

diagnostic criteria for study entry. There are no details reported for how the outcomes in the study were assessed, and by whom. The length of follow-up for the outcomes in the model are questionable in relation to whether there was sufficient time for GnRH analogues to have a measurable effect. The time points used are start of GnRH analogues and start of gender-affirming hormones. Overall, the mean time between starting GnRH analogues and gender-affirming hormones was 1.88 (± 1.05) years, but the range is as low as just 5 months between the 2 time points, which may be insufficient for any difference in outcome to have occurred in some individuals.

The fourth study ([Joseph et al. 2019](#)) was a retrospective, longitudinal observational single centre study which assessed bone mineral density in adolescents with gender dysphoria in the UK. For inclusion in the study, participants had to have been assessed by the Gender Identity Development Service multi-disciplinary psychosocial health team for at least 4 assessments over a minimum of 6 months. No other diagnostic criteria, such as the DSM-IV-TR, are discussed. Bone density was assessed using dual energy X-ray absorptiometry (DAXA) scan of the lumbar spine (L1-L4) and the femoral neck at baseline (n=70), 1 year (n=70) and 2 years after starting GnRH analogues (n=39). The results suggest a possible association between GnRH analogues and bone mineral apparent density. However, the evidence is of poor quality, and the results could be due to bias or chance. No concomitant treatments or comorbidities were reported.

The fifth study ([Khatchadourian et al. 2014](#)) was an uncontrolled retrospective observational study which describes patient characteristics at presentation, treatment, and response to treatment in 84 adolescents with gender dysphoria, of whom 27 received GnRH analogues. The study used clinical records to show outcomes for up to 13 years (continuing use of GnRH analogues, reasons for stopping GnRH analogues and onward care such as gender-affirming hormone use). The methods are well reported but the results for those taking GnRH analogues are poorly and incompletely reported, particularly for transfemales, and no analysis of data was undertaken. It is difficult to assess the results for stopping GnRH analogues due to incomplete reporting of this outcome.

The sixth study ([Klink et al. 2015](#)) was a retrospective longitudinal observational single centre study which assessed bone mineral density in adolescents with gender dysphoria, diagnosed with the DSM-IV-TR criteria. Bone density was assessed when starting GnRH analogues and then when starting gender-affirming hormones. Results are reported for transmales and transfemales separately and no results for the whole cohort are given. Statistical analyses were reported for all outcomes of interest but, because there was no comparator group and participants acted as their own controls, it is not known whether the findings are associated with GnRH analogues or due to changes over time. The authors reported z-scores which allows for comparison with the expected increase in bone density in the general population. However, because no concomitant treatments or comorbidities were reported it is possible that the findings may not be because of GnRH analogues and there is another way in which the study population differs from the general population.

The seventh study ([Schagen et al. 2016](#)) was a prospective observational study of 116 adolescents which provided very low certainty non-comparative evidence on change in serum creatinine between starting GnRH analogues and 1 year, and liver function during treatment. Statistical analyses were reported for changes in serum creatinine but not for liver function. Because there was no comparator group and participants acted as their own

controls, it is not known whether the findings are associated with GnRH analogues or due to changes over time, or concomitant treatments.

The eighth study ([Staphorsius et al. 2015](#)) was a cross-sectional study of 85 adolescents, 40 with gender dysphoria (of whom 20 were receiving GnRH analogues) and 45 matched controls (not further reported in this evidence review). The study includes 1 outcome of interest for clinical effectiveness (CBCL) and 1 outcome of interest for safety (cognitive development or functioning). The mean (\pm SD) CBCL, IQ test, reaction time and accuracy scores were given for each group, but the statistical analysis is unclear. It is not reported what analysis was used or which of the groups were compared, therefore it is difficult to interpret the results.

The ninth study ([Vlot et al. 2017](#)) was a retrospective observational study which assessed bone mineral apparent density in adolescents with DSM-IV-TR gender dysphoria. Measurements were taken at the start of GnRH analogues and at the start of gender-affirming hormones. Results are reported for young bone age and old bone age in transmales and transfemales separately, and no results for the whole cohort are given. Statistical analyses were reported for all outcomes of interest but, because there was no comparator group and participants acted as their own controls, it is not known whether the findings are associated with GnRH analogues or due to changes over time. The authors reported z-scores which allows for comparison with the expected increase in bone density in the general population. However, because no concomitant treatments or comorbidities were reported it is possible that the findings may not be because of GnRH analogues and there is another way in which the study population differs from the general population.

7. Conclusion

The results of the studies that reported impact on the critical outcomes of gender dysphoria and mental health (depression, anger and anxiety), and the important outcomes of body image and psychosocial impact (global and psychosocial functioning) in children and adolescents with gender dysphoria are of very low certainty using modified GRADE. They suggest little change with GnRH analogues from baseline to follow-up.

Studies that found differences in outcomes could represent changes that are either of questionable clinical value, or the studies themselves are not reliable and changes could be due to confounding, bias or chance. It is plausible, however, that a lack of difference in scores from baseline to follow-up is the effect of GnRH analogues in children and adolescents with gender dysphoria, in whom the development of secondary sexual characteristics might be expected to be associated with an increased impact on gender dysphoria, depression, anxiety, anger and distress over time without treatment. One study reported statistically significant reductions in the Child Behaviour Checklist/Youth Self-Report (CBCL/YSR) scores from baseline to follow up, and given that the purpose of GnRH analogues is to reduce distress caused by the development of secondary sexual characteristics and the CBCL/YSR in part measures distress, this could be an important finding. However, as the studies all lack reasonable controls not receiving GnRH analogues, the natural history of the outcomes measured in the studies is not known and any positive changes could be a regression to mean.

The results of the studies that reported bone density outcomes suggest that GnRH analogues may reduce the increase in bone density which is expected during puberty. However, as the studies themselves are not reliable, the results could be due to confounding, bias or chance. While controlled trials may not be possible, comparative studies are needed to understand this association and whether the effects of GnRH analogues on bone density are seen after treatment is stopped. All the studies that reported safety outcomes provided very low certainty evidence.

No cost-effectiveness evidence was found to determine whether or not GnRH analogues are cost-effective for children and adolescents with gender dysphoria.

The results of the studies that reported outcomes for subgroups of children and adolescents with gender dysphoria, suggest there may be differences between sex assigned at birth males (transfemales) and sex assigned at birth females (transmales).

Appendix A PICO document

The review questions for this evidence review are:

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

PICO table

P – Population and Indication	<p>Children and adolescents aged 18 years or less who have gender dysphoria, gender identity disorder or gender incongruence of childhood as defined by study:</p> <p>The following subgroups of children and adolescents with gender dysphoria, gender identity disorder or gender incongruence of childhood need to be considered:</p> <ul style="list-style-type: none"> • Sex assigned at birth males. • Sex assigned at birth females. • The duration of gender dysphoria: less than 6 months, 6-24 months, and more than 24 months. • The age of onset of gender dysphoria. • The age at which treatment was initiated. • The age of onset of puberty. • Tanner stage at which treatment was initiated. • Children and adolescents with gender dysphoria who have a pre-existing diagnosis of autistic spectrum disorder. • Children and adolescents with gender dysphoria who had a significant mental health symptom load at diagnosis including anxiety, depression (with or without a history of self-harm and suicidality), suicide attempts, psychosis, personality disorder, Attention Deficit Hyperactivity Disorder and eating disorders.
I – Intervention	<p>Any GnRH analogue including: triptorelin*; buserelin; histrelin; goserelin (Zoladex); leuprorelin/leuprolide (Prostap); nafarelin.</p>

	* Triptorelin (brand names Gonapeptyl and Decapeptyl) are used in Leeds Hospital, England. The search should include brand names as well as generic names.
C – Comparator(s)	One or a combination of: <ul style="list-style-type: none"> • Psychological support. • Social transitioning to the gender with which the individual identifies. • No intervention.
O – Outcomes	<p>There are no known minimal clinically important differences and there are no preferred timepoints for the outcome measures selected.</p> <p>All outcomes should be stratified by:</p> <ul style="list-style-type: none"> • The age at which treatment with GnRH analogues was initiated. • The length of treatment with GnRH analogues where possible. <p><u>A: Clinical Effectiveness</u></p> <p><i>Critical to decision making</i></p> <ul style="list-style-type: none"> • Impact on Gender Dysphoria This outcome is critical because gender dysphoria in adolescents and children is associated with significant distress and problems functioning. Impact on gender dysphoria may be measured by the Utrecht Gender Dysphoria Scale. Other measures as reported in studies may be used as an alternative to the stated measure. • Impact on mental health Examples of mental health problems include self-harm, thoughts of suicide, suicide attempts, eating disorders, depression/low mood and anxiety. These outcomes are critical because self-harm and thoughts of suicide have the potential to result in significant physical harm and for completed suicides the death of the young person. Disordered eating habits may cause significant morbidity in young people. Depression and anxiety are also critical outcomes because they may impact on social, occupational, or other areas of functioning of children and adolescents. The Child and Adolescent Psychiatric Assessment (CAPA) may be used to measure depression and anxiety. The impact on self-harm and suicidality (ideation and behaviour) may be measured using the Suicide Ideation Questionnaire Junior. Other measures may be used as an alternative to the stated measures. • Impact on Quality of Life This outcome is critical because gender dysphoria in children and adolescents may be associated with a significant reduction in health-related quality of life. Quality of Life may be measured by the KINDL questionnaire, Kidscreen 52. Other measures as reported in studies may be used as an alternative to the stated measure. <p><i>Important to decision making</i></p> <ul style="list-style-type: none"> • Impact on body Image This outcome is important because some transgender young people may desire to take steps to suppress features of their physical appearance associated with their sex assigned at birth or accentuate physical features of their desired gender. The Body Image Scale could be used as a measure. Other measures

	<p>as reported in studies may also be used as an alternative to the stated measure.</p> <ul style="list-style-type: none"> • Psychosocial Impact Examples of psychosocial impact are: coping mechanisms which may impact on substance misuse; family relationships; peer relationships. This outcome is important because gender dysphoria in adolescents and children is associated with internalising and externalising behaviours and emotional and behavioural problems which may impact on social and occupational functioning. The child behavioural check list (CBCL) may be used to measure the impact on psychosocial functioning. Other measures as reported in studies may be used as an alternative to the stated measure. • Engagement with health care services This outcome is important because patient engagement with healthcare services will impact on their clinical outcomes. Engagement with health care services may be measured using the Youth Health Care measure-satisfaction, utilization, and needs (YHC-SUN) questionnaire. Loss to follow up should also be ascertained as part of this outcome. Alternative measures to the YHC-SUN questionnaire may be used as reported in studies. • Transitioning surgery – Impact on extent of and satisfaction with surgery This outcome is important because some children and adolescents with gender dysphoria may proceed to transitioning surgery. Stated measures of the extent of transitioning surgery and satisfaction with surgery in studies may be reported. • Stopping treatment The proportion of patients who stop treatment with GnRH analogues and the reasons why. This outcome is important to patients because there is uncertainty about the short- and long-term safety and adverse effects of GnRH analogues in children and adolescents being treated for gender dysphoria. <p><u>B: Safety</u></p> <ul style="list-style-type: none"> • Short and long-term safety and adverse effects of taking GnRH analogues are important because GnRH analogues are not licensed for the treatment of adolescents and children with gender dysphoria. Aspects to be reported on should include: <ul style="list-style-type: none"> ○ Impact of the drug use such as its impact on bone density, arterial hypertension, cognitive development/functioning ○ Impact of withdrawing the drug such as, slipped upper femoral epiphysis, reversibility on the reproductive system, and any others as reported. <p><u>C: Cost effectiveness</u></p> <p>Cost effectiveness studies should be reported.</p>
Inclusion criteria	
Study design	<p>Systematic reviews, randomised controlled trials, controlled clinical trials, cohort studies. If no higher level quality evidence is found, case series can be considered.</p>

Language	English only
Patients	Human studies only
Age	18 years or less
Date limits	2000-2020
Exclusion criteria	
Publication type	Conference abstracts, non-systematic reviews, narrative reviews, commentaries, letters, editorials, guidelines and pre-publication prints
Study design	Case reports, resource utilisation studies

Appendix B Search strategy

Medline, Embase, the Cochrane Library, HTA and APA PsycInfo were searched on 23 July 2020, limiting the search to papers published in English language in the last 20 years. Conference abstracts and letters were excluded.

Database: Medline

Platform: Ovid

Version: Ovid MEDLINE(R) <1946 to July 21, 2020>

Search date: 23/7/2020

Number of results retrieved: 144

Search strategy:

- 1 Gender Dysphoria/ (485)
- 2 Gender Identity/ (18452)
- 3 "Sexual and Gender Disorders"/ (75)
- 4 Transsexualism/ (3758)
- 5 Transgender Persons/ (3143)
- 6 Health Services for Transgender Persons/ (136)
- 7 exp Sex Reassignment Procedures/ (836)
- 8 (gender* adj3 (dysphori* or affirm* or incongruen* or identi* or disorder* or confus* or minorit* or queer*).tw. (7435)
- 9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (12678)
- 10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (102343)
- 11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*).tw. (6974)
- 12 (male-to-female or m2f or female-to-male or f2m).tw. (114841)
- 13 or/1-12 (252702)
- 14 exp Infant/ or Infant Health/ or Infant Welfare/ (1137479)
- 15 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (852400)
- 16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1913257)

17 Minors/ (2574)
 18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2361686)
 19 exp pediatrics/ (58118)
 20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (836269)
 21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (2024207)
 22 Puberty/ (13278)
 23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert*
 or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn.
 (424246)
 24 Schools/ (38104)
 25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7199)
 26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or
 pupil* or student*).ti,ab,jn. (468992)
 27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or
 "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or
 aged)).ti,ab. (89353)
 28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19")
 adj2 (year or years or age or ages or aged)).ti,ab. (887838)
 29 or/14-28 (5534171)
 30 13 and 29 (79263)
 31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (7)
 32 30 or 31 (79263)
 33 Gonadotropin-Releasing Hormone/ (27588)
 34 (pubert* adj3 block*).ti,ab. (78)
 35 ((gonadotrophin or gonadotropin) and releasing).ti,ab. (17299)
 36 (GnRH adj2 analog*).ti,ab. (2541)
 37 GnRH*.ti,ab. (20991)
 38 "GnRH agonist".ti,ab. (4040)
 39 Triptorelin Pamoate/ (1906)
 40 triptorelin.ti,ab. (677)
 41 arvekap.ti,ab. (1)
 42 ("AY 25650" or AY25650).ti,ab. (1)
 43 ("BIM 21003" or BIM21003).ti,ab. (0)
 44 ("BN 52014" or BN52014).ti,ab. (0)
 45 ("CL 118532" or CL118532).ti,ab. (0)
 46 Debio.ti,ab. (83)
 47 diphereline.ti,ab. (17)
 48 moapar.ti,ab. (0)
 49 pamorelin.ti,ab. (0)
 50 trelstar.ti,ab. (3)
 51 triptodur.ti,ab. (1)
 52 ("WY 42422" or WY42422).ti,ab. (0)
 53 ("WY 42462" or WY42462).ti,ab. (0)
 54 gonapeptyl.ti,ab. (0)
 55 decapeptyl.ti,ab. (210)
 56 salvacyl.ti,ab. (0)
 57 Buserelin/ (2119)
 58 buserelin.ti,ab. (1304)

59 bigonist.ti,ab. (0)
60 ("hoe 766" or hoe-766 or hoe766).ti,ab. (69)
61 profact.ti,ab. (2)
62 receptal.ti,ab. (30)
63 suprecur.ti,ab. (4)
64 suprefact.ti,ab. (22)
65 tiloryth.ti,ab. (0)
66 histrelin.ti,ab. (55)
67 "LHRH-hydrogel implant".ti,ab. (1)
68 ("RL 0903" or RL0903).ti,ab. (1)
69 ("SPD 424" or SPD424).ti,ab. (1)
70 goserelin.ti,ab. (875)
71 Goserelin/ (1612)
72 ("ici 118630" or ici118630).ti,ab. (51)
73 ("ZD-9393" or ZD9393).ti,ab. (0)
74 zoladex.ti,ab. (379)
75 leuprorelin.ti,ab. (413)
76 carcinil.ti,ab. (0)
77 enanton*.ti,ab. (23)
78 ginecrin.ti,ab. (0)
79 leuplin.ti,ab. (13)
80 Leuprolide/ (2900)
81 leuprolide.ti,ab. (1743)
82 lucrin.ti,ab. (11)
83 lupron.ti,ab. (162)
84 provren.ti,ab. (0)
85 procrin.ti,ab. (3)
86 ("tap 144" or tap144).ti,ab. (40)
87 (a-43818 or a43818).ti,ab. (3)
88 Trenantone.ti,ab. (1)
89 staladex.ti,ab. (0)
90 prostap.ti,ab. (6)
91 Nafarelin/ (327)
92 nafarelin.ti,ab. (251)
93 ("76932-56-4" or "76932564").ti,ab. (0)
94 ("76932-60-0" or "76932600").ti,ab. (0)
95 ("86220-42-0" or "86220420").ti,ab. (0)
96 ("rs 94991 298" or rs94991298).ti,ab. (0)
97 synarel.ti,ab. (12)
98 deslorelin.ti,ab. (263)
99 gonadorelin.ti,ab. (201)
100 ("33515-09-2" or "33515092").ti,ab. (0)
101 ("51952-41-1" or "51952411").ti,ab. (0)
102 ("52699-48-6" or "52699486").ti,ab. (0)
103 cetrotide.ti,ab. (463)
104 cetrotide.ti,ab. (41)
105 ("NS 75A" or NS75A).ti,ab. (0)
106 ("NS 75B" or NS75B).ti,ab. (0)

- 107 ("SB 075" or SB075).ti,ab. (0)
- 108 ("SB 75" or SB75).ti,ab. (63)
- 109 gonadoliberin.ti,ab. (143)
- 110 kryptocur.ti,ab. (6)
- 111 cetorelix.ti,ab. (463)
- 112 cetrotide.ti,ab. (41)
- 113 antagon.ti,ab. (17)
- 114 ganirelix.ti,ab. (138)
- 115 ("ORG 37462" or ORG37462).ti,ab. (3)
- 116 orgalutran.ti,ab. (20)
- 117 ("RS 26306" or RS26306).ti,ab. (5)
- 118 ("AY 24031" or AY24031).ti,ab. (0)
- 119 factrel.ti,ab. (11)
- 120 fertagyl.ti,ab. (11)
- 121 lutrelef.ti,ab. (5)
- 122 lutrepulse.ti,ab. (3)
- 123 relect.ti,ab. (10)
- 124 fertiral.ti,ab. (0)
- 125 (hoe471 or "hoe 471").ti,ab. (6)
- 126 relisorm.ti,ab. (4)
- 127 cystorelin.ti,ab. (18)
- 128 dirigestran.ti,ab. (5)
- 129 or/33-128 (42216)
- 130 32 and 129 (416)
- 131 limit 130 to english language (393)
- 132 limit 131 to (letter or historical article or comment or editorial or news or case reports)
(36)
- 133 131 not 132 (357)
- 134 animals/ not humans/ (4686361)
- 135 133 not 134 (181)
- 136 limit 135 to yr="2000 -Current" (144)

Database: Medline in-process

Platform: Ovid

Version: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to July 21, 2020>

Search date: 23/7/2020

Number of results retrieved:

Search strategy: 42

- 1 Gender Dysphoria/ (0)
- 2 Gender Identity/ (0)
- 3 "Sexual and Gender Disorders"/ (0)
- 4 Transsexualism/ (0)
- 5 Transgender Persons/ (0)
- 6 Health Services for Transgender Persons/ (0)
- 7 exp Sex Reassignment Procedures/ (0)

- 8 (gender* adj3 (dysphori* or affirm* or incongruen* or identi* or disorder* or confus* or minorit* or queer*)).tw. (1645)
- 9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (2333)
- 10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (20884)
- 11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (968)
- 12 (male-to-female or m2f or female-to-male or f2m).tw. (15513)
- 13 or/1-12 (39905)
- 14 exp Infant/ or Infant Health/ or Infant Welfare/ (0)
- 15 (prematu* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (80723)
- 16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)
- 17 Minors/ (0)
- 18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (321871)
- 19 exp pediatrics/ (0)
- 20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (119783)
- 21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)
- 22 Puberty/ (0)
- 23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (60264)
- 24 Schools/ (0)
- 25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)
- 26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (69233)
- 27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (10319)
- 28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (112800)
- 29 or/14-28 (525529)
- 30 13 and 29 (9196)
- 31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (3)
- 32 30 or 31 (9197)
- 33 Gonadotropin-Releasing Hormone/ (0)
- 34 (pubert* adj3 block*).ti,ab. (19)
- 35 ((gonadotrophin or gonadotropin) and releasing).ti,ab. (1425)
- 36 (GnRH adj2 analog*).ti,ab. (183)
- 37 GnRH*.ti,ab. (1695)
- 38 "GnRH agonist".ti,ab. (379)
- 39 Triptorelin Pamoate/ (0)
- 40 triptorelin.ti,ab. (72)
- 41 arvekap.ti,ab. (0)
- 42 ("AY 25650" or AY25650).ti,ab. (0)
- 43 ("BIM 21003" or BIM21003).ti,ab. (0)
- 44 ("BN 52014" or BN52014).ti,ab. (0)
- 45 ("CL 118532" or CL118532).ti,ab. (0)

46 Debio.ti,ab. (11)
47 diphereline.ti,ab. (6)
48 moapar.ti,ab. (0)
49 pamorelin.ti,ab. (0)
50 trelstar.ti,ab. (0)
51 triptodur.ti,ab. (0)
52 ("WY 42422" or WY42422).ti,ab. (0)
53 ("WY 42462" or WY42462).ti,ab. (0)
54 gonapeptyl.ti,ab. (0)
55 decapeptyl.ti,ab. (8)
56 salvacyl.ti,ab. (0)
57 Buserelin/ (0)
58 buserelin.ti,ab. (59)
59 bigonist.ti,ab. (0)
60 ("hoe 766" or hoe-766 or hoe766).ti,ab. (3)
61 profact.ti,ab. (0)
62 receptal.ti,ab. (0)
63 suprecur.ti,ab. (1)
64 suprefact.ti,ab. (2)
65 tiloryth.ti,ab. (0)
66 histrelin.ti,ab. (9)
67 "LHRH-hydrogel implant".ti,ab. (0)
68 ("RL 0903" or RL0903).ti,ab. (0)
69 ("SPD 424" or SPD424).ti,ab. (0)
70 goserelin.ti,ab. (68)
71 Goserelin/ (0)
72 ("ici 118630" or ici118630).ti,ab. (0)
73 ("ZD-9393" or ZD9393).ti,ab. (0)
74 zoladex.ti,ab. (6)
75 leuprorelin.ti,ab. (47)
76 carcinil.ti,ab. (0)
77 enanton*.ti,ab. (1)
78 ginecrin.ti,ab. (0)
79 leuplin.ti,ab. (1)
80 Leuprolide/ (0)
81 leuprolide.ti,ab. (121)
82 lucrin.ti,ab. (4)
83 lupron.ti,ab. (10)
84 provren.ti,ab. (0)
85 procrin.ti,ab. (0)
86 ("tap 144" or tap144).ti,ab. (0)
87 (a-43818 or a43818).ti,ab. (0)
88 Trenantone.ti,ab. (1)
89 staladex.ti,ab. (0)
90 prostap.ti,ab. (0)
91 Nafarelin/ (0)
92 nafarelin.ti,ab. (5)
93 ("76932-56-4" or "76932564").ti,ab. (0)

- 94 ("76932-60-0" or "76932600").ti,ab. (0)
- 95 ("86220-42-0" or "86220420").ti,ab. (0)
- 96 ("rs 94991 298" or rs94991298).ti,ab. (0)
- 97 synarel.ti,ab. (0)
- 98 deslorelin.ti,ab. (14)
- 99 gonadorelin.ti,ab. (13)
- 100 ("33515-09-2" or "33515092").ti,ab. (0)
- 101 ("51952-41-1" or "51952411").ti,ab. (0)
- 102 ("52699-48-6" or "52699486").ti,ab. (0)
- 103 cetorelix.ti,ab. (31)
- 104 cetrotide.ti,ab. (5)
- 105 ("NS 75A" or NS75A).ti,ab. (0)
- 106 ("NS 75B" or NS75B).ti,ab. (0)
- 107 ("SB 075" or SB075).ti,ab. (0)
- 108 ("SB 75" or SB75).ti,ab. (2)
- 109 gonadoliberin.ti,ab. (4)
- 110 kryptocur.ti,ab. (1)
- 111 cetorelix.ti,ab. (31)
- 112 cetrotide.ti,ab. (5)
- 113 antagonist.ti,ab. (0)
- 114 ganirelix.ti,ab. (8)
- 115 ("ORG 37462" or ORG37462).ti,ab. (0)
- 116 orgalutran.ti,ab. (3)
- 117 ("RS 26306" or RS26306).ti,ab. (0)
- 118 ("AY 24031" or AY24031).ti,ab. (0)
- 119 factrel.ti,ab. (2)
- 120 fertagyl.ti,ab. (1)
- 121 lutrelef.ti,ab. (0)
- 122 lutrepulse.ti,ab. (0)
- 123 relefact.ti,ab. (0)
- 124 fertiral.ti,ab. (0)
- 125 (hoe471 or "hoe 471").ti,ab. (0)
- 126 relisorm.ti,ab. (0)
- 127 cystorelin.ti,ab. (1)
- 128 dirigestran.ti,ab. (0)
- 129 or/33-128 (2332)
- 130 32 and 129 (45)
- 131 limit 130 to english language (45)
- 132 limit 131 to yr="2000 -Current" (42)

Database: Medline epubs ahead of print

Platform: Ovid

Version: Ovid MEDLINE(R) Epub Ahead of Print <July 21, 2020>

Search date: 23/7/2020

Number of results retrieved: 8

Search strategy:

1 Gender Dysphoria/ (0)

- 2 Gender Identity/ (0)
- 3 "Sexual and Gender Disorders"/ (0)
- 4 Transsexualism/ (0)
- 5 Transgender Persons/ (0)
- 6 Health Services for Transgender Persons/ (0)
- 7 exp Sex Reassignment Procedures/ (0)
- 8 (gender* adj3 (dysphori* or affirm* or incongruen* or identi* or disorder* or confus* or minorit* or queer*).tw. (486)
- 9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (640)
- 10 (trans or crossgender* or cross-gender* or crosssex* or cross-sex* or genderqueer*).tw. (1505)
- 11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*).tw. (178)
- 12 (male-to-female or m2f or female-to-male or f2m).tw. (2480)
- 13 or/1-12 (4929)
- 14 exp Infant/ or Infant Health/ or Infant Welfare/ (0)
- 15 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (15496)
- 16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)
- 17 Minors/ (0)
- 18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (53563)
- 19 exp pediatrics/ (0)
- 20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (22796)
- 21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)
- 22 Puberty/ (0)
- 23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (13087)
- 24 Schools/ (0)
- 25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)
- 26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (12443)
- 27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (1416)
- 28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (20166)
- 29 or/14-28 (88366)
- 30 13 and 29 (1638)
- 31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (1)
- 32 30 or 31 (1638)
- 33 Gonadotropin-Releasing Hormone/ (0)
- 34 (pubert* adj3 block*).ti,ab. (2)
- 35 ((gonadotrophin or gonadotropin) and releasing).ti,ab. (176)
- 36 (GnRH adj2 analog*).ti,ab. (30)
- 37 GnRH*.ti,ab. (223)
- 38 "GnRH agonist*".ti,ab. (49)
- 39 Triptorelin Pamoate/ (0)

40 triptorelin.ti,ab. (12)
41 arvekap.ti,ab. (0)
42 ("AY 25650" or AY25650).ti,ab. (0)
43 ("BIM 21003" or BIM21003).ti,ab. (0)
44 ("BN 52014" or BN52014).ti,ab. (0)
45 ("CL 118532" or CL118532).ti,ab. (0)
46 Debio.ti,ab. (2)
47 diphereline.ti,ab. (1)
48 moapar.ti,ab. (0)
49 pamorelin.ti,ab. (0)
50 trelstar.ti,ab. (0)
51 triptodur.ti,ab. (0)
52 ("WY 42422" or WY42422).ti,ab. (0)
53 ("WY 42462" or WY42462).ti,ab. (0)
54 gonapeptyl.ti,ab. (0)
55 decapeptyl.ti,ab. (0)
56 salvacyl.ti,ab. (0)
57 Buserelin/ (0)
58 buserelin.ti,ab. (7)
59 bigonist.ti,ab. (0)
60 ("hoe 766" or hoe-766 or hoe766).ti,ab. (0)
61 profact.ti,ab. (0)
62 receptal.ti,ab. (0)
63 suprecur.ti,ab. (0)
64 suprefact.ti,ab. (1)
65 tiloryth.ti,ab. (0)
66 histrelin.ti,ab. (2)
67 "LHRH-hydrogel implant".ti,ab. (0)
68 ("RL 0903" or RL0903).ti,ab. (0)
69 ("SPD 424" or SPD424).ti,ab. (0)
70 goserelin.ti,ab. (11)
71 Goserelin/ (0)
72 ("ici 118630" or ici118630).ti,ab. (0)
73 ("ZD-9393" or ZD9393).ti,ab. (0)
74 zoladex.ti,ab. (1)
75 leuprorelin.ti,ab. (13)
76 carcinil.ti,ab. (0)
77 enanton*.ti,ab. (1)
78 ginecrin.ti,ab. (0)
79 leuplin.ti,ab. (0)
80 Leuprolide/ (0)
81 leuprolide.ti,ab. (22)
82 lucrin.ti,ab. (0)
83 lupron.ti,ab. (2)
84 provren.ti,ab. (0)
85 procrin.ti,ab. (0)
86 ("tap 144" or tap144).ti,ab. (1)
87 (a-43818 or a43818).ti,ab. (0)

88 Trenantone.ti,ab. (0)
89 staladex.ti,ab. (0)
90 prostap.ti,ab. (0)
91 Nafarelin/ (0)
92 nafarelin.ti,ab. (4)
93 ("76932-56-4" or "76932564").ti,ab. (0)
94 ("76932-60-0" or "76932600").ti,ab. (0)
95 ("86220-42-0" or "86220420").ti,ab. (0)
96 ("rs 94991 298" or rs94991298).ti,ab. (0)
97 synarel.ti,ab. (0)
98 deslorelin.ti,ab. (3)
99 gonadorelin.ti,ab. (3)
100 ("33515-09-2" or "33515092").ti,ab. (0)
101 ("51952-41-1" or "51952411").ti,ab. (0)
102 ("52699-48-6" or "52699486").ti,ab. (0)
103 cetorelix.ti,ab. (6)
104 cetrotide.ti,ab. (2)
105 ("NS 75A" or NS75A).ti,ab. (0)
106 ("NS 75B" or NS75B).ti,ab. (0)
107 ("SB 075" or SB075).ti,ab. (0)
108 ("SB 75" or SB75).ti,ab. (0)
109 gonadoliberin.ti,ab. (0)
110 kryptocur.ti,ab. (0)
111 cetorelix.ti,ab. (6)
112 cetrotide.ti,ab. (2)
113 antagon.ti,ab. (1)
114 ganirelix.ti,ab. (1)
115 ("ORG 37462" or ORG37462).ti,ab. (0)
116 orgalutran.ti,ab. (0)
117 ("RS 26306" or RS26306).ti,ab. (0)
118 ("AY 24031" or AY24031).ti,ab. (0)
119 factrel.ti,ab. (0)
120 fertagyl.ti,ab. (0)
121 lutrelef.ti,ab. (0)
122 lutrepulse.ti,ab. (0)
123 relect.ti,ab. (0)
124 fertiral.ti,ab. (0)
125 (hoe471 or "hoe 471").ti,ab. (0)
126 relisorm.ti,ab. (0)
127 cystorelin.ti,ab. (0)
128 dirigestran.ti,ab. (0)
129 or/33-128 (310)
130 32 and 129 (8)
131 limit 130 to english language (8)
132 limit 131 to yr="2000 -Current" (8)

Database: Medline daily update

Platform: Ovid

Version: Ovid MEDLINE(R) Daily Update <July 21, 2020>

Search date: 23/7/2020

Number of results retrieved: 1

Search strategy

- 1 Gender Dysphoria/ (4)
- 2 Gender Identity/ (38)
- 3 "Sexual and Gender Disorders"/ (0)
- 4 Transsexualism/ (2)
- 5 Transgender Persons/ (26)
- 6 Health Services for Transgender Persons/ (1)
- 7 exp Sex Reassignment Procedures/ (3)
- 8 (gender* adj3 (dysphori* or affirm* or incongruen* or identi* or disorder* or confus* or minorit* or queer*)).tw. (24)
- 9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (39)
- 10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (87)
- 11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (15)
- 12 (male-to-female or m2f or female-to-male or f2m).tw. (181)
- 13 or/1-12 (358)
- 14 exp Infant/ or Infant Health/ or Infant Welfare/ (932)
- 15 (prematu* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (981)
- 16 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1756)
- 17 Minors/ (3)
- 18 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (3672)
- 19 exp pediatrics/ (75)
- 20 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (1658)
- 21 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (2006)
- 22 Puberty/ (8)
- 23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (732)
- 24 Schools/ (56)
- 25 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (5)
- 26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (622)
- 27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (98)
- 28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (1301)
- 29 or/14-28 (6705)
- 30 13 and 29 (130)
- 31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw. (0)
- 32 30 or 31 (130)
- 33 Gonadotropin-Releasing Hormone/ (11)

34 (pubert* adj3 block*).ti,ab. (0)
35 ((gonadotrophin or gonadotropin) and releasing).ti,ab. (10)
36 (GnRH adj2 analog*).ti,ab. (2)
37 GnRH*.ti,ab. (14)
38 "GnRH agonist*".ti,ab. (4)
39 Triptorelin Pamoate/ (1)
40 triptorelin.ti,ab. (1)
41 arvekap.ti,ab. (0)
42 ("AY 25650" or AY25650).ti,ab. (0)
43 ("BIM 21003" or BIM21003).ti,ab. (0)
44 ("BN 52014" or BN52014).ti,ab. (0)
45 ("CL 118532" or CL118532).ti,ab. (0)
46 Debio.ti,ab. (1)
47 diphereline.ti,ab. (0)
48 moapar.ti,ab. (0)
49 pamorelin.ti,ab. (0)
50 trelstar.ti,ab. (0)
51 triptodur.ti,ab. (0)
52 ("WY 42422" or WY42422).ti,ab. (0)
53 ("WY 42462" or WY42462).ti,ab. (0)
54 gonapeptyl.ti,ab. (0)
55 decapeptyl.ti,ab. (0)
56 salvacyl.ti,ab. (0)
57 Buserelin/ (0)
58 buserelin.ti,ab. (0)
59 bigonist.ti,ab. (0)
60 ("hoe 766" or hoe-766 or hoe766).ti,ab. (0)
61 profact.ti,ab. (0)
62 receptal.ti,ab. (0)
63 suprecur.ti,ab. (0)
64 suprefact.ti,ab. (0)
65 tiloryth.ti,ab. (0)
66 histrelin.ti,ab. (0)
67 "LHRH-hydrogel implant".ti,ab. (0)
68 ("RL 0903" or RL0903).ti,ab. (0)
69 ("SPD 424" or SPD424).ti,ab. (0)
70 goserelin.ti,ab. (1)
71 Goserelin/ (2)
72 ("ici 118630" or ici118630).ti,ab. (0)
73 ("ZD-9393" or ZD9393).ti,ab. (0)
74 zoladex.ti,ab. (0)
75 leuprorelin.ti,ab. (0)
76 carcinil.ti,ab. (0)
77 enanton*.ti,ab. (0)
78 ginecrin.ti,ab. (0)
79 leuplin.ti,ab. (0)
80 Leuprolide/ (0)
81 leuprolide.ti,ab. (0)

82 lucrin.ti,ab. (0)
83 lupron.ti,ab. (0)
84 provren.ti,ab. (0)
85 procrin.ti,ab. (0)
86 ("tap 144" or tap144).ti,ab. (0)
87 (a-43818 or a43818).ti,ab. (0)
88 Trenantone.ti,ab. (0)
89 staladex.ti,ab. (0)
90 prostap.ti,ab. (0)
91 Nafarelin/ (0)
92 nafarelin.ti,ab. (0)
93 ("76932-56-4" or "76932564").ti,ab. (0)
94 ("76932-60-0" or "76932600").ti,ab. (0)
95 ("86220-42-0" or "86220420").ti,ab. (0)
96 ("rs 94991 298" or rs94991298).ti,ab. (0)
97 synarel.ti,ab. (0)
98 deslorelin.ti,ab. (0)
99 gonadorelin.ti,ab. (0)
100 ("33515-09-2" or "33515092").ti,ab. (0)
101 ("51952-41-1" or "51952411").ti,ab. (0)
102 ("52699-48-6" or "52699486").ti,ab. (0)
103 cetorelix.ti,ab. (0)
104 cetrotide.ti,ab. (0)
105 ("NS 75A" or NS75A).ti,ab. (0)
106 ("NS 75B" or NS75B).ti,ab. (0)
107 ("SB 075" or SB075).ti,ab. (0)
108 ("SB 75" or SB75).ti,ab. (0)
109 gonadoliberin.ti,ab. (0)
110 kryptocur.ti,ab. (0)
111 cetorelix.ti,ab. (0)
112 cetrotide.ti,ab. (0)
113 antagon.ti,ab. (0)
114 ganirelix.ti,ab. (0)
115 ("ORG 37462" or ORG37462).ti,ab. (0)
116 orgalutran.ti,ab. (0)
117 ("RS 26306" or RS26306).ti,ab. (0)
118 ("AY 24031" or AY24031).ti,ab. (0)
119 factrel.ti,ab. (0)
120 fertagyl.ti,ab. (0)
121 lutrelef.ti,ab. (0)
122 lutrepulse.ti,ab. (0)
123 relefact.ti,ab. (0)
124 fertiral.ti,ab. (0)
125 (hoe471 or "hoe 471").ti,ab. (0)
126 relisorm.ti,ab. (0)
127 cystorelin.ti,ab. (0)
128 dirigestran.ti,ab. (0)
129 or/33-128 (23)

130 32 and 129 (1)
131 limit 130 to english language (1)
132 limit 131 to yr="2000 -Current" (1)

Database: Embase

Platform: Ovid

Version: Embase <1974 to 2020 July 22>

Search date: 23/7/2020

Number of results retrieved: 367

Search strategy:

1 exp Gender Dysphoria/ (5399)
2 Gender Identity/ (16820)
3 "Sexual and Gender Disorders"/ (24689)
4 Transsexualism/ (3869)
5 exp Transgender/ (6597)
6 Health Services for Transgender Persons/ (158848)
7 exp Sex Reassignment Procedures/ or sex transformation/ (3058)
8 (gender* adj3 (dysphori* or affirm* or incongru* or identi* or disorder* or confus* or minorit* or queer*)).tw. (13005)
9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (22509)
10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (154446)
11 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (10327)
12 (male-to-female or m2f or female-to-male or f2m).tw. (200166)
13 or/1-12 (582812)
14 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3437324)
15 (prematu* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (1186161)
16 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (3586795)
17 exp pediatrics/ (106214)
18 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (1491597)
19 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (105108)
20 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (641660)
21 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (103791)
22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (687437)
23 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or aged)).ti,ab. (138908)
24 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj2 (year or years or age or ages or aged)).ti,ab. (1562903)

25 or/14-24 (7130881)
26 13 and 25 (182161)
27 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw.
(17)
28 26 or 27 (182161)
29 gonadorelin/ (37580)
30 (pubert* adj3 block*).ti,ab. (142)
31 ((gonadotrophin or gonadotropin) and releasing).ti,ab. (21450)
32 (GnRH adj2 analog*).ti,ab. (4013)
33 GnRH*.ti,ab. (29862)
34 "GnRH agonist".ti,ab. (6719)
35 exp gonadorelin agonist/ or gonadorelin derivative/ or gonadorelin acetate/ (23304)
36 Triptorelin/ (5427)
37 triptorelin.ti,ab. (1182)
38 arvekap.ti,ab. (3)
39 ("AY 25650" or AY25650).ti,ab. (1)
40 ("BIM 21003" or BIM21003).ti,ab. (0)
41 ("BN 52014" or BN52014).ti,ab. (0)
42 ("CL 118532" or CL118532).ti,ab. (0)
43 Debio.ti,ab. (185)
44 diphereline.ti,ab. (51)
45 moapar.ti,ab. (0)
46 pamorelin.ti,ab. (0)
47 trelstar.ti,ab. (5)
48 triptodur.ti,ab. (1)
49 ("WY 42422" or WY42422).ti,ab. (0)
50 ("WY 42462" or WY42462).ti,ab. (0)
51 gonapeptyl.ti,ab. (10)
52 decapeptyl.ti,ab. (307)
53 salvacyl.ti,ab. (1)
54 buserelin acetate/ or buserelin/ (5164)
55 buserelin.ti,ab. (1604)
56 bigonist.ti,ab. (1)
57 ("hoe 766" or hoe-766 or hoe766).ti,ab. (89)
58 profact.ti,ab. (4)
59 receptal.ti,ab. (37)
60 suprecur.ti,ab. (8)
61 suprefact.ti,ab. (30)
62 tiloryth.ti,ab. (0)
63 histrelin/ (446)
64 histrelin.ti,ab. (107)
65 "LHRH-hydrogel implant".ti,ab. (1)
66 ("RL 0903" or RL0903).ti,ab. (1)
67 ("SPD 424" or SPD424).ti,ab. (1)
68 goserelin.ti,ab. (1487)
69 Goserelin/ (7128)
70 ("ici 118630" or ici118630).ti,ab. (49)
71 ("ZD-9393" or ZD9393).ti,ab. (0)

72 zoladex.ti,ab. (501)
73 leuprorelin/ (11312)
74 leuprorelin.ti,ab. (727)
75 carcinil.ti,ab. (0)
76 enanton*.ti,ab. (38)
77 ginecrin.ti,ab. (1)
78 leuplin.ti,ab. (26)
79 leuprolide.ti,ab. (2788)
80 lucrin.ti,ab. (47)
81 lupron.ti,ab. (361)
82 provren.ti,ab. (0)
83 procrin.ti,ab. (11)
84 ("tap 144" or tap144).ti,ab. (63)
85 (a-43818 or a43818).ti,ab. (3)
86 Trenantone.ti,ab. (7)
87 staladex.ti,ab. (0)
88 prostap.ti,ab. (11)
89 nafarelin acetate/ or nafarelin/ (1441)
90 nafarelin.ti,ab. (324)
91 ("76932-56-4" or "76932564").ti,ab. (0)
92 ("76932-60-0" or "76932600").ti,ab. (0)
93 ("86220-42-0" or "86220420").ti,ab. (0)
94 ("rs 94991 298" or rs94991298).ti,ab. (0)
95 synarel.ti,ab. (28)
96 deslorelin/ (452)
97 deslorelin.ti,ab. (324)
98 gonadorelin.ti,ab. (338)
99 ("33515-09-2" or "33515092").ti,ab. (0)
100 ("51952-41-1" or "51952411").ti,ab. (0)
101 ("52699-48-6" or "52699486").ti,ab. (0)
102 cetorelix/ (2278)
103 cetorelix.ti,ab. (717)
104 cetrotide.ti,ab. (113)
105 ("NS 75A" or NS75A).ti,ab. (0)
106 ("NS 75B" or NS75B).ti,ab. (0)
107 ("SB 075" or SB075).ti,ab. (1)
108 ("SB 75" or SB75).ti,ab. (76)
109 gonadoliberin.ti,ab. (152)
110 kryptocur.ti,ab. (6)
111 cetorelix.ti,ab. (717)
112 cetrotide.ti,ab. (113)
113 antagon.ti,ab. (32)
114 ganirelix/ (1284)
115 ganirelix.ti,ab. (293)
116 ("ORG 37462" or ORG37462).ti,ab. (4)
117 orgalutran/ (1284)
118 orgalutran.ti,ab. (68)
119 ("RS 26306" or RS26306).ti,ab. (6)

120 ("AY 24031" or AY24031).ti,ab. (0)
 121 factrel.ti,ab. (14)
 122 fertagyl.ti,ab. (20)
 123 lutrelef.ti,ab. (7)
 124 lutrepulse.ti,ab. (6)
 125 reifact.ti,ab. (10)
 126 fertiral.ti,ab. (0)
 127 (hoe471 or "hoe 471").ti,ab. (4)
 128 relisorm.ti,ab. (6)
 129 cystorelin.ti,ab. (26)
 130 dirigestran.ti,ab. (5)
 131 or/29-130 (80790)
 132 28 and 131 (988)
 133 limit 132 to english language (940)
 134 133 not (letter or editorial).pt. (924)
 135 134 not (conference abstract or conference paper or conference proceeding or "conference review").pt. (683)
 136 nonhuman/ not (human/ and nonhuman/) (4649157)
 137 135 not 136 (506)
 138 limit 137 to yr="2000 -Current" (420)
 139 elsevier.cr. (25912990)
 140 138 and 139 (372)
 141 remove duplicates from 140 (367)

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

Platform: Wiley

Version:

CDSR – Issue 7 of 12, July 2020

CENTRAL – Issue 7 of 12, July 2020

Search date: 23/7/2020

Number of results retrieved: CDSR – 1; CENTRAL - 8.

#1 [mh ^"Gender Dysphoria"] 3
 #2 [mh ^"gender identity"] 227
 #3 [mh ^"sexual and gender disorders"] 2
 #4 [mh ^"transsexualism"] 27
 #5 [mh ^"transgender persons"] 36
 #6 [mh ^"health services for transgender persons"] 0
 #7 [mh "sex reassignment procedures"] 4
 #8 (gender* NEAR/3 (dysphori* or affirm* or incongruen* or identi* or disorder* or confus* or minorit* or queer*)):ti,ab 308
 #9 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*):ti,ab 929
 #10 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*):ti,ab 3915
 #11 ((sex or gender*) NEAR/3 (reassign* or chang* or transform* or transition*)):ti,ab 493
 #12 (male-to-female or m2f or female-to-male or f2m):ti,ab 489

#13 {or #1-#12} 6142
 #14 [mh infant] or [mh ^"infant health"] or [mh ^"infant welfare"] 27769
 #15 (prematu* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*):ti,ab 69476
 #16 [mh child] or [mh "child behavior"] or [mh ^"child health"] or [mh ^"child welfare"] 42703
 #17 [mh ^minors] 8
 #18 (child* or minor or minors or boy* or girl* or kid or kids or young*):ti,ab 175826
 #19 [mh pediatrics]661
 #20 (pediatric* or paediatric* or peadiatric*):ti,ab 30663
 #21 [mh ^adolescent] or [mh ^"adolescent behavior"] or [mh ^"adolescent health"] 102154
 #22 [mh ^puberty] 295
 #23 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*):ti,ab 34139
 #24 [mh ^schools] 1914
 #25 [mh ^"Child Day Care Centers"] or [mh nurseries] or [mh ^"schools, nursery"] 277
 #26 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*):ti,ab 54723
 #27 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen" or "nineteen") NEAR/2 (year or years or age or ages or aged)):ti,ab 6710
 #28 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") NEAR/2 (year or years or age or ages or aged)):ti,ab 196881
 #29 {or #14-#28} 469351
 #30 #13 and #29 2146
 #31 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*):ti,ab 0
 #32 #30 or #31 2146
 #33 [mh ^"Gonadotropin-Releasing Hormone"] 1311
 #34 (pubert* NEAR/3 block*):ti,ab 1
 #35 ((gonadotrophin or gonadotropin) and releasing):ti,ab 2095
 #36 (GnRH NEAR/2 analog*):ti,ab 493
 #37 GnRH*:ti,ab 3764
 #38 "GnRH agonist*":ti,ab 1399
 #39 [mh ^"Triptorelin Pamoate"] 451
 #40 triptorelin:ti,ab 451
 #41 arvekap:ti,ab 4
 #42 ("AY 25650" or AY25650):ti,ab 0
 #43 ("BIM 21003" or BIM21003):ti,ab 0
 #44 ("BN 52014" or BN52014):ti,ab 0
 #45 ("CL 118532" or CL118532):ti,ab 0
 #46 Debio:ti,ab 301
 #47 diphereline:ti,ab 25
 #48 moapar:ti,ab 0
 #49 pamorelin:ti,ab 5
 #50 trelstar:ti,ab 3

#51	triptodur:ti,ab	0	
#52	("WY 42422" or WY42422):ti,ab	0	
#53	("WY 42462" or WY42462):ti,ab	0	
#54	gonapeptyl:ti,ab	11	
#55	decapeptyl:ti,ab	135	
#56	salvacyl:ti,ab	0	
#57	[mh ^Buserelin]	290	
#58	Buserelin:ti,ab	339	
#59	bigonist:ti,ab	0	
#60	("hoe 766" or hoe-766 or hoe766):ti,ab	11	
#61	profact:ti,ab	1	
#62	receptal:ti,ab	4	
#63	suprecur:ti,ab	0	
#64	suprefact:ti,ab	28	
#65	tiloryth:ti,ab	0	
#66	histrelin:ti,ab	5	
#67	"LHRH-hydrogel implant":ti,ab	0	
#68	("RL 0903" or RL0903):ti,ab	0	
#69	("SPD 424" or SPD424):ti,ab	0	
#70	goserelin:ti,ab	761	
#71	[mh ^goserelin]	568	
#72	("ici 118630" or ici118630):ti,ab	7	
#73	("ZD-9393" or ZD9393):ti,ab	1	
#74	zoladex:ti,ab	318	
#75	leuprorelin:ti,ab	248	
#76	carcinil:ti,ab	0	
#77	enanton*:ti,ab	21	
#78	ginecrin:ti,ab	1	
#79	leuplin:ti,ab	7	
#80	[mh ^Leuprolide]	686	
#81	leuprolide:ti,ab	696	
#82	lucrin:ti,ab	21	
#83	lupron:ti,ab	77	
#84	provren:ti,ab	0	
#85	procrin:ti,ab	2	
#86	("tap 144" or tap144):ti,ab	24	
#87	(a-43818 or a43818):ti,ab	0	
#88	Trenantone:ti,ab	3	
#89	staladex:ti,ab	0	
#90	prostap:ti,ab	9	
#91	[mh ^Nafarelin]	77	
#92	nafarelin:ti,ab	114	
#93	("76932-56-4" or "76932564"):ti,ab	0	
#94	("76932-60-0" or "76932600"):ti,ab	2	
#95	("86220-42-0" or "86220420"):ti,ab	0	
#96	("rs 94991 298" or rs94991298):ti,ab	0	
#97	synarel:ti,ab	10	
#98	deslorelin:ti,ab	16	

#99 gonadorelin:ti,ab 11
 #100 ("33515-09-2" or "33515092"):ti,ab 0
 #101 ("51952-41-1" or "51952411"):ti,ab 0
 #102 ("52699-48-6" or "52699486"):ti,ab 0
 #103 cetorelix:ti,ab 221
 #104 cetrotide:ti,ab 111
 #105 ("NS 75A" or NS75A):ti,ab 0
 #106 ("NS 75B" or NS75B):ti,ab 0
 #107 ("SB 075" or SB075):ti,ab 0
 #108 ("SB 75" or SB75):ti,ab 10
 #109 gonadoliberin:ti,ab 5
 #110 kryptocur:ti,ab 0
 #111 cetorelix:ti,ab 221
 #112 cetrotide:ti,ab 111
 #113 antagonist:ti,ab 12
 #114 ganirelix:ti,ab 142
 #115 ("ORG 37462" or ORG37462):ti,ab 4
 #116 orgalutran:ti,ab 45
 #117 ("RS 26306" or RS26306):ti,ab 0
 #118 ("AY 24031" or AY24031):ti,ab 0
 #119 factrel:ti,ab 1
 #120 fertagyl:ti,ab 0
 #121 lutrelef:ti,ab 0
 #122 lutrepulse:ti,ab 1
 #123 relect:ti,ab 1
 #124 fertiral:ti,ab 0
 #125 (hoe471 or "hoe 471"):ti,ab 3
 #126 relisorm:ti,ab 0
 #127 cystorelin:ti,ab 0
 #128 dirigestran:ti,ab 0
 #129 {or #33-#128} 6844
 #130 #32 and #129 27
 #131 #130 with Cochrane Library publication date Between Jan 2000 and Jul 2020, in Cochrane Reviews 1
 #132 #130 27
 #133 "conference":pt or (clinicaltrials or trialsearch):so 492465
 #134 #132 not #1339
 #135 #134 with Publication Year from 2000 to 2020, in Trials 8

Database: HTA

Platform: CRD

Version: HTA

Search date: 23/7/2020

Number of results retrieved: 26

Search strategy:

1 MeSH DESCRIPTOR Gender Dysphoria EXPLODE ALL TREES 0
 2 MeSH DESCRIPTOR Gender Identity EXPLODE ALL TREES 14

3 MeSH DESCRIPTOR Sexual and Gender Disorders EXPLODE ALL TREES 2

4 MeSH DESCRIPTOR Transsexualism EXPLODE ALL TREES 12

5 MeSH DESCRIPTOR Transgender Persons EXPLODE ALL TREES 3

6 MeSH DESCRIPTOR Health Services for Transgender Persons EXPLODE ALL TREES 0

7 MeSH DESCRIPTOR Sex Reassignment Procedures EXPLODE ALL TREES 1

8 ((gender* adj3 (dysphori* or affirm* or incongruen* or identi* or disorder* or confus* or minorit* or queer*))) 28

9 ((transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*)) 76

10 ((trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*)) 83

11 (((sex or gender*) adj3 (reassign* or chang* or transform* or transition*))) 24

12 (male-to-female or m2f or female-to-male or f2m) 86

13 ((transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*)) 0

14 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 262

15 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13) IN HTA 30

*26 results are from 200 onwards. Downloaded as a set to sift for drug terms rather than continuing with search strategy.

Database: APA PsycInfo

Search date: July 2020 (Week 2)

Search Strategy:

1 Gender Dysphoria/ (936)

2 Gender Identity/ (8648)

3 Transsexualism/ (2825)

4 Transgender/ (5257)

5 exp Gender Reassignment/ (568)

6 (gender* adj3 (dysphori* or affirm* or incongruen* or identi* or disorder* or confus* or minorit* or queer*)).tw. (15471)

7 (transgend* or transex* or transsex* or transfem* or transwom* or transma* or transmen* or transperson* or transpeopl*).tw. (13028)

8 (trans or crossgender* or cross-gender* or crossex* or cross-sex* or genderqueer*).tw. (7679)

9 ((sex or gender*) adj3 (reassign* or chang* or transform* or transition*)).tw. (5796)

10 (male-to-female or m2f or female-to-male or f2m).tw. (63688)

11 or/1-10 (99560)

12 exp Infant Development/ (21841)

13 (prematu* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (150219)

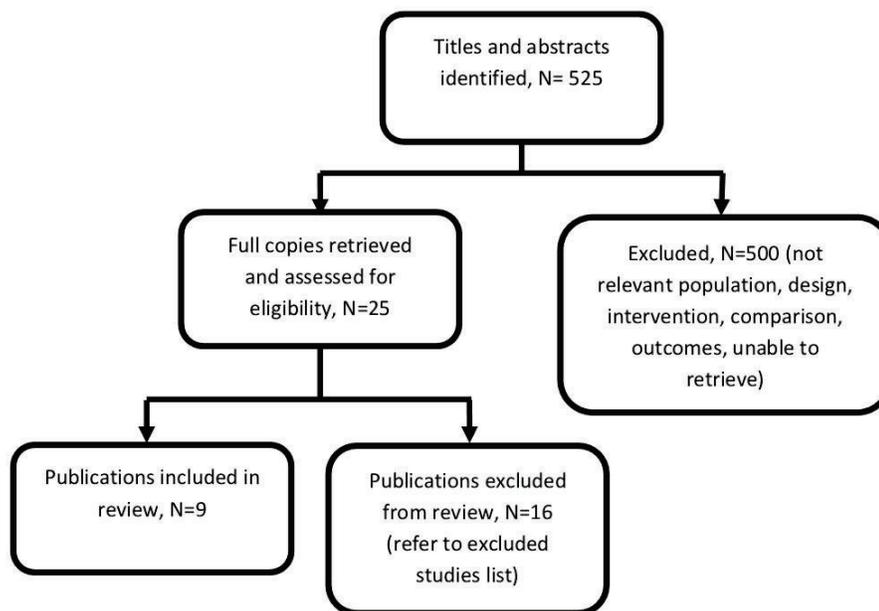
- 14 Child Characteristics/ or exp Child Behavior/ or Child Psychology/ or exp Child Welfare/
or Child Psychiatry/ (23423)
- 15 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (984230)
- 16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (78962)
- 17 Adolescent Psychiatry/ or Adolescent Behavior/ or Adolescent Development/ or
Adolescent Psychology/ or Adolescent Characteristics/ or Adolescent Health/ (62142)
- 18 Puberty/ (2753)
- 19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert*
or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn.
(347604)
- 20 Schools/ or exp elementary school students/ or high school students/ or junior high
school students/ or middle school students/ (113053)
- 21 Child Day Care/ or Nursery Schools/ (2836)
- 22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or
pupil* or student*).ti,ab,jn. (772814)
- 23 (("eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or
"sixteen" or "seventeen" or "eighteen" or "nineteen") adj2 (year or years or age or ages or
aged)).ti,ab. (21475)
- 24 (("8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19")
adj2 (year or years or age or ages or aged)).ti,ab. (285697)
- 25 or/12-24 (1772959)
- 26 11 and 25 (49612)
- 27 (transchild* or transyouth* or transteen* or transadoles* or transgirl* or transboy*).tw.
(14)
- 28 26 or 27 (49613)
- 29 exp Gonadotropic Hormones/ (4226)
- 30 (pubert* adj3 block*).ti,ab. (29)
- 31 ((gonadotrophin or gonadotropin) and releasing).ti,ab. (1060)
- 32 (GnRH adj2 analog*).ti,ab. (49)
- 33 GnRH*.ti,ab. (998)
- 34 "GnRH agonist".ti,ab. (72)
- 35 triptorelin.ti,ab. (25)
- 36 arvekap.ti,ab. (0)
- 37 ("AY 25650" or AY25650).ti,ab. (0)
- 38 ("BIM 21003" or BIM21003).ti,ab. (0)
- 39 ("BN 52014" or BN52014).ti,ab. (0)
- 40 ("CL 118532" or CL118532).ti,ab. (0)
- 41 Debio.ti,ab. (7)
- 42 diphereline.ti,ab. (0)
- 43 moapar.ti,ab. (0)
- 44 pamorelin.ti,ab. (0)
- 45 trelstar.ti,ab. (0)
- 46 triptodur.ti,ab. (0)
- 47 ("WY 42422" or WY42422).ti,ab. (0)
- 48 ("WY 42462" or WY42462).ti,ab. (0)
- 49 gonapeptyl.ti,ab. (0)
- 50 decapeptyl.ti,ab. (3)
- 51 salvacyl.ti,ab. (1)

52 buserelin.ti,ab. (6)
53 bigonist.ti,ab. (0)
54 ("hoe 766" or hoe-766 or hoe766).ti,ab. (0)
55 profact.ti,ab. (0)
56 receptal.ti,ab. (0)
57 suprecur.ti,ab. (0)
58 suprefact.ti,ab. (0)
59 tiloryth.ti,ab. (0)
60 histrelin.ti,ab. (1)
61 "LHRH-hydrogel implant".ti,ab. (0)
62 ("RL 0903" or RL0903).ti,ab. (0)
63 ("SPD 424" or SPD424).ti,ab. (0)
64 goserelin.ti,ab. (30)
65 ("ici 118630" or ici118630).ti,ab. (0)
66 ("ZD-9393" or ZD9393).ti,ab. (0)
67 zoladex.ti,ab. (3)
68 leuprorelin.ti,ab. (12)
69 carcinil.ti,ab. (0)
70 enanton*.ti,ab. (1)
71 ginecrin.ti,ab. (0)
72 leuplin.ti,ab. (0)
73 leuprolide.ti,ab. (79)
74 lucrin.ti,ab. (1)
75 lupron.ti,ab. (18)
76 provren.ti,ab. (0)
77 procrin.ti,ab. (0)
78 ("tap 144" or tap144).ti,ab. (1)
79 (a-43818 or a43818).ti,ab. (0)
80 Trenantone.ti,ab. (0)
81 staladex.ti,ab. (0)
82 prostap.ti,ab. (0)
83 nafarelin.ti,ab. (1)
84 ("76932-56-4" or "76932564").ti,ab. (0)
85 ("76932-60-0" or "76932600").ti,ab. (0)
86 ("86220-42-0" or "86220420").ti,ab. (0)
87 ("rs 94991 298" or rs94991298).ti,ab. (0)
88 synarel.ti,ab. (0)
89 deslorelin.ti,ab. (8)
90 gonadorelin.ti,ab. (3)
91 ("33515-09-2" or "33515092").ti,ab. (0)
92 ("51952-41-1" or "51952411").ti,ab. (0)
93 ("52699-48-6" or "52699486").ti,ab. (0)
94 cetorelix.ti,ab. (9)
95 cetrotide.ti,ab. (0)
96 ("NS 75A" or NS75A).ti,ab. (0)
97 ("NS 75B" or NS75B).ti,ab. (0)
98 ("SB 075" or SB075).ti,ab. (0)
99 ("SB 75" or SB75).ti,ab. (1)

100 gonadoliberin.ti,ab. (1)
101 kryptocur.ti,ab. (0)
102 cetorelix.ti,ab. (9)
103 cetrotide.ti,ab. (0)
104 antagon.ti,ab. (0)
105 ganirelix.ti,ab. (0)
106 ("ORG 37462" or ORG37462).ti,ab. (0)
107 orgalutran.ti,ab. (0)
108 ("RS 26306" or RS26306).ti,ab. (0)
109 ("AY 24031" or AY24031).ti,ab. (0)
110 factrel.ti,ab. (0)
111 fertagyl.ti,ab. (0)
112 lutrelef.ti,ab. (0)
113 lutrepulse.ti,ab. (0)
114 relect.ti,ab. (0)
115 fertiral.ti,ab. (0)
116 (hoe471 or "hoe 471").ti,ab. (0)
117 relisorm.ti,ab. (0)
118 cystorelin.ti,ab. (0)
119 dirigestran.ti,ab. (0)
120 or/29-119 (4869)
121 28 and 120 (130)
122 limit 121 to english language (120)
123 limit 122 to yr="2000 -Current" (93)

Appendix C Evidence selection

The literature searches identified 525 references. These were screened using their titles and abstracts and 25 references were obtained and assessed for relevance. Of these, 9 references are included in the evidence review. The remaining 16 references were excluded and are listed in [appendix D](#).

Figure 1 – Study selection flow diagram

References submitted with Preliminary Policy Proposal

There is no preliminary policy proposal for this policy.

Appendix D Excluded studies table

Study reference	Reason for exclusion
Achille, C., Taggart, T., Eaton, N.R. et al. (2020) Longitudinal impact of gender-affirming endocrine intervention on the mental health and well-being of transgender youths: Preliminary results. <i>International Journal of Pediatric Endocrinology</i> 2020(1): 8	Intervention – data for GnRH analogues not reported separately from other interventions
Bechard, Melanie, Vanderlaan, Doug P, Wood, Hayley et al. (2017) Psychosocial and Psychological Vulnerability in Adolescents with Gender Dysphoria: A "Proof of Principle" Study. <i>Journal of sex & marital therapy</i> 43(7): 678-688	Population – no GnRH analogues at time of study
Chew, Denise, Anderson, Jemma, Williams, Katrina et al. (2018) Hormonal Treatment in Young People With Gender Dysphoria: A Systematic Review. <i>Pediatrics</i> 141(4)	All primary studies included apart from 1 conference abstract
de Vries, Annelou L C, McGuire, Jenifer K et al. (2014) Young adult psychological outcome after puberty suppression and gender reassignment. <i>Pediatrics</i> 134(4): 696-704	Population – relevant population included in de Vries et al. 2011
Ghelani, Rahul, Lim, Cheryl, Brain, Caroline et al. (2020) Sudden sex hormone withdrawal and the effects on body composition in late pubertal adolescents with gender dysphoria. <i>Journal of pediatric endocrinology & metabolism: JPEM</i> 33(1): 107-112	Outcomes – not in the PICO

Study reference	Reason for exclusion
Giovanardi, G, Morales, P, Mirabella, M et al. (2019) Transition memories: experiences of trans adult women with hormone therapy and their beliefs on the usage of hormone blockers to suppress puberty. Journal of endocrinological investigation 42(10): 1231-1240	Population – adults only
Hewitt, Jacqueline K, Paul, Campbell, Kasiannan, Porpavai et al. (2012) Hormone treatment of gender identity disorder in a cohort of children and adolescents. The Medical journal of Australia 196(9): 578-81	Outcomes – no data reported for relevant outcomes
Jensen, R.K., Jensen, J.K., Simons, L.K. et al. (2019) Effect of Concurrent Gonadotropin-Releasing Hormone Agonist Treatment on Dose and Side Effects of Gender-Affirming Hormone Therapy in Adolescent Transgender Patients. Transgender Health 4(1): 300-303	Outcomes – not in the PICO
Klaver, Maartje, de Mutsert, Renee, Wiepjes, Chantal M et al. (2018) Early Hormonal Treatment Affects Body Composition and Body Shape in Young Transgender Adolescents. The journal of sexual medicine 15(2): 251-260	Outcomes – not in the PICO
Klaver, Maartje, de Mutsert, Renee van der Loos, Maria A T C et al. (2020) Hormonal Treatment and Cardiovascular Risk Profile in Transgender Adolescents. Pediatrics 145(3)	Outcomes – not in the PICO
Lopez, Carla Marisa, Solomon, Daniel, Boulware, Susan D et al. (2018) Trends in the use of puberty blockers among transgender children in the United States. Journal of pediatric endocrinology & metabolism : JPEM 31(6): 665-670	Outcomes – not in the PICO
Schagen, Sebastian E E, Lustenhouwer, Paul, Cohen-Kettenis, Peggy T et al. (2018) Changes in Adrenal Androgens During Puberty Suppression and Gender-Affirming Hormone Treatment in Adolescents With Gender Dysphoria. The journal of sexual medicine 15(9): 1357-1363	Outcomes – not in the PICO
Swendiman, Robert A, Vogiatzi, Maria G, Alter, Craig A et al. (2019) Histrelin implantation in the pediatric population: A 10-year institutional experience. Journal of pediatric surgery 54(7): 1457-1461	Population – less than 10% of participants had gender dysphoria; data not reported separately
Turban, Jack L, King, Dana, Carswell, Jeremi M et al. (2020) Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation. Pediatrics 145(2)	Intervention – data for GnRH analogues not reported separately from other interventions
Vrouenraets, Lieke Josephina Jeanne Johanna, Fredriks, A Miranda, Hannema, Sabine E et al. (2016) Perceptions of Sex, Gender, and Puberty Suppression: A Qualitative Analysis of Transgender Youth. Archives of sexual behavior 45(7): 1697-703	Outcomes – not in the PICO
Zucker, Kenneth J, Bradley, Susan J, Owen-Anderson, Allison et al. (2010) Puberty-blocking hormonal therapy for adolescents with gender identity disorder: A descriptive clinical study. Journal of Gay & Lesbian Mental Health 15(1): 58-82	Intervention – data for GnRH analogues not reported separately from other interventions

Appendix E Evidence tables

Study details	Population	Interventions	Study outcomes	Appraisal and Funding
<p>Brik T, Vrouenraets L, de Vries M, et al. (2020) Trajectories of adolescents treated with gonadotropin-releasing hormone analogues for gender dysphoria. Archives of Sexual Behaviour https://doi.org/10.1007/s10508-020-01660-8</p> <p>Netherlands</p> <p>Retrospective observational single-centre study</p> <p>To document trajectories after the initiation of GnRH analogue and explore reasons for extended use and discontinuation of GnRH analogues.</p> <p>Includes participants seen between November 2010 and January 1, 2018.</p>	<p>Inclusion criteria were adolescents with gender dysphoria, according to the DSM-5 criteria, seen at the single centre and treated with GnRH analogues between November 2010 and January 1, 2018.</p> <p>The study excluded adolescents without a diagnosis of gender dysphoria, those who had coexisting problems that interfered with the diagnostic process and/or might interfere with successful treatment (not further defined), those adolescents not wanting hormones, those with ongoing diagnostic evaluation and those who did not attend appointments.</p> <p>The sample consisted of 143 adolescents meeting the inclusion/exclusion criteria, 38 transfemales, 105 transmales, with median ages of 15.0 years (range 11.1 to 18.6 years) and 16.1 years (range 10.1 to 17.9</p>	<p>The study only reports that GnRH analogues were given, no specific drug, dose, route, or frequency of administration are reported.</p> <p>No comparator cohort was used in the study.</p> <p>Follow-up was at (up to) 9 years (last follow-up July 2019).</p>	<p>Critical outcomes No critical outcomes assessed.</p> <p>Important outcomes Psychosocial impact Not assessed.</p> <p>Engagement with health care services Not formally assessed but the study reported that out of 214 age and developmentally appropriate adolescents for potential inclusion in the study, 9 were excluded as they stopped attending appointments (4.2%).</p> <p>Stopping treatment Of the 143 adolescents, 9 (6.2%, 1 transfemale and 8 transmales) stopped taking GnRH analogues after a median duration of 0.8 years (range 0.1 to 3.0). Four adolescents (2.8%) discontinued GnRH analogues although they wanted to continue endocrine treatments for gender dysphoria:</p> <ul style="list-style-type: none"> 1 transmale stopped due to increase in mood problems, suicidal thoughts and confusion attributed to GnRH analogues (later had gender-affirming hormones at an adult gender clinic)¹ 1 transmale experienced hot flushes, increased migraines, had a fear of injections, stress at school and unrelated medical issues, and temporarily discontinued treatment (after 4 months)² 	<p>This study was appraised using the Newcastle-Ottawa tool for cohort studies.</p> <p>Domain 1: Selection</p> <ol style="list-style-type: none"> 1. somewhat representative 2. no-non exposed cohort 3. secure record 4. yes <p>Domain 2: Comparability</p> <ol style="list-style-type: none"> 1. no comparator <p>Domain 3: Outcome</p> <ol style="list-style-type: none"> 1. record linkage 2. yes 3. complete follow-up <p>Overall quality is assessed as poor.</p> <p>Other comments: Physical and psychological comorbidity was poorly reported, concomitant use of other medicines was not reported.</p> <p>Source of funding: not reported.</p>

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	<p>years), respectively at commencement of GnRH analogues.</p> <p>Of the 143 adolescents in the study, 125 (87%, 36 transfemales and 89 transmales) subsequently started treatment with gender-affirming hormones after median 1.0 (range 0.5 to 3.8) years and 0.8 (0.3 to 3.7) years, respectively. Median age at the start of gender-affirming hormones was 16.2 years (range 14.5 to 18.6 years) in transfemales and 17.1 years (range 14.9 to 18.8 years) in transmales.</p> <p>Five adolescents who used GnRH analogues had not started gender-affirming hormones at the time of data collection as they were not yet eligible for this treatment due to age. At the time of data collection, they had used GnRH analogues for a median duration of 2.1 years (range 1.6 to 2.8). Tanner stage was not reported.</p> <p>Six adolescents had been referred to a gender clinic elsewhere for further</p>		<ul style="list-style-type: none"> 1 transmale experienced mood swings 4 months after commencing GnRH analogues. After 2.2 years he developed unexplained severe nausea and rapid weight loss and due to his general condition discontinued GnRH analogues after 2.4 years³ 1 transmale stopped GnRH analogues as his parents were unable to regularly collect medication from the pharmacy and take him to appointments for the injections⁴ <p>Five adolescents (3.5%) stopped treatment as they no longer wished to continue with gender-affirming treatment.</p> <ul style="list-style-type: none"> 1 adolescent had been very distressed about breast development at the start of GnRH analogues and later thought that she might want to live as a woman without breasts. She did not want to live as a boy and discontinued GnRH analogues, although dreaded breast development and menstruation. 1 adolescent experienced concurrent psychosocial problems interfering with the exploration of gender identity and did not currently want treatment.⁵ 1 adolescent felt more in between male and female and therefore did not want to continue with GnRH analogues.⁶ 1 adolescent made a social transition while using GnRH analogues and shortly after decided to discontinue treatment.⁷ 	

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	treatment, including 1 who had prolonged use.		<ul style="list-style-type: none"> 1 adolescent discontinued after using GnRH analogues as the treatment allowed them to feel who they were.⁸ 	

¹ The adolescent later indicated "I was already fully matured when I started GnRH analogues, menstruations were already suppressed by contraceptives. For me, it had no added value" (transmale, age 19 years).

² The adolescent restarted endocrine treatment (testosterone) 5 months later.

³ The adolescent recovered over the next 2 years and subsequently started lynestrol and testosterone treatment.

⁴ The adolescent subsequently started lynestrol to suppress menses, he was not yet eligible for testosterone treatment.

⁵ The adolescent later reflected that "The decision to stop GnRH analogues to my mind was made by the gender team, because they did not think gender dysphoria was the right diagnosis. I do still feel like a man, but for me it is okay to be just me instead of a he or a she, so for now I do not want any further treatment" (adolescent assigned female sex at birth, age 16 years).

⁶ The adolescent stated "At the moment, I feel more like 'I am' instead of 'I am a woman' or 'I am a man'" (adolescent assigned female sex at birth, age 16 years).

⁷ The adolescent stated that "he had fallen in love with a girl and had never had such feelings, which made him question his gender identity. At subsequent visits, he indicated that he was happy living as a man.

⁸ The adolescent stated "After using GnRH analogues for the first time, I could feel who I was without the female hormones, this gave me peace of mind to think about my future. It was an inner feeling that said I am a woman" (adolescent assigned female sex at birth, age 18 years).

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<p>Costa R, Dunsford M, Skagerberg E, et al. (2015) <u>Psychological support, puberty suppression, and psychosocial functioning in adolescents with gender dysphoria</u>. Journal of Sexual Medicine 12(11):2206-14.</p> <p>United Kingdom</p> <p>Prospective longitudinal observational single centre cohort study</p> <p>Includes participants referred to the service between 2010 and 2014.</p>	<p>Adolescents with gender dysphoria who completed a 6-month diagnostic process using DSM-IV-TR criteria for gender dysphoria (comprising the gender dysphoria assessment and psychological interventions) either immediately eligible for treatment with GnRH analogues or delayed eligible for treatment with GnRH analogues (received psychological support without any physical intervention).</p> <p>No exclusion criteria were reported.</p> <p>The sample consisted of 201 adolescents (sex assigned at birth male to female ratio 1:1.6) mean (±SD) age 15.52±1.41 years) from a sampling frame of</p>	<p>Intervention 101 individuals were assessed as being immediately eligible for use of GnRH analogues (no specific treatment, dose or route, or frequency of administration reported but all received psychological support).</p> <p>Comparison The analyses were between the immediately eligible and delayed eligible (n=100) adolescents,</p>	<p>Critical outcomes Impact on gender dysphoria The Utrecht gender dysphoria scale (UGDS) was used to assess adolescents' gender dysphoria related discomfort. The Cronbach's alpha (α) for the study was reported as 0.76 to 0.88, suggesting good internal consistency. UGDS was only reported once, for 160 adolescents (50 sex assigned at birth males and 110 sex assigned at birth females). The assessment time point is not reported (baseline or follow-up) and the comparison for gender related discomfort was between sex assigned at birth males and sex assigned at birth females. Sex assigned at birth males had a mean (±SD) UGDS score of 51.6 [±9.7] versus sex assigned at birth females score of 56.1 [±4.3], t-test 4.07; p<0.001.</p>	<p>This study was appraised using the Newcastle-Ottawa tool for cohort studies.</p> <p>Domain 1: Selection</p> <ol style="list-style-type: none"> 1. somewhat representative 2. drawn from the same community as the exposed cohort. 3. secure record 4. no <p>Domain 2: Comparability</p> <ol style="list-style-type: none"> 1. partial comparator <p>Domain 3: Outcome</p> <ol style="list-style-type: none"> 1. independent assessment (unclear if blinded) 2. yes 3. incomplete follow-up <p>Overall quality is assessed as poor.</p>

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	<p>436 consecutive adolescents referred to the service between 2010 and 2014. The mean (\pmSD) age ($n=201$) at the start of GnRH analogues was 16.48 [\pm1.26], range 13 to 17 years. The interval from the start of the diagnostic procedure to the start of puberty suppression took approximately 1.5 years [\pm0.63] from baseline.</p> <p>None of the delayed eligible individuals received puberty suppression at the time of this study. Tanner stage was not reported.</p>	<p>Baseline assessment (following diagnostic procedure) was followed by follow-up at 6 months from baseline (T1), 12 months from baseline (T2) and 18 months from baseline (T3).</p>	<p>Impact on mental health Not assessed.</p> <p>Impact on quality of life Not assessed.</p> <p>Important outcomes Psychosocial impact The Children's Global Assessment Scale (CGAS) was used to assess adolescents' psychosocial functioning. The CGAS was administered by psychologists, psychotherapists, and psychiatrists (intra-class correlation assessment was $0.76 \leq$ Cronbach's $\alpha \leq 0.94$).</p> <p>At baseline, CGAS scores were not associated with any demographic variable, in both sex assigned at birth males and sex assigned at birth females (all $p > 0.1$).</p> <p>In comparison with sex assigned at birth females, sex assigned at birth males had statistically significantly lower mean (\pmSD) baseline CGAS scores (55.4 [\pm12.7] versus 59.2 [\pm11.8]; t-test 2.15; $p=0.03$).</p> <p>There was no statistically significant difference in mean (\pmSD) CGAS scores at baseline (T0) between immediately eligible adolescents and delayed eligible adolescents ($n=201$, 58.72 [\pm11.38] versus 56.63 [\pm13.14]; t-test 1.21; $p=0.23$).</p> <p>Immediately eligible compared with delayed eligible participants At follow-up, there was no statistically significant difference in mean (\pmSD) CGAS scores at any follow-up time point (T1, T2 or T3) between immediately</p>	<p>Other comments: Physical and psychological comorbidity was poorly reported, concomitant use of other medicines was not reported. Large unexplained loss to follow-up (64.7%) at T3.</p> <p>Source of funding: not reported.</p>

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			<p>eligible adolescents and delayed eligible adolescents:</p> <ul style="list-style-type: none"> • T1, n=201, 60.89 [±12.17] versus 60.29 [±12.81]; t-test 0.34; p=0.73 • T2, n=121, 64.70 [±13.34] versus 62.97 [±14.10]; t-test 0.69; p=0.49 • T3, n=71, 67.40 [±13.93] versus 62.53 [±13.54]; t-test 1.49; p=0.14. <p>All participants There was a statistically significant increase in mean (±SD) CGAS scores at any follow-up time point (T1, T2 or T3) compared with baseline (T0) for the all adolescents group:</p> <ul style="list-style-type: none"> • T0 (n=201) versus T1 (n=201), 57.73 [±12.27] versus 60.68 [±12.47]; t-test 4.87; p<0.001 • T0 (n=201) versus T2 (n=121), 57.73 [±12.27] versus 63.31 [±14.41]; t-test 3.70; p<0.001 • T0 (n=201) versus T3 (n=71), 57.73 [±12.27] versus 64.93 [±13.85]; t-test 4.11; p<0.001 <p>There was a statistically significant increase in mean (±SD) CGAS scores when comparing the follow-up period T1 to T3 but not for the periods T1 to T2 and T2 to T3, for all adolescents:</p> <ul style="list-style-type: none"> • T1 (n=201) versus T2 (n=121), 60.68 [±12.47] versus 63.31 [±14.41]; t-test 1.73; p<0.08 • T1 (n=201) versus T3 (n=71), 60.68 [±12.47] versus 64.93 [±13.85], t-test 2.40; p<0.02 • T2 (n=121) versus T3 (n=71), 63.31 [±14.41] versus 64.93 [±13.85], t-test 0.76; p=0.45 <p>There were no statistically significant differences in CGAS scores between sex assigned at birth males and sex</p>	

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			<p>assigned at birth females with gender dysphoria in all the follow-up evaluations (all $p > 0.1$). Delayed eligible and immediately eligible adolescents with gender dysphoria were not statistically significantly different for demographic variables (all $p > 0.1$).</p> <p>Immediately eligible participants</p> <p>There was a statistically significant increase in mean (\pmSD) CGAS scores at follow-up times T2 and T3 compared with baseline (T0) but not for T0 versus T1, for the immediately eligible adolescents:</p> <ul style="list-style-type: none"> • T0 (n=101) versus T1 (n=101), 58.72 [\pm11.38] versus 60.89 [\pm12.17]; <i>t</i>-test 1.31; $p=0.19$ • T0 (n=101) versus T2 (n=60), 58.72 [\pm11.38] versus 64.70 [\pm13.34]; <i>t</i>-test 3.02; $p=0.003$ • T0 (n=101) versus T3 (n=35), 58.72 [\pm11.38] versus 67.40 [\pm13.93]; <i>t</i>-test 3.66; $p < 0.001$ <p>There was a statistically significant increase in mean (\pmSD) CGAS scores when comparing the follow-up period T1 to T3 with each other but not for the periods T1 to T2 and T2 to T3, for the immediately eligible adolescents:</p> <ul style="list-style-type: none"> • T1 (n=101) versus T2 (n=60), 60.89 [\pm12.17] versus 64.70 [\pm13.34]; <i>t</i>-test 1.85; $p=0.07$ • T1 (n=101) versus T3 (n=35), 60.89 [\pm12.17] versus 67.40 [\pm13.93], <i>t</i>-test 2.63; $p < 0.001$ • T2 (n=60) versus T3 (n=35), 64.70 [\pm13.34] versus 67.40 [\pm13.93], <i>t</i>-test 0.94; $p=0.35$ <p>The immediately eligible adolescents had a CGAS score which was not</p>	

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<p>de Vries A, Steensma T, Doreleijers T, et al. (2011) Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. The Journal of Sexual Medicine 8 (8):2276-83.</p> <p>Netherlands</p> <p>Prospective longitudinal observational single centre before and after study.</p>	<p>The sample size was 70 adolescents receiving GnRH analogues (mean age [\pmSD] at assessment 13.6\pm1.8 years) from a sampling frame of 196 consecutive adolescents referred to the service between 2000 and 2008. Inclusion criteria were if they subsequently started gender-affirming hormones between 2003 and 2009 (mean [\pmSD] age at start of GnRH analogues was 14.75 [\pm1.92] years)¹. No specific exclusion criteria were described.</p> <p>No diagnostic criteria or concomitant treatments were reported. Tanner stage of the included adolescents was not reported.</p>	<p>Intervention 70 adolescents were assessed at baseline (T0) before the start of GnRH analogues (no specific treatment, dose or route of administration reported).</p> <p>Comparison The same 70 adolescents were assessed again at follow-up (T1), shortly before starting gender-affirming hormones. Not all adolescents completed all assessments for all items².</p>	<p>statistically significantly different compared to the sample of children/adolescents without observed psychological /psychiatric symptoms after 12 months of puberty suppression (T3, $t=0.01$, $p=0.99$).</p>	
<p>Study details</p> <p>de Vries A, Steensma T, Doreleijers T, et al. (2011) Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. The Journal of Sexual Medicine 8 (8):2276-83.</p> <p>Netherlands</p> <p>Prospective longitudinal observational single centre before and after study.</p>	<p>The sample size was 70 adolescents receiving GnRH analogues (mean age [\pmSD] at assessment 13.6\pm1.8 years) from a sampling frame of 196 consecutive adolescents referred to the service between 2000 and 2008. Inclusion criteria were if they subsequently started gender-affirming hormones between 2003 and 2009 (mean [\pmSD] age at start of GnRH analogues was 14.75 [\pm1.92] years)¹. No specific exclusion criteria were described.</p> <p>No diagnostic criteria or concomitant treatments were reported. Tanner stage of the included adolescents was not reported.</p>	<p>Intervention 70 adolescents were assessed at baseline (T0) before the start of GnRH analogues (no specific treatment, dose or route of administration reported).</p> <p>Comparison The same 70 adolescents were assessed again at follow-up (T1), shortly before starting gender-affirming hormones. Not all adolescents completed all assessments for all items².</p>	<p>Study outcomes</p> <p>Critical outcomes Impact on gender dysphoria Impact on gender dysphoria was assessed using the Utrecht Gender Dysphoria Scale (UGDS).</p> <ul style="list-style-type: none"> There was no statistically significant difference in UGDS scores between T0 and T1 (n=41). There was a statistically significant difference between sex assigned at birth males and sex assigned at birth females, with sex assigned at birth females reporting more gender dysphoria, F (df, errdf), P: 15.98 (1,39), $p<0.001$. <p>Impact on mental health Depressive symptoms were assessed using the Beck Depression Inventory (BDI-II).</p> <ul style="list-style-type: none"> There was a statistically significant reduction in BDI score between T0 and T1, $n=41$, 8.31 [\pm7.12] versus 4.95 [\pm6.72], F (df, errdf), P: 9.28 (1,39), $p=0.004$. There was no statistically significant difference between sex assigned at birth males and sex assigned at birth females, F (df, errdf), P: 3.85 (1,39), $p=0.057$. 	<p>This study was appraised using the Newcastle-Ottawa tool for cohort studies.</p> <p>Domain 1: Selection</p> <ol style="list-style-type: none"> 1. somewhat representative of children and adolescents who have gender dysphoria 2. no non-exposed cohort 3. no description 4. no <p>Domain 2: Comparability</p> <ol style="list-style-type: none"> 1. study controls for age, age at start of treatment, IQ, and parental factors <p>Domain 3: Outcome</p> <ol style="list-style-type: none"> 1. no description 2. no/unclear 3. complete <p>Overall quality is assessed as poor.</p> <p>Other comments: Physical and psychological comorbidity was not reported, concomitant use of other medicines was not reported.</p> <p>Source of funding: This study was supported by a personal</p>

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			<p>Anger and anxiety were assessed using Trait Anger and Anxiety (TPI and STAI, respectively) Scales of the State-Trait Personality Inventory.</p> <ul style="list-style-type: none"> There was no statistically significant difference in anger (TPI) scale scores between T0 and T1 (n=41). There was a statistically significant difference between sex assigned at birth males and sex assigned at birth females, with sex assigned at birth females reporting increased anger compared with sex assigned at birth males, $F(df, errdf), P: 5.70(1,39), p=0.022$. Similarly, there was no statistically significant difference in anxiety (STAI) scale scores between T0 and T1 (n=41). There was a statistically significant difference between sex assigned at birth males and sex assigned at birth females, with sex assigned at birth females reporting increased anxiety compared with sex assigned at birth males, $F(df, errdf), P: 16.07(1,39), p<0.001$. <p>Impact on quality of life Not assessed.</p> <p>Important outcomes Impact on body image Impact on body image was assessed using the Body Image Scale to measure body satisfaction (BIS). There was no statistically significant difference between T0 and T1 for any of the 3 BIS scores (primary sex characteristics, secondary sex characteristics or neutral characteristics,</p>	<p>grant awarded to the first author by the Netherlands Organization for Health Research and Development.</p>

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			<p>n=57). There were statistically significant differences between sex assigned at birth males and sex assigned at birth females, with sex assigned at birth females reporting more dissatisfaction, for:</p> <ul style="list-style-type: none"> • primary sexual characteristics, F (df, $errdf$), P: 4.11 (1,55), $p=0.047$. • secondary sexual characteristics, F (df, $errdf$), P: 11.57 (1,55), $p=0.001$. <p>But no statistically significant difference between sex assigned at birth males and sex assigned at birth females was found for neutral characteristics. However, there was a significant interaction effect between sex assigned at birth sex and the changes of gender dysphoria between T0 and T1; sex assigned at birth females became more dissatisfied with their secondary sex characteristics compared with sex assigned at birth males, F (df, $errdf$), P: 14.59 (1,55), $p<0.001$) and neutral characteristics, F (df, $errdf$), P: 15.26 (1,55), $p<0.001$).</p> <p>Psychosocial impact</p> <p>Psychosocial impact was assessed using both the Child Behaviour Checklist (CBCL) and the Youth Self-Report (YSR) to parents and adolescents, respectively. The Children's Global Assessment Scale was also reported.</p> <p>There was a statistically significant decrease in mean (\pmSD) total, internalising, and externalising³ parental CBCL scores between T0 and T1⁴ for all adolescents (n=54):</p> <ul style="list-style-type: none"> • Total score (T0 – T1) 60.70 [\pm12.76] versus 54.46 [\pm11.23], F (df, $errdf$), P: 26.17 (1,52), $p<0.001$. 	

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			<ul style="list-style-type: none"> • Internalising score (T0 – T1) 61.00 [±12.21] versus 54.56 [±10.22], <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 22.93 (1,52), <i>p</i><0.001. • Externalising score (T0 – T1) 58.04 [±12.99] versus 53.81 [±11.86], <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 12.04 (1,52), <i>p</i>=0.001. <p>There was no statistically significant difference between sex assigned at birth males and sex assigned at birth females for total and internalising CBCL score but there was a significant difference for the externalising score:</p> <ul style="list-style-type: none"> • Externalising score, <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 6.29 (1,52), <i>p</i>=0.015. <p>There was a statistically significant decrease in mean (±SD) total, internalising, and externalising³ YSR scores between T0 and T1 for all adolescents (n=54):</p> <ul style="list-style-type: none"> • Total score (T0 – T1) 55.46 [±11.56] versus 50.00 [±10.56], <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 16.24 (1,52), <i>p</i><0.001. • Internalising score (T0 – T1) 56.04 [±12.49] versus 49.78 [±11.63], <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 15.05 (1,52), <i>p</i><0.001. • Externalising score (T0 – T1) 53.30 [±11.87] versus 49.98 [±9.35], <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 7.26 (1,52), <i>p</i>=0.009. <p>There was no statistically significant difference between sex assigned at birth males and sex assigned at birth females for total and internalising YSR score but there was a significant difference for the externalising score:</p> <ul style="list-style-type: none"> • Externalising score, <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 9.14 (1,52), <i>p</i>=0.004. <p>There was a statistically significant increase in CGAS mean (±SD) score between T0 and T1 (n=41), 70.24 [±10.12] versus 73.90 [±9.63], <i>F</i> (<i>df</i>, <i>errdf</i>), <i>P</i>: 8.76</p>	