seeking gender-affirming care. The most relevant conclusions from these studies are that insistent cross-gender identification in adolescence most often correlates with persistent TGD identities in adulthood”).

⁶⁴ de Vries et al. 2011, cited in note 43 (“None of the gender dysphoric adolescents in this study renounced their wish for [gender reassignment] during puberty suppression. This finding supports earlier studies showing that young adolescents who had been carefully diagnosed show persisting gender dysphoria into late adolescence or young adulthood”).

⁶⁵ Wagner S, Panagiotakopoulos L, Nash R, Bradlyn A, Getahun D, Lash TL, Roblin D, Silverberg MJ, Tangpricha V, Vupputuri S, Goodman M. Progression of Gender Dysphoria in Children and Adolescents: A Longitudinal Study. *Pediatrics*. 2021 Jul;148(1):e2020027722. doi: 10.1542/peds.2020-027722. Epub 2021 Jun 7. PMID: 34099504; PMCID: PMC8276590. Wagner et. al (2021) studied this cohort for only (on average) 3.5 years; by the end of the study period, roughly 35% of teens but only about 15-18% of prepubertal children received a formal diagnosis of gender dysphoria. Note that these data do *not* establish that only 35% of teens *with gender dysphoria* persist in their diagnosis. This was not a population already diagnosed with dysphoria, and so the persistence rate cannot be calculated. Rather, Wagner et al. (2021) shows that, among a population with some evidence of dysphoria, adolescents are far more likely than young children to continue to a formal diagnosis.

in adolescence.”⁶⁶ A reasonable summary of the literature would be that around 50% of prepubertal children diagnosed with gender dysphoria (using older, less stringent diagnostic criteria) will not persist in identifying as transgender into adolescence and adulthood.⁶⁷

Recent evidence suggests that the spontaneous resolution of true gender dysphoria among prepubertal children is likely even lower. Earlier studies likely overstate the spontaneous resolution of gender dysphoria among children diagnosed before puberty, because their data incorporated broader diagnostic criteria.⁶⁸ That is, the studies likely included prepubertal children with gender variant behavior (e.g., boys with feminine interests or “tomboy” girls) alongside children who would meet today’s diagnostic criteria for gender dysphoria – a deeply felt and lasting transgender identity with clinically significant distress and impaired functioning.⁶⁹ Consistent with this hypothesis is the recent finding that “the intensity of early dysphoria appears to be an important predictor” of the persistence of dysphoria into adolescence.⁷⁰ The evidence thus implies that, had the earlier studies focused on prepubertal children with intense gender dysphoria, the rates of spontaneous resolution of dysphoria would be lower.

To summarize, then, the key to the question of whether gender dysphoria persists over time is whether the patient is diagnosed with gender dysphoria in adolescence. (This might be a new diagnosis or it might be a persistent diagnosis from childhood.) Put plainly: *adolescents with gender dysphoria rarely find that their dysphoria resolves without treatment.*

“*Rapid-onset*” gender dysphoria. The AG Opinion also asserts that there has been a recent spike in gender dysphoria diagnosis and gender-affirming treatment among U.S. adolescents.⁷¹ The AG insists that this is a “novel cohort” of youth and implies that their gender dysphoria is transient.⁷²

As evidence, the AG Opinion again fails to consult reputable science and instead cites the SEGM website, which features a graph showing an increase from 2010 to 2020 in referrals of British adolescents to a specialized gender clinic.⁷³ The graph is calibrated to look as if the

⁶⁶ Endocrine Society (2017). See Wallien MS, Cohen-Kettenis PT. Psychosexual outcome of gender-dysphoric children. *J Am Acad Child Adolesc Psychiatry*. 2008 Dec;47(12):1413-23. doi: 10.1097/CHI.0b013e31818956b9. PMID: 18981931.

⁶⁷ American Psychological Association (2015), pp. 841-2 (“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”).

⁶⁸ See Temple Newhook J, Pyne J, Winters K, Feder S, Holmes C, Tosh J, Sinnott ML, Jamieson A, and Pickett S, A critical commentary on follow-up studies and “desistance” theories about transgender and gender-nonconforming children, *International Journal of Transgenderism*, vol. 19(2), pp. 212-224 (2018) doi: 10.1080/15532739.2018.1456390.

⁶⁹ Endocrine Society (2017).

⁷⁰ Steensma TD, McGuire JK, Kreukels BP, Beekman AJ, Cohen-Kettenis PT. Factors associated with desistance and persistence of childhood gender dysphoria: a quantitative follow-up study. *J Am Acad Child Adolesc Psychiatry*. 2013 Jun;52(6):582-90 (finding that “children with persistent GID are characterized by more extreme gender dysphoria in childhood than children with desisting gender dysphoria”).

⁷¹ AG Opinion, at 3 (stating that “the spike in [surgical and drug] procedures is a relatively recent development”).

⁷² AG Opinion, at 4.

⁷³ The AG Opinion cites to the website of the Society for Evidence-Based Gender Medicine (SEGM). SEGM’s homepage provides an uncredited and unverifiable graph, which claims to depict referrals to an undefined term,

increase is very large, but in fact, the absolute numbers are small. The information depicted cannot be verified, because SEGM provides no citation. But taking the data at face value, in 2020 about 2600 children and teens sought treatment at the U.K. gender clinic. That is a very small percentage of Britain's child population. Further, the data appear to show only the number of children and adolescents referred for consultation; only a subset of these will ultimately be diagnosed with gender dysphoria and will continue with medical treatment.⁷⁴ The claimed "spike" in referrals certainly reflects the reduction in social stigma over the past decade and the expansion of care options.

By contrast, reliable recent data shows that, among high-school students, the percentage who identify as transgender is under 2% (1.8%).⁷⁵ These data come from the Centers for Disease Control's Youth Risk Behavior Surveillance System, which is the largest repository of data on self-reported behaviors in the United States. Because not all transgender people seek medical treatment, the percentage seeking medical care would be smaller.

The AG Opinion also repeats a discredited claim that a novel wave of "adolescent-onset gender dysphoria" is sweeping the U.S.⁷⁶ This statement echoes (without citing or quoting) a poor-quality study by Lisa Littman.⁷⁷ Littman's 2018 article contended that a novel pathology, "rapid-onset gender dysphoria" was leading teenagers to claim a transgender identity because of peer influence. WPATH, among other authorities, has taken a skeptical view of Littman's claim,⁷⁸ and the study has been criticized for serious methodological errors, including the use of parent reports instead of clinical data and the recruitment of its sample of parents from anti-transgender websites.⁷⁹ The journal of publication required an extensive correction of the

"GIDS." SEGM [Internet]. c2020 [cited 2022 Apr 1]. Available from: <https://segm.org/>. Although GIDS is not defined on the SEGM site, it appears to refer to the Gender Identity Development Service, a specialized UK gender clinic for children and adolescents. GIDS [Internet]. c2022 [cited 2022 Apr 1]. Available from: <https://gids.nhs.uk/about-us#main-content>.

⁷⁴ A referral means that a medical provider (or, possibly, the patient) has suggested an appointment with GIDS. A referral does not equate to the receipt of gender-affirming care. See GIDS [internet]. Available from <https://gids.nhs.uk/about-us#main-content>.

⁷⁵ Johns MM, Lowry R, Andrzejewski J, Barrios LC, Demissie Z, McManus T, Rasberry CN, Robin L, Underwood JM. Transgender Identity and Experiences of Violence Victimization, Substance Use, Suicide Risk, and Sexual Risk Behaviors Among High School Students – 19 States and Large Urban School Districts, 2017. *MMWR Morb Mortal Wkly Rep*. 2019 Jan 25;68(3):67-71.

⁷⁶ AG Opinion, at 4.

⁷⁷ Littman L. Parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria. *PLoS One*. 2018 Aug 16;13(8):1-44; Littman L. Correction: Parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria. *PLoS One*. 2019 Mar 19;14(3):1-7.

⁷⁸ WPATH Global Board of Directors. WPATH Position on "Rapid-Onset Gender Dysphoria" [Internet]. 2018 Sep 4 [cited 2022 Apr 1]. Available from: https://www.wpath.org/media/cms/Documents/Public%20Policies/2018/9_Sept/WPATH%20Position%20on%20Rapid-Onset%20Gender%20Dysphoria_9-4-2018.pdf (stating that ROGD "constitutes nothing more than an acronym created to describe a proposed clinical phenomenon that may or may not warrant further peer-reviewed scientific investigation").

⁷⁹ Restar AJ. Methodological Critique of Littman's (2018) Parental-Respondents Accounts of "Rapid-Onset Gender Dysphoria". *Arch Sex Behav*. 2020 Jan;49(1):61-66. doi: 10.1007/s10508-019-1453-2 (hereinafter, "Restar 2020"); Temple Newhook, J, Pyne, J, Winters, K, Feder, S, Holmes, C, Tosh, J, and Pickett, S. A critical commentary on follow-up studies and "desistance" theories about transgender and gender-nonconforming children. *International Journal of Transgenderism*, 19(2), 212-224. (2018).

original Littman article because of its misstatements.⁸⁰ Such a correction in reputable, peer-reviewed academic journals is taken only when a panel of experts, in retrospect, came to recognize the methodological flaws of the original study and concluded that it would be unscientific to allow the originally published findings to stand.

Littman's hypothesis that rapid-onset gender dysphoria exists as a distinct condition has not been supported by studies of clinical data.⁸¹ Neither the American Psychiatric Association nor any other reputable professional organization has recognized rapid-onset gender dysphoria as a distinct clinical condition or diagnosis.⁸²

Section 3. The AG Opinion and the Alabama Law greatly exaggerate the risks of gender-affirming drug therapy.

The AG Opinion claims that "sex change procedures," including surgery and drug therapies "often ha[ve] the effect of permanently sterilizing those minor children."⁸³ The Alabama Law makes similar claims.⁸⁴ Section 1 of this report has established that the AG Opinion's claim with respect to surgery is false: current medical protocols state that individuals must be the age of majority or older before undergoing surgery on genitals or reproductive organs. In this Section, we focus on the AG Opinion's (and Alabama Law's) claims regarding the medical effects of drug treatment for transgender adolescents.

a. The AG Opinion and the Alabama Law greatly overstate the risks of puberty-blocking medication and incorrectly state that it results in sterilization.

The Texas Attorney General claims that "[t]here is insufficient medical evidence available to demonstrate that discontinuing [puberty-blocking] medication resumes a normal puberty process."⁸⁵ The Alabama Law contains similar statements.⁸⁶ The claim is false: puberty-blocking medication has been shown to be safe, effective, and fully reversible.

As noted in Section 1 of this report, puberty-blocking medication (gonadotropin-releasing hormone agonists, or GnRHa's) can be part of a staged approach to gender-affirming care for

⁸⁰ Littman L. Correction: Parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria. PLoS One. 2019 Mar 19;14(3):1-7 (altering the original article to, inter alia, clarify that the article collected no data from adolescents or clinicians and generates only a hypothesis for further exploration).

⁸¹ Bauer GR, Lawson ML, Metzger DL; Trans Youth CAN! Research Team. Do Clinical Data from Transgender Adolescents Support the Phenomenon of "Rapid Onset Gender Dysphoria"? J Pediatr. 2022 Apr; 243:224-227. See also Arnoldussen M, Steensma TD, Popma A, van der Miesen AIR, Twisk JWR, de Vries ALC. Re-evaluation of the Dutch approach: are recently referred transgender youth different compared to earlier referrals? Eur Child Adolesc Psychiatry. 2020 Jun;29(6):803-811. Erratum in: Eur Child Adolesc Psychiatry. 2020 Dec 16 (concluding that there has been no marked change in the characteristics of the population of adolescents referred for gender dysphoria from 2000 to 2016; the authors hypothesize that the increase in number of referrals reflects the increasing social acceptability of seeking treatment).

⁸² Restar (2018), cited in note 79.

⁸³ AG Opinion, at 2-3. The AG Opinion repeats its claim about sterilization. Id. at 5 ("The surgical and chemical procedures you ask about can and do cause sterilization.")

⁸⁴ Alabama Law, Sections 2(9), 2(11), 2(12), 2(13) and 2(14).

⁸⁵ AG Opinion, at 5.

⁸⁶ Alabama Law, Sections 2(7), (11), (12) and (13).

adolescents. By stalling pubertal maturation, the medication relieves adolescents of the intense gender dysphoria that can accompany pubertal development along the pathway of their assigned sex. During this pause, the adolescent is given time to confirm their gender identity and to consider the need for appropriate gender-affirming hormone therapy without having had their body mature along pubertal path incongruent with their gender identity. Adolescents who continue to identify as transgender will be able to proceed with gender-affirming hormone therapy when they, their parents, and their providers determine that treatment is medically appropriate. Puberty blockers not only alleviate gender dysphoria in adolescence but have beneficial lifelong effects on dysphoria and can minimize the need for subsequent treatments, including surgery in adulthood. In the unlikely event that a teen realizes that they identify as cisgender, they can discontinue the blocker and spontaneous pubertal maturation will resume.

The scientific evidence clearly shows that treatment with puberty blockers is fully reversible. GnRHa therapy has been used since the 1980's in children with precocious puberty, and a solid body of evidence documents that pubertal progression stops with drug therapy and that spontaneous pubertal development occurs after discontinuation of the medication.⁸⁷

Recent studies suggest that puberty-blocking medication has negligible or small effects on bone development in adolescents, and any negative effects are temporary and reversible. The most recent studies show that puberty-blocking drug therapy either has no effect on bone mineral density (BMD), a proxy measure of bone strength, or is associated with a very small decrease.⁸⁸

⁸⁷ Manasco PK, Pescovitz OH, Feuillan PP, Hench KD, Barnes KM, Jones J, Hill SC, Loriaux DL, Cutler Jr GB. Resumption of puberty after long term luteinizing hormone-releasing hormone agonist treatment of central precocious puberty. *J Clin Endocrinol Metab.* 1988 Aug 1;67(2):368-72; Heger S, Muller M, Ranke M, Schwarz H, Waldhauser F, Partsch C, Sippell WG. Long-term GnRH agonist treatment for female central precocious puberty does not impair reproductive function. *Mol Cell Endocrinol.* 2006 Jul 25;254-255:217-220; Feuillan PP, Jones JV, Barnes K, Oerter-Klein K, Cutler Jr GB. Reproductive Axis after Discontinuation of Gonadotropin-Releasing Hormone Analog Treatment of Girls with Precocious Puberty: Long Term Follow-Up Comparing Girls with Hypothalamic Hamartoma to Those with Idiopathic Precocious Puberty. *J Clin Endocrinol Metab.* 1999 Jan;84(1):44-49; Bertelloni S, Baroncelli GI, Ferdeghini M, Menchini-Fabris F, Saggese G. Final height, gonadal function and bone mineral density of adolescent males with central precocious puberty after therapy with gonadotropin-releasing hormone analogues. *Eur J Pediatr.* 2000 May;159(5):369-74 (hereinafter, "Bertelloni et al (2000)"); Bertelloni S, Mul D. Treatment of central precocious puberty by GnRH analogs: long-term outcome in men. *Asian J Androl.* 2008 Jul;10(4):525-34; Luo X, Liang Y, Hou L, Wu W, Ying Y, Ye F. Long-term efficacy and safety of gonadotropin-releasing hormone analog treatment in children with idiopathic central precocious puberty: A systematic review and meta-analysis. *Clin Endocrinol.* 2021 May; 94(5):786-96.

⁸⁸ Klink D, Caris M, Heijboer A, van Trotsenburg M, Rotteveel J. Bone mass in young adulthood following gonadotropin-releasing hormone analog treatment and cross-sex hormone treatment in adolescents with gender dysphoria. *J Clin Endocrinol Metab.* 2015 Feb;100(2):E270-75 (hereinafter, "Klink et al. 2015"); Schagen SEE, Wouters FM, Cohen-Kettenis PT, Gooren LJ, Hannema SE. Bone Development in Transgender Adolescents Treated With GnRH Analogues and Subsequent Gender-Affirming Hormones. *J Clin Endocrinol Metab.* 2020 Dec 1;105(12): e4252-e4263 (hereinafter, Schagen et al. 2020"); Delemarre-van de Waal HA, Cohen-Kettenis PT. Clinical management of gender identity disorder in adolescents: a protocol on psychological and paediatric endocrinology aspects. *Eur J Endocrinol.* 2006;155:S131-S137. Studies of children treated for precocious puberty found that BMD was normal at final height attainment. Alessandri SB, Pereira F de A, Villela RA, Antonini SRR, Elias PCL, Martinelli Jr CE, de Castro M, Moreira AC, de Paula FJA. Bone mineral density and body composition in girls with idiopathic central precocious puberty before and after treatment with a gonadotropin-releasing hormone agonist. *Clinics (Sao Paulo).* 2012;67(6):591-96; Antoniazzi F, Zamboni G, Bertoldo F, Lauriola S, Mengarda F, Pietrobelli A, Tato L. Bone mass at final height in precocious puberty after gonadotropin-releasing hormone agonist with and without calcium supplementation. *J Clin Endocrinol Metab.* 2003 Mar;88(3):1096-1101 (hereinafter,

Calcium supplementation has been shown to protect patients from bone loss.⁸⁹ Critically, any reduction in BMD is recovered when adolescents cease taking puberty-blocking medication, whether or not they continue to gender-affirming hormone therapy.⁹⁰

Tellingly, the AG Opinion does not cite scientific evidence for its claim regarding “insufficient medical evidence.”⁹¹ Instead, it cites two legal cases, neither of which contains sound scientific evidence on this subject.⁹² One of the cited cases is irrelevant, because it involves legal claims about surgery, not puberty blockers.⁹³ The other cited case, *Bell v. Tavistock and Portman NHS Foundation Trust* (2020), was reversed on appeal in the U.K. in 2021 because the decision relied on biased and inexperienced scientific testimony.⁹⁴

The AG Opinion also attacks puberty blockers by claiming that their use “is not approved by the federal Food and Drug Administration and is considered an ‘off-label’ use of the medications.”⁹⁵ The Alabama Law makes a similar claim.⁹⁶ The implication is that off-label use of medication is harmful, but this claim is unfounded.

“Antoniazzi et al. (2003)”); Heger S, Partsch CJ, Sippell WG. Long-term outcome after depot gonadotropin-releasing hormone agonist treatment of central precocious puberty: final height, body proportions, body composition, bone mineral density, and reproductive function. *J Clin Endocrinol Metab.* 1999 Dec;84(12):4583-90; Neely EK, Bachrach LK, Hintz RL, Habiby RL, Slemenda CW, Feezle L, Pescovitz OH. Bone mineral density during treatment of central precocious puberty. *J Pediatr.* 1995 Nov;127(5):819-22.

⁸⁹ Antoniazzi et al. (2003), cited in note 88.

⁹⁰ Klink et al. (2015), cited in note 88; Schagen et al. (2020), cited in note 88. Bertelloni et al. (2000), cited in note 87; Pasquino AM, Pucarelli I, Accardo F, Demiraj V, Segni M, Di Nardo R. Long-term observation of 87 girls with idiopathic central precocious puberty treated with gonadotropin-releasing hormone analogs: impact on adult height, body mass index, bone mineral content, and reproductive function. *J Clin Endocrinol Metab.* 2008 Jan;93(1):190-195; Magiakou MA, Manousaki D, Papadaki M, Hadjidakis D, Levidou G, Vakaki M, Papaefstathiou A, Lalioti N, Kanaka-Gantenbein C, Piaditis G, Chrousos GP, Dacou-Voutetakis C. The efficacy and safety of gonadotropin-releasing hormone analog treatment in childhood and adolescence: a single center, long-term follow-up study. *J Clin Endocrinol Metab.* 2010 Jan;95(1):109-17; Bertelloni S, Baroncelli GI, Sorrentino MC, Perri G, Saggese G. Effect of central precocious puberty and gonadotropin-releasing hormone analogue treatment on peak bone mass and final height in females. *Eur J Pediatr.* 1998 May;157(5):363-67.

⁹¹ AG Opinion, at 5.

⁹² The AG Opinion’s citation is “see generally *Hennessy-Waller v. Snyder*, 529 F. Supp. 3d 1031, 1042 (D. Ariz. 2021), citing *Bell v. Tavistock and Portman NHS Foundation Trust*, 2020 EWHC 3274, para. 134 (Dec. 1, 2020) (referring to Bell’s conclusion that a clinic’s practice of prescribing puberty-suppressing medication to individuals under age 18 with gender dysphoria and determining such treatment was experimental).” *Id.* at 5-6.

⁹³ *Hennessy-Waller* is a decision that denies a motion for preliminary injunction against an insurance company for failure to cover gender-affirming surgery. The decision involves surgery, not puberty blockers, and it is not a fully-adjudicated factual determination about either surgery or puberty blockers. *Hennessy-Waller v. Snyder*, 529 F. Supp. 3d 1031 (D. Ariz. 2021).

⁹⁴ *Bell v. The Tavistock and Portman NHS Foundation Trust* [2021] EWCA (Civ) 1363 [38] (Eng.) (noting that the claimant’s (plaintiff’s) expert evidence was faulty: “None of it complied with the rules regarding expert evidence and a good deal of it is argumentative and adversarial.”). For a scientific review of the evidence in the lower court decision, see de Vries ALC, Richards C, Tishelman AC, Motmans J, Hannema SE, Green J, Rosenthal SM. *Bell v. Tavistock and Portman NHS Foundation Trust* [2020] EWHC 3274: Weighing current knowledge and uncertainties in decisions about gender-related treatment for transgender adolescents. *Int J Transgend Health.* 2021 Apr 5;22(3):217-24.

⁹⁵ AG Opinion, at 5.

⁹⁶ Alabama Law, Section 2(7).

“Off label” means only that the FDA has not specifically approved a particular medication for a particular use. The off-label use of medications for children is quite common and often necessary, because an “overwhelming number of drugs” have no FDA-approved instructions for use in pediatric patients.⁹⁷ This is in part because pharmaceutical companies often lack financial incentives to support research required for FDA approval for specific use in children.⁹⁸ Indeed, the American Academy of Pediatrics specifically approves the off-label use of drugs:

The purpose of off-label use is to benefit the individual patient. Practitioners use their professional judgment to determine these uses. As such, *the term “off-label” does not imply an improper, illegal, contraindicated, or investigational use.* Therapeutic decision-making must always rely on the best available evidence and the importance of the benefit for the individual patient.⁹⁹

Many common medications, including hormones, are used off-label in adults and minors. In fact, pediatricians prescribe off-label drugs in 20% of patient visits.¹⁰⁰ Estrogen and testosterone are often used off-label to treat adolescents with intersex conditions. Common hormonal medications used off-label include norethindrone, a progesterone analogue used off-label for the treatment of heavy menstrual bleeding in those with polycystic ovarian syndrome, bleeding disorder, and anovulatory bleeding of early puberty. It is also used to treat endometriosis, which is a painful inflammatory condition. Many forms of combined hormonal contraception, as well as a testosterone-blocking medication (spironolactone), are used off-label to treat acne. Other examples include clonidine, a blood pressure medication used off-label for the treatment of ADHD, migraine headaches, disorders of behavioral regulation, and insomnia; and propranolol, a blood pressure medication used off-label for the treatment of performance anxiety.

b. The AG Opinion and the Alabama Law exaggerate the fertility risks of gender-affirming hormonal treatment.

⁹⁷ The quote is from the American Academy of Pediatrics Committee on Drugs. See Frattarelli DA, Galinkin JL, Green TP, Johnson TD, Neville KA, Paul IM, Van Den Anker JN; American Academy of Pediatrics Committee on Drugs. Off-label use of drugs in children. *Pediatrics*. 2014 Mar;133(3):563-7 (hereinafter, “AAP Committee on Drugs (2014)”); see also Allen HC, Garbe MC, Lees J, Aziz N, Chaaban H, Miller JL, Johnson P, DeLeon S. Off-Label Medication use in Children, More Common than We Think: A Systematic Review of the Literature. *J Okla State Med Assoc*. 2018 Oct;111(8):776-783.

⁹⁸ AAP Committee on Drugs (2014), cited in note 97.

⁹⁹ AAP Committee on Drugs (2014), cited in note 97 (emphasis added). See also Schrier L, Hadjipanayis A, Stiris T, Ross-Russell RI, Valiulis A, Turner MA, Zhao W, De Cock P, de Wildt SN, Allegaert K, van den Anker J. Off-label use of medicines in neonates, infants, children, and adolescents: a joint policy statement by the European Academy of Paediatrics and the European society for Developmental Perinatal and Pediatric Pharmacology. *Eur J Pediatr*. 2020 May;179(5):839-847.

¹⁰⁰ Hoon D, Taylor MT, Kapadia P, Gerhard T, Strom BL, Horton DB. Trends in Off-Label Drug Use in Ambulatory Settings: 2006-2015. *Pediatrics*. 2019 Oct;144(4):1-10 (emphasis added).

The AG Opinion claims that gender-affirming hormone treatments cause infertility.¹⁰¹ The Alabama Law contains a similar statement.¹⁰² These are unwarranted exaggerations, which ignore the substantial evidence of reversibility of the fertility effects of hormone therapy.

Treatment with gender-affirming sex hormones impacts fertility while drug therapy is ongoing, but the effect is anticipated to be reversible if medication is discontinued. Importantly, hormone therapy is always individualized, and some transgender and non-binary teens remain on puberty blockers up to the age of majority without proceeding to hormone treatment.

For transgender men (persons assigned female sex at birth who retain ovaries), testosterone treatment can affect ovarian function, inhibiting menses in the majority of those on therapy. The evidence shows that most transgender men who had regular menses before starting testosterone therapy are reported to resume menses if testosterone is discontinued.¹⁰³ Some transgender men may retain fertility during hormone treatment: spontaneous pregnancies have occurred in testosterone-treated transgender men, some while still amenorrheic.¹⁰⁴ Further, a number of transgender men have discontinued testosterone therapy prior to undergoing assisted reproductive technology and have carried pregnancies to term with delivery of normal infants.¹⁰⁵

The effects of gender-affirming estrogen treatment on testicular histology vary among individuals. Reduced spermatogenesis is common while patients remain on estrogen, but fully normal spermatogenic activity has been documented.¹⁰⁶ Importantly, return of spermatogenesis occurred quickly in patients who discontinued hormone treatment.¹⁰⁷ Patients who were treated with puberty blockers (GnRHa's) starting at the onset of pubertal development and estrogen at

¹⁰¹ AG Opinion, at 3.

¹⁰² Alabama Law, Section 2(13).

¹⁰³ Endocrine Society (2017). Light AD, Obedin-Maliver J, Sevelius JM, Kerns JL. Transgender men who experienced pregnancy after female-to-male gender transitioning. *Obstet Gynecol.* 2014;124(6):1120–1127 (hereinafter, “Light et al. 2014”); Pelusi C, Costantino A, Martelli V, et al. Effects of three different testosterone formulations in female-to-male transsexual persons. *J Sex Med.* 2014;11(12):3002–3011.; Smith KP, Madison CM, Milne NM. Gonadal suppressive and cross-sex hormone therapy for gender dysphoria in adolescents and adults. *Pharmacotherapy.* 2014;34(12):1282–1297.

¹⁰⁴ Light et al. (2014), cited in note 103; Light A, Wang LF, Zeymo A, Gomez-Lobo V. Family planning and contraception use in transgender men. *Contraception.* 2018 Oct;98(4):266-69.

¹⁰⁵ Leung A, Sakkas D, Pang S, Thornton K, Resetkova N. Assisted reproductive technology outcomes in female-to-male transgender patients compared with cisgender patients: a new frontier in reproductive medicine. *Fertil Steril.* 2019 Nov;112(5):858-65; Wallace SA, Blough KL, Kondapalli LA. Fertility preservation in the transgender patient: expanding oncofertility care beyond cancer. *Gynecol Endocrinol.* 2014;30(12):868-71; Maxwell S, Noyes N, Keefe D, Berkeley AS, Goldman KN. Pregnancy outcomes after fertility preservation in transgender men. *Obstet Gynecol.* 2017 Jun;129(6):1031-34.; Gale J, Magee B, Forsyth-Greig A, Visram H, Jackson A. Oocyte cryopreservation in a transgender man on long-term testosterone therapy: a case report. *F S Rep.* 2021 Feb 20;2(2):249-51.

¹⁰⁶ Schneider F, Kliesch S, Schlatt S, Neuhaus N. Andrology of male -to-female transsexuals: influence of cross-sex hormone therapy on testicular function. *Andrology.* 2017 Sept;5(5):873-80.

¹⁰⁷ Schneider F, Neuhaus N, Wistuba J, Zitzmann M, Heß J, Mahler D, van Ahlen H, Schlatt S, Kliesch S. Testicular functions and clinical characterization of patients with gender dysphoria (GD) undergoing sex reassignment surgery (SRS). *J Sex Med.* 2015 Nov;12(11):2190-2200.

16 years of age were shown to have normal-appearing, immature sperm-producing cells in the testes, suggesting those individuals retained fertility potential.¹⁰⁸

As with any other medical decision, parents and providers carefully weigh the risks of treating the individual adolescent against the risks of not treating them, including the mental health impact and potential suicide risk of not beginning gender-affirming care.

As the standard protocols summarized in Section 1 of this report demonstrate, there is no push by physicians to proceed to hormone therapy. On the contrary, the decision to proceed with drug therapy and the choice of therapy are determined after assessing each adolescent's medical history as well as their past and ongoing mental health concerns. The standard of care specifically states that any existing mental health issues must be stable prior to moving forward with gender-affirming medical interventions. When counseling transgender adolescents who are considering gender-affirming drug therapy, physicians can also offer sperm or oocyte (egg) cryopreservation.

In addition to its claims about fertility, the AG Opinion offers a list of asserted medical harms without citation to any existing medical authority. The cited source is a healthcare website, and the underlying document has been removed from the site and is not otherwise available on the Internet.¹⁰⁹ The opinion offers no scientific foundation for its claims but seems to conflate long-outdated practice with the current standard of care.¹¹⁰

A more accurate perspective begins with an understanding of the role of hormones in the body. Hormones play a role in determining the medical profile of cisgender people. Generally speaking, cisgender women have relatively higher levels of estrogen and lower levels of testosterone, and cisgender men have the reverse. Each hormonal profile carries with it medical benefits and risks. Cisgender women, for example, have lower rates of cardiovascular disease than cisgender men but higher risks of venous thromboembolism. When a transgender individual receives gender-affirming hormone treatment, they take doses of exogenous sex hormones that approximate the physiologic state of their identified gender. Put simply, a transgender female is supplied an amount of estrogen similar to the estrogen that a cisgender woman's ovaries typically produce. Similarly, a transgender male receives a dose of testosterone that approximates what a cisgender male's testicles typically produce. Protocols provide explicit dosage guidelines to approximate the physiology of the patient's identified gender rather than to develop desired physical characteristics.

The medical result is that transgender individuals move toward the typical medical profile of their identified gender. And so transgender women, like cisgender women, have lower risks of

¹⁰⁸ de Nie I, Mulder CL, Meißner A, Schut Y, Holleman EM, van der Sluis WB, Hannema SE, den Heijer M, Huirne J, van Pelt AMM, van Mello NM. Histological study on the influence of puberty suppression and hormonal treatment on developing germ cells in transgender women. *Hum Reprod.* 2022 Jan 28;37(1):297-308.

¹⁰⁹ The AG Opinion cites to Timothy Cavanaugh, M.D., Cross-Sex Hormone Therapy, FENWAY HEALTH (2015), <https://www.lgbtqihealtheducation.org/wp-content/uploads/Cross-Sex-Hormone-Therapy1.pdf>. A search conducted in March 2022 found that the link was broken and the document could not be found on the Fenway Health website or elsewhere on the Internet.

¹¹⁰ The iatrogenic (drug-induced) risks of hepatotoxicity, meningioma, and prolactinoma are now zero, because the medication associated with those risks (cyproterone) is no longer in use in the United States. WPATH (2012), p. 48.

cardiovascular disease than cisgender men.¹¹¹ Transgender women, like cisgender women, have a slightly higher risk of venous thromboembolism than cisgender men. In fact, transgender women have a *lower* risk of venous thromboembolism than cisgender women, and the overall risk is extremely low (less than 1%) for all transgender individuals, both women and men.¹¹² The risk of venous thromboembolism in transgender women and non-pregnant cisgender women is less than the risk in pregnancy, which is the highest estrogenic physiologic state known.

It is also critical to note that the medical impact of gender-affirming treatment is generally the same in transgender people as in cisgender people who take the same hormone medications. For example, physicians commonly prescribe hormonal contraceptives containing ethinyl estradiol (a synthetic estrogen) to adolescents for reasons including birth control, management of irregular or painful menstrual periods, and acne. In other words, similar doses of exogenous sex hormones are commonly administered to cisgender individuals for a host of reasons and are well tolerated.

¹¹¹ Connelly PJ, Marie Freel E, Perry C, Ewan J, Touyz RM, Currie G, Delles C. Gender-Affirming Hormone Therapy, Vascular Health and Cardiovascular Disease in Transgender Adults. *Hypertension*. 2019 Dec;74(6):1266-1274. doi: 10.1161/HYPERTENSIONAHA.119.13080. Epub 2019 Oct 28. Erratum in: *Hypertension*. 2020 Apr;75(4):e10. PMID: 31656099; PMCID: PMC6887638.

¹¹² Oral estradiol, the preferred estrogen formulation that is given to transgender women in the United States, carries a VTE risk of <1%. T'Sjoen G, Arcelus J, Gooren L, Klink DT, Tangpricha V. Endocrinology of Transgender Medicine. *Endocr Rev*. 2019 Feb 1;40(1):97-117. In transgender men, the overall risk of VTE ranges from 0% to 0.34%. Maraka S, Singh Ospina N, Rodriguez-Gutierrez R, Davidge-Pitts CJ, Nippoldt TB, Prokop LJ, Murad MH. Sex Steroids and Cardiovascular Outcomes in Transgender Individuals: A Systematic Review and Meta-Analysis. *J Clin Endocrinol Metab*. 2017 Nov 1;102(11):3914-23.

Appendix A: Additional Information on Biased Sources of Information in the AG Opinion

Here, we address two sources of information mischaracterized by the AG Opinion as authorities on, respectively, science and medical ethics.

a. The Society for Evidence-Based Gender Medicine

The AG Opinion twice cites the Society for Evidence-Based Gender Medicine (“SEGM”). SEGM claims to be “an international group of over 100 clinicians and researchers concerned about the lack of quality evidence for the use of hormonal and surgical interventions as first-line treatment for young people with gender dysphoria.”¹¹³

Despite SEGM’s statement, the group appears to be nothing more than a website; it does not appear to hold meetings, screen its members, or publish a journal. The original content on the website includes statements unsupported by any citations. When the content does provide citations, they are often unreliable or misleading. The SEGM website includes a list of citations to more than 100 articles as evidence for the medical risks of gender-affirming care, but we reviewed each article and found the vast majority to be of low quality. The site’s content omits mention of the standards of care published by mainstream scientific organizations, and it falsely claims that the standard protocols permit gender-affirming surgery before the age of majority. The long list of citations omits mainstream scientific articles that do not support the SEGM agenda, and the list includes a large number of letters to the editor, which are not peer-reviewed or fact-checked,¹¹⁴ as well as other sources of little scientific value, including opinion pieces and case studies.

Although the SEGM site claims “over 100 clinicians and researchers” as members, it lists as “clinical and academic advisors” a group of only 14 people, many of whom have limited (or no) scientific qualifications related to the study of medical treatment for transgender people. Of the 14, only eight claim academic credentials above the master’s degree level (and, of these, two of the PhD’s are in sociology and evolutionary biology). None have academic appointments in pediatric medicine or child psychology; none have published original empirical research on the medical treatment of transgender people in a peer-reviewed publication; and none currently treat patients in a recognized gender clinic.¹¹⁵

A contextual examination reveals that SEGM is an ideological organization without apparent ties to mainstream scientific or professional organizations. Its 14 core members are a small group of repeat players in anti-trans activities – a fact that the SEGM website does not disclose. These 14 often write letters to the editor of mainstream scientific publications; these letters appear in the list of publications on the website (even though letters to the editor typically are not peer-reviewed or fact-checked). (Our review shows that the group of 14 has a total of 39 relevant publications and that 75% of these are letters to the editor.)

¹¹³ All SEGM.org website citations reflect visits to the site in March 2022.

¹¹⁴ Of the 123 listed papers (some are listed more than once), 49 (or 40%) are letters to the editor or opinion pieces.

¹¹⁵ These findings are based on the biographical data posted on the SEGM.org website, supplemented with searches of Google (to determine academic appointments and listed publications) and the database PubMed (to determine medical publication records).

The core members of SEGM frequently serve together on the boards of other organizations that oppose gender-affirming treatment and, like SEGM, feature biased and unscientific content. These include Genspect, Gender Identity Challenge (GENID), Gender Health Query, Rethink Identity Medicine Ethics, Sex Matters, Gender Exploratory Therapy Team, Gender Dysphoria Working Group, and the Institute for Comprehensive Gender Dysphoria Research.

b. Purported bioethics experts

The AG Opinion cites two purported ethics experts for the proposition that “it is particularly unethical to radically intervene in the normal physical development of a child to ‘affirm’ a ‘gender identity’ that is at odds with bodily sex.”¹¹⁶

This is an unreliable citation for two reasons. First, the cited item is not published in a peer-reviewed or mainstream legal or ethics journal. It appears, instead, in *Public Discourse*, an online journal on the website of an organization with no clear academic or professional affiliation.¹¹⁷ Second, the two authors have strong ties to anti-trans activism. The first author, Ryan T. Anderson, is the president of a right-wing, Catholic-identified think tank.¹¹⁸ (Anderson is also the founder of the publishing journal, *Public Discourse*, further undermining the credibility of the citation.) The second author, Robert George, is a professor at Princeton who has long been engaged in anti-trans political activism. George is the founder of The American Principles Project, which states: “We want to impose a political cost on the Left’s anti-family extremism. If they want to attack parental rights [or] confuse young children about their gender...they are going to be punished at the polls.”¹¹⁹

By contrast, academic experts in bioethics consider gender-affirming treatment to be ethical.¹²⁰ They emphasize “the importance of balanced decision making when counseling and

¹¹⁶ AG Opinion, at 4 (citing Anderson RT, George RP. Physical Interventions on the Bodies of Children to “Affirm” their “Gender Identity” Violate Sound Medical Ethics and Should Be Prohibited [Internet]. *Public Discourse: The Journal of the Witherspoon Institute*; 2019 Dec 8 [cited 2022 Mar]. Available from: <https://www.thepublicdiscourse.com/2019/12/58839/>).

¹¹⁷ “*Public Discourse* is the online journal of the Witherspoon Institute, a 501(c)3 research center located in Princeton, New Jersey”. Our Mission. *Public Discourse: The Journal of the Witherspoon Institute*; c2022 [cited 2022 Mar]. Available from: <https://www.thepublicdiscourse.com/our-mission/>.

¹¹⁸ “Founded in 1976, the Ethics and Public Policy Center” works “to apply the riches of the Judeo-Christian tradition to contemporary questions of law, culture, and politics, in pursuit of America’s continued civic and cultural renewal.” About. Ethics & Public Policy Center; c2022 [cited 2022 Mar]. Available from: <https://eppc.org/about/>. The EPPC’s programs include “Catholic Studies” and the “Catholic Women’s Forum. Programs. Ethics & Public Policy Center; c2022 [cited 2022 Mar]. Available from: <https://eppc.org/program/>. Anderson is listed as the president. Ryan T. Anderson. Ethics & Public Policy Center; c2022 [cited 2022 Mar]. Available from: https://eppc.org/author/ryan_anderson/.

¹¹⁹ About. American Principles Project; c2020 [cited 2022 Mar]. Available from: <https://americanprinciplesproject.org/about/>. On another page, the website states that the American Principles Project was founded in 2009 by George and “veteran political strategist Frank Cannon.” History. American Principles Project; c2020 [cited 2022 Mar]. Available from: <https://americanprinciplesproject.org/about/history-story/>.

¹²⁰ For examples, see Kimberly LL, Folkers KM, Friesen P, Sultan D, Quinn GP, Bateman-House A, Parent B, Konnoth C, Janssen A, Shah LD, Bluebond-Langner R, Salas-Humara C. Ethical Issues in Gender-Affirming Care for Youth. *Pediatrics*. 2018 Dec;142(6):e20181537; Bizic MR, Jevtovic M, Pusica S, Stojanovic B, Duisin D,

treating adolescents with nonconforming gender identities,”¹²¹ and they have evaluated decision-making procedures that can ensure that adolescents and their parents give fully-informed consent to treatment.¹²² These considerations align with the consent processes prescribed by standard medical protocols, which we discuss in Section 1.

Vujovic S, Rakic V, Djordjevic ML. Gender Dysphoria: Bioethical Aspects of Medical Treatment. *BioMed Res Int*. 2018 Jun 13;2018:9652305; Strang JF, Powers MD, Knauss M, Sibarium E, Leibowitz SF, Kenworthy L, Sadikova E, Wyss S, Willing L, Caplan R, Pervez N, Nowak J, Gohari D, Gomez-Lobo V, Call D, Anthony LG. “They Thought It Was an Obsession”: Trajectories and Perspectives of Autistic Transgender and Gender-Diverse Adolescents. *J Autism Dev Disord*. 2018 Dec;48(12):4039-55.

¹²¹ Steensma TD, Wensing-Kruger SA, Klink DT. How Should Physicians Help Gender-Transitioning Adolescents Consider Potential Iatrogenic Harms of Hormone Therapy? *AMA J Ethics*. 2017 Aug 1;19(8):762-70.

¹²² Vrouwenraets LJJJ, Hartman LA, Hein IM, de Vries ALC, de Vries MC, Molewijk BAC. Dealing with Moral Challenges in Treatment of Transgender Children and Adolescents: Evaluating the Role of Moral Case Deliberation. *Arch Sex Behav*. 2020 Oct;49(7):2619-34.



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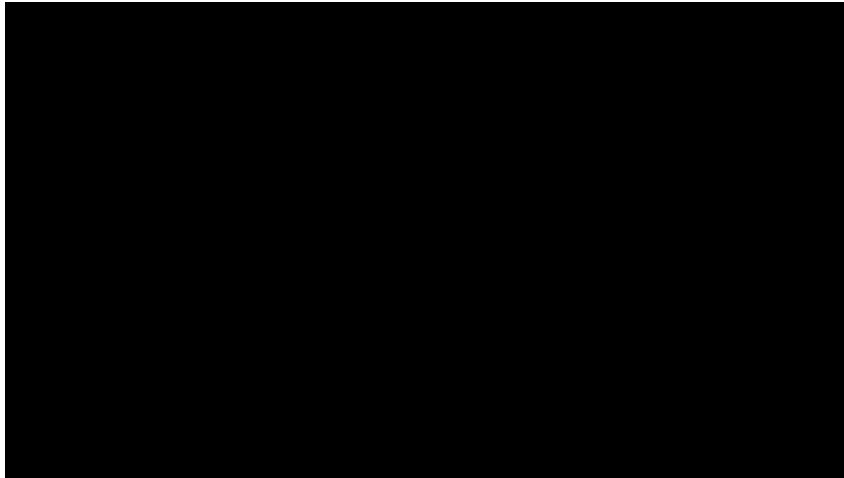
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Alabama governor signs 'Don't Say Gay,' trans care and bathroom ban bills

Alabama is one of several Republican-led states backing such bills.

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Classroom hardships amid wave of anti-trans laws

A record number of anti-transgender bills have been introduced in state legislatures in 2...[Read More](#)
Mickey Welsh/AP, FILE

In the latest salvo of legislation targeting LGBTQ youth, Alabama Gov. Kay Ivey has signed into law two bills banning transgender health care for minors and teaching about gender identity and sexual orientation in kindergarten through fifth grade.

The Alabama legislature passed the two bills focusing on transgender youth a day prior. SB 184 bans gender-affirming care, while HB 322 bans trans students from using bathrooms and locker rooms that align with their gender identity. HB 322 also limits LGBTQ content in classrooms due to a last-minute amendment.

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SB 184, the Vulnerable Child Protection Act, states that anyone who provides gender-affirming care -- including puberty blockers, hormone therapy or physical gender-affirming surgeries -- to anyone under 18 could be convicted of a felony and face up to 10 years in prison and a \$15,000 fine.

Several [Alabama physicians has said the legislation](#) is riddled with misinformation about how gender-affirming care actually affects children.

"When lawmakers attempt to practice medicine with a life without a license, they realize quickly that there was a lot more they didn't understand than what they thought they did," Morissa Ladinsky, an associate professor of pediatrics at the University of Alabama at Birmingham, previously told ABC News.



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Jodi Womack holds a sign that reads "We Love Our Trans Youth" during a rally at the Alab...[Read More](#)

For instance, the bill would ban minors from receiving gender-affirming "surgical procedures," but in Alabama, such surgeries aren't allowed until a patient reaches the age of legal majority for medical decisions, which is 19.

The legislation also makes the claim that puberty blockers can cause infertility or other health risks. According to Ladinsky, these potential side effects only present real risks after puberty and are not a risk to youth taking puberty blockers.

"I believe very strongly that if the Good Lord made you a boy, you are a boy, and if he made you a girl, you are a girl," Ivey said in a statement after signing the bill into law. "We should especially protect our children from

these radical, life-altering drugs and surgeries when they are at such a vulnerable stage in life. Instead, let us all focus on helping them to properly develop into the adults God intended them to be."

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The bill's sponsor, Republican Sen. Shay Shelnett, has called gender-affirming health care "child abuse."

"We don't want parents to be abusing their children. We don't want to make that an option, because that's what it is; it's child abuse. This is just to protect children," Shelnett said Feb. 23 on the state Senate floor.

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Courtney Roark, the Alabama policy & movement building director for the youth-led reproductive rights nonprofit URGE, slammed the bill's passage as an attack on bodily autonomy for trans youth and their families.

"In yet another attack on our bodies, our autonomy, and our desire to live happy and healthy lives, Alabama politicians have passed and signed into law a bill that would criminalize doctors, principals, teachers, school counselors and nurses for providing gender-affirming care and support to trans and non-binary youth," Roark said. "Trans and non-binary youth in our state and across the country already face extraordinary barriers to accessing the liberated and joyous lives they deserve."

HB 322 would require students in public K-12 schools to only use bathrooms and locker rooms that correspond with their assigned sex at birth.

Alabama state Rep. Scott Stadthagen, the sponsor of the bill, said the bill does not target transgender students.

"Almost every school district in this state is dealing with this issue with opposite genders wanting to use opposite bathrooms," Stadthagen [has said in debate](#). "I find this to be a safety issue. It is for protection of our students."

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"Here in Alabama, men use the men's room, and ladies use the ladies' room -- it's really a no brainer," Ivey said in a statement. "This bill will also ensure our elementary school classrooms remain free from any kind of sex talk."

An amendment to this bill would also prohibit classroom instruction or discussion on sexual orientation or gender identity for students in kindergarten through the fifth grade in public K-12 schools. The language mirrors the controversial so-called "Don't Say Gay" bills popping up across the country.

Ivey took issue with that characterization, saying in a statement, "Let me be clear to the media and opponents who like to incorrectly dub this the 'Don't Say Gay' amendment: That is misleading, false and just plain wrong. We don't need to be teaching young children about sex. We are talking about five-year-olds for crying out loud. We need to focus on what matters – core instruction like reading and math."

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LGBTQ suicide awareness group The Trevor Project condemned the passage of such bills.

"On likely the last day of Alabama's legislative session, lawmakers have added last-minute votes to push the most extreme anti-transgender agenda we've seen to date -- all within a matter of hours," said Sam Ames, director of advocacy and government affairs for The Trevor Project.

"These policies are not only cruel and unnecessary, they are unpopular among a majority of Americans," they continued. "Criminalizing doctors, isolating trans youth from their support systems and stigmatizing conversations around LGBTQ identity will only fuel more bullying, anxiety and suicide risk among these youth."

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