

Supplementary Table 2 - Study characteristics

Study ID	Country	Relevant study aim*	Setting	Population*	Primary sample size (age, gender/)	Hormones	Reports data on puberty suppression	Intervention	Comparator	Comparator category	Other control group (size (age, gender/))	Study design	Study follow-up	Data collection period
<b>Cohort</b>														
Achille 2020	US	To examine the associations of endocrine intervention with depression and quality of life scores over time in transgender youths	Paediatric endocrine department for gender dysphoria	Children and adolescents age 9-25 years referred to the department for gender dysphoria	50 (mean age 16.2 (SD 2.2); 33 brf, 17 brm)	Yes	Yes	Puberty suppressants and/or cross-sex hormones	Participants who had received nothing at all or only puberty suppressants	Non-exposed individuals from primary sample	N/A	Prospective cohort study	Baseline and two follow-ups at ~6-monthly intervals (time-points not linked to treatment initiation)	Questionnaires completed between Dec 2013 to Dec 2018
Becker-Hebly 2020	Germany	To describe how dimensions of psychosocial health are distributed among different intervention groups of adolescents with a gender dysphoria diagnosis before and after treatment	Gender identity service for children and adolescents	Young people age 11 and over who were seeking and eligible for medication interventions	75 (mean age at baseline 15.56 range 11-18; 64 brf, 11 brm)	Yes	Yes	GnRHs; cross-sex hormones and GnRHs; cross-sex hormones and surgery	No hormone treatment	Non-exposed individuals from primary sample	N/A	Retrospective cohort study	Baseline (at intake) and single follow-up follow-up ranged 13 to 38 months after baseline, mean 21.4 months - not linked to treatment start)	Clinical entry Sep 2013 to Jun 2017 (follow-up to Mar 2018)
Beking 2020	Netherlands	To investigate the effect of testosterone treatment in trans boys on functional lateralization of the amygdala and compare this with cisgender male and female control groups	Center for Gender Dysphoria for all ages	Birth-registered females with gender dysphoria who had received puberty suppressants and were starting testosterone treatment	21 (mean age 16.1 SD 0.7)	Yes	No	Testosterone	Two age-matched control groups presumed no GD recruited from schools and friends of treated participants	Other control group	(20 boys, mean 15.9 (SD 0.6); 21 girls, mean 16.4 (SD 1.0))	Prospective cohort study	Baseline and single follow-up (on average 10 months after baseline, treatment duration range 5.6-14.8 months, mean average 9.8)	Not reported
Burke 2016	Netherlands	To investigate whether adolescent girls with gender dysphoria, before and after testosterone treatment, would show male- or female-typical brain activity during a mental rotation task	Center for Gender Dysphoria for all ages	Adolescent birth-registered females with gender dysphoria who had been gender dysphoric since childhood and had received puberty suppressants	21 (mean age 16.1 years SD 0.8)	Yes	No	Testosterone	Two age-matched control groups presumed no GD	Other control group	(21 girls, mean age 16.3 (SD 1.0); 20 boys, mean age 15.9 (SD 0.6))	Prospective cohort study	Baseline and single follow-up (on average 10 months after baseline, treatment duration range 6-15 months, average 10)	Not reported
Cantu 2020	US	To examine changes in anxiety, depression and suicidality in young people receiving gender-affirming care	Paediatric gender clinic	Transgender and gender-nonconforming youth seeking gender-affirming care ages 11-18 who attended an initial visit and one follow-up and completed distress measures at both visits	80 (mean age 15.1 SD 1.8; 15 affirmed gender female, 58 affirmed gender male, 7 non-binary)	Yes	Yes	Puberty suppressants; cross-sex hormones (with or without puberty suppressants)	No hormone treatment	Non-exposed individuals from primary sample	N/A	Retrospective cohort study	Baseline (initial appointment) and single follow-up (average 4 months after baseline, range <1 to 11 months)	Initial appointment Sep 2017 to Jun 2019
de Nie 2022	Netherlands	To evaluate the influence of puberty suppression and/or gender affirming hormonal treatment on exocrine testicular function in transgender women	Center for Gender Dysphoria for all ages	Transgender women who underwent bilateral orchiectomy combined with vaginoplasty	214 (mean age at time of surgery 29.6 years SD 12.4)	Yes	Yes	Puberty suppressants and/or cross-sex hormones initiated in adolescence	Hormones initiated in adulthood	Individuals from primary sample receiving hormones in adulthood	N/A	Retrospective cohort study	Single time-point	Underwent surgery from 2006 to 2019
Grimstad 2021b	US	To identify the impact of oxandrolone in the presence or absence of GnRHs on adult height in trans-masculine youth	Multi-disciplinary gender identity clinic at paediatric medical centre	Sex assigned female at birth and diagnosis of gender dysphoria and whose final adult heights were available	154 (mean age of referral 15.7 SD 1.9)	Yes	Yes	Oxandrolone with or without GnRHs; Testosterone with or without GnRHs; GnRHs only; Progesterone only	No hormone therapy	Non-exposed individuals from primary sample	N/A	Retrospective cohort study	All heights available in the medical record were collected up to adult height	Seen between 2013 and 2018 (data collected to 2020)
Jensen 2019	US	To determine whether dosages of gender-affirming hormones in transgender adolescents taking GnRHs differ from those not taking GnRHs, and identify the frequency of associated side effects	Paediatric gender clinic	Patients who started or were currently receiving gender-affirming hormone therapy	85 (62 brf; median age at CSH+GnRH 15.0 range 13.7-16.5; at CSH only 16.9 range 13.4-22.1; 23 brm; median age at CSH+GnRH 14.9 range 14.1-15.7; CSH only 16.7 range 14.4-18.2)	Yes	No	Cross-sex hormones with GnRHs	Cross-sex hormones without GnRHs	Individuals from primary sample receiving hormones in combination with another medication	N/A	Retrospective cohort study	Relevant data from medical record (follow-up ranged from 6.4 to 53.0 months)	Treatment started before Mar 2016 (data extracted to Jan 2018)
Lopez de Lara 2020	Spain	To evaluate the psychosocial status of paediatric patients with gender incongruity and to establish the impact on this after one year of cross hormonal therapy	Paediatric endocrinology clinic	Adolescents age 14-18 with gender incongruity, at Tanner stage 2 or higher	23 (mean age 16; 16 brf, 7 brm)	Yes	No	Cross-sex hormones	Age, ethnicity and socio-economically matched controls presumed no GD	Other control group	30 (mean age 16 (range 14-18); 12 females, males)	Prospective cohort study	Baseline and 12 month follow-up	Attended clinic during 2018 and 2019
Tordoff 2022	US	To investigate whether initiation of puberty blockers and gender affirming hormones is associated with changes in depression, anxiety, and suicidality in transgender and nonbinary youths	Urban multidisciplinary children's gender clinic	Transgender and nonbinary adolescents and young adults who completed the initial clinic appointment	104 (mean age 15.8 range 13-20; 63 trans males, 27 trans females, 10 nonbinary / fluid, 4 don't know)	Yes	Yes	Puberty suppressants and cross-sex hormones	No hormone treatment	Non-exposed individuals from primary sample	N/A	Prospective cohort study	Baseline (initial appointment), 3, 6 and 12 month follow-up (follow-up timepoints not linked to initiation of medical intervention)	Initial appointment from Aug 2017 to Jun 2018
Valentine 2021	US	To examine changes in BMI and lipids in transgender youth on testosterone therapy compared to cisgender females	Multidisciplinary gender identity programme at a large pediatric centre	Transgender males age 14-21 on testosterone therapy with available follow-up data	42 (mean age 16.6 SD 1.3)	Yes	No	Testosterone	BMI-matched female adolescents presumed no GD	Other control group	82 (mean age 15.5 (SD 1.8))	Retrospective cohort study	Baseline and available short- and long-term follow-up data (average short-term 4.9 months range 0.5-17.7, long-term 10.8 months range 2.6-25.7)	Treated from 2014 to 2018
van de Grift 2020	Netherlands	To describe the development of sex characteristics in a transgender adolescent cohort of early and later-initiated puberty suppressant treatment compared with young adults without treatment	Patients were identified using local registries (single centre)	Adolescents with gender dysphoria who initiated and continued puberty suppression treatment, and were less than age 18 at initiation	300 (mean age at start of puberty suppressants 15 SD 2.0; 184 brf, 116 brm)	Yes	Yes	Puberty suppressants and cross-sex hormones	No puberty suppressants prior to hormones	Non-exposed individuals from primary sample	N/A	Retrospective cohort study	Baseline, and follow-ups at initiation of cross-sex hormones, and initiation of surgery	Sought treatment from 2006 to 2013 (data collected until 2018)
<b>Pre-post</b>														
Allen 2019	US	To evaluate the effectiveness of gender-affirming hormones for improving psychological well-being and decreasing suicidality among transgender youth	Gender identity clinic at a large children's hospital	Young people age 13-20 years who were treated with gender-affirming hormones for at least 3 months	47 (mean age at treatment initiation 16.50; 33 brf, 14 brm)	Yes	No	Cross-sex hormones (with and without previous GnRHs)	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline and single follow-up (at least 3 months after start of treatment - treatment duration ranged 113-1016 days, mean 349)	Presented to clinic between 2015 and 2018
Chiniera 2018	Canada	To examine characteristics, including mental health comorbidities, among adolescents presenting to a transgender clinic and to compare these data to previous reports.	Specialist gender service based in children's hospital	12-18 year olds with gender dysphoria who desired pubertal suppression or cross-gender hormones	75 (no information on characteristics provided)	Yes	Yes	GnRHs and cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	Follow-up at 4.7 ± 3.7 months after starting gender-affirming hormones	Recruited Apr 2011 to Apr 2014 (commenced GnRHs between Jun 2011 and Apr 2015)
de Vries 2014	Netherlands	To investigate whether gender dysphoric youth improve over time with medical intervention consisting of puberty suppressants followed by cross-sex hormones and gender reassignment surgery	Center for Gender Dysphoria for all ages	Young adults who had received puberty suppressants followed by cross-sex hormones and gender reassignment surgery	55 (mean age at GnRHs initiation 14.8 range 11.5-18.5; 22 brm, 33 brf)	Yes	Yes	Puberty suppression followed cross-sex hormones and surgery	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline and follow-ups at initiation of cross-sex hormones, and 1 year after surgery	Referred between 2000 and 2008 (follow-up between 2008 and 2012)
Delemar-van de Waal 2006	Netherlands	To investigate the efficacy and safety of GnRHs treatment in adolescents with gender dysphoria	Center for Gender Dysphoria for all ages	Adolescents receiving GnRHs under the Dutch protocol for 2 years or longer	21 (age not reported; 11 brf, 10 brm)	Yes	Yes	GnRHs and cross-sex hormones	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline, 12 months and 24 months for some outcomes, and 24 months for others	Not reported
Grimstad 2021a	US	To evaluate breakthrough bleeding in transgender adolescents receiving testosterone treatment	Gender service at children's hospital	Sex assigned female at birth with functional uterus and ovaries present at start of testosterone treatment, received treatment for 12 months plus	232 (age 13-28 years, mean age 16.3)	Yes	No	Testosterone	No comparator	No comparator	N/A	Retrospective pre-post single group study	All outcome data available in the medical record after 12 months of testosterone treatment (duration of follow-up varied)	Seen between 2010 and 2020
Hamema 2017	Netherlands	To evaluate the efficacy and safety of estrogen treatment for pubertal induction in transgirls	Center for Gender Dysphoria for all ages	Birth-registered males diagnosed with gender dysphoria and treated with estrogen for 12 months or longer	28 (median age 16.0 range 13.9-18.9)	Yes	No	Estrogen	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline, and 12, 24 and 36 month follow-up	Seen between 1998 and 2009
Hilde-Gorman 2021	US	To examine mental health and psychotropic medication use among transgender adolescents following gender-affirming pharmaceutical care (secondary aim of sub-group of primary sample)	Military Healthcare Data Repository	Transgender military dependent youth who received care for gender dysphoria before age 18	963 (median age study start 12 IQR 10-14; 300 brm, 663 brf)	Yes	Yes	Puberty suppressants or cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	All available data before and after initiation of treatment (followed for mean 1.5 years [IQR 0.8-2.8] after start of treatment)	Received care between Oct 2010 and Sep 2018

Jarin 2017	US	To identify patterns in metabolic and cardiovascular parameters in transgender adolescents receiving cross-sex hormones	Four medical centers / hospitals (two paediatric)	Adolescents age 14-25 diagnosed with gender dysphoria and receiving cross-sex hormones	116 (72 brf mean age 16 range 13-22, 44 brm mean age 18 range 14-25)	Yes	No	Cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline, and 1-3 months, 4-6 months, and 6 plus months follow-up	Seen in clinics between 2008 and 2014
Kahiala 2020	Finland	To assess how adolescent development progresses and psychosocial functioning changes among transgender adolescents after starting cross-sex hormone treatment	Gender identity unit for minors	Adolescents diagnosed with transsexualism who were offered cross-sex hormones (referred before age 18)	52 (mean age 18.1 at diagnosis, range 15.2-19.9 years; 11 brm, 41 brf)	Yes	No	Cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline (during initial assessment) and 12 months follow-up (during real-life phase)	Offered treatment between 2011 and 2017
Khatshadourian 2014	Canada	To describe patient characteristics at presentation, treatment, and response to treatment in youth with gender dysphoria	Children's gender identity programme	Youth with a diagnosis of gender dysphoria and achieved at least Tanner stage 2	84 (median age at first visit 16.8 range 11.4-22.5; 45 brf, 37 brm)	Yes	Yes	GnRH <sub>a</sub> , spironolactone, cross-sex hormones, surgery	No comparator	No comparator	N/A	Retrospective pre-post single group study	All relevant clinic notes (follow-up ranged from 0.0 to 11.3 years)	Seen from Jan 1998 to Dec 2011
Klaver 2018	Netherlands	To examine the change in body shape and composition in transgender adolescents receiving hormone treatments	Center for Gender Dysphoria for all ages	All persons who started hormone treatment before 18 years old and had undergone x-rays and medical checkups to adulthood	192 (71 brm mean age at start of GnRH <sub>a</sub> 14.5 SD 1.8, 121 brf mean age 15.3 SD 2.0)	Yes	Yes	GnRH <sub>a</sub> followed by cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline and follow-ups at addition of cross-sex hormones, and 22 years of age	Started treatment between 1998 and 2014
Klaver 2020	Netherlands	To investigate cardiovascular risk factors, and assess obesity and dyslipidemia prevalence in transgender adolescents receiving hormone treatments	Center for Gender Dysphoria for all ages	All persons who started hormone treatment before 18 years old and had undergone x-rays and medical checkups to adulthood	192 (71 brm mean age at start of GnRH <sub>a</sub> 14.6 SD 1.8, 121 brf mean age 15.2 SD 2.0)	Yes	Yes	GnRH <sub>a</sub> followed by cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline and follow-ups at addition of cross-sex hormones, and 22 years of age	Diagnosed with gender dysphoria from 1998 to Dec 2015
Klink 2015	Netherlands	To assess peak bone mass in young adults with gender dysphoria who had been treated with GnRH <sub>a</sub> and cross-sex hormones during their pubertal years	Tertiary referral center	At least 21 years, gonadectomy had taken place, and data on bone development at start of GnRH <sub>a</sub> treatment, at start of cross-sex hormone therapy, and at the age of 22 years were available	34 (15 brm mean age at start of GnRH <sub>a</sub> 14.9 SD 1.9, 19 brf mean age at start of GnRH <sub>a</sub> 15.0 SD 2.0)	Yes	Yes	GnRH <sub>a</sub> followed by cross-sex hormones followed by gonadectomy	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline and follow-ups at addition of cross-sex hormones, and 22 years of age	Received gonadectomy from Jun 1998 to Aug 2012
Kuper 2020	US	To examine how transgender youth body dissatisfaction, depression, and anxiety symptoms change over the first year of receiving gender-affirming hormone therapy	Multi-disciplinary programme	Youth who received gender-affirming hormone therapy	n = 148 (mean age 14.9 range 9-18; 55 brm, 94 brf)	Yes	Yes	GnRH <sub>a</sub> and cross-sex hormones	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline (initial assessment) and 12 month follow-up (mean 14.9 months, range 11-18 months)	Initial assessments between 2014 and Mar 2018
Laurenzano 2021	US	To assess the effectiveness and safety of subcutaneous testosterone in achieving recommended testosterone levels and cessation of menses in transmasculine and gender-diverse adolescents	Gender management clinic for children and adolescents (not explicitly stated)	Transmasculine and gender diverse youth who started subcutaneous testosterone at age 13-19 and received it for > 6 months	119 (mean age at presentation 16.0; transmale 110, nonbinary 3, other 6)	Yes	No	Subcutaneous testosterone	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline and follow-up to most recent data available (median follow-up 1.9 years range 6 months to 5.5 years)	Received treatment between Aug 2012 and Feb 2020
Madsen 2021	Netherlands	To study the prevalence and determinants in the development of erythrocytosis in trans men on testosterone therapy	Center for Gender Dysphoria for all ages	Trans men who started testosterone and had at least one follow-up visit and laboratory results	1073 (mean age at initiation of treatment 22.5, IQR 18.4-31.8)	Yes	No	Testosterone	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline and regular follow-up data up to 20 years (follow-up varied in terms of frequency and length)	Seen between 1972 and 2015 (data collection Jan 2004 to Dec 2018)
Millington 2019	US	To assess prevalence of hyperkalemia in gender-diverse adolescents taking spironolactone for gender transition	Gender Management Service Programme at children's hospital	Adolescents prescribed spironolactone for gender transition	85 (mean age 16.6 SD 1.7; 82 female gender identity, 3 nonbinary gender identity)	Yes	No	Spironolactone	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline and follow-up of all measures recorded during treatment (up to 7 years, variation in follow-up period not reported, median no. of measures 3 (range 1-10))	Seen from 2007 to 2017
Millington 2022	US	To examine changes in serum creatinine during gender-affirming hormone treatment in transgender and gender diverse youth	Four specialist gender services based in children's hospitals	Transgender and gender diverse adolescents prior to initiation of gender-affirming treatment with no prior GnRH <sub>a</sub> treatment	286 (92 brm median age 17.3 IQR 16.2-18.6, 194 brf median age 16.2 IQR 15.1-17.5)	Yes	No	Testosterone, estradiol (with or without spironolactone)	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline, and 6, 12, 18 and 24 month follow-up	Recruitment Jul 2016 to Sep 2018
Mullins 2021	US	To examine thrombosis and thrombosis risk factors among an exclusively adolescent and young adult transgender population receiving gender-affirming hormone therapy	Pediatric hospital-associated gender identity clinic	Age 13 to 24 at initiation of gender-affirming hormone treatment	611 (median age at presentation to clinic 17.0 IQR 16.0-19.0; 428 brf, 183 brm)	Yes	No	Testosterone, estrogen	No comparator	No comparator	N/A	Retrospective pre-post single group study	All relevant data before and during treatment (mean 9 months SD 0), initiation of treatment (mean 554 days IQR 283-1037, testosterone 577 days IQR 283-923)	Seen from Jul 2013 to Mar 2019
Olson 2014	US	To determine if subcutaneous delivery of testosterone resulted in menstrual cessation and the normal male ranges of serum testosterone in female-to-male transgender youth	Large, gender identity youth-specialized multidisciplinary clinic	Transgender males age 12 to 24 receiving testosterone cypionate via subcutaneous injections for masculinization	36 (mean age 18.7 SD 2.6)	Yes	No	Subcutaneous testosterone	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline and 6 month follow-up	Recruited from 2011 to 2012
Olson-Kennedy 2018	US	To examine the physiologic impact of gender-affirming hormones in a cohort of adolescents with gender dysphoria	Large, gender identity youth-specialized multidisciplinary clinic	Transgender youth age 12-24 with gender dysphoria who wished to undergo phenotypic gender transition	59 (mean age 18 range 12-23; 34 brf, 25 brm)	Yes	No	Cross-sex hormones	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline and 24 month follow-up (range 21-31 months)	Presented for care between Feb 2011 and Jun 2013
Peri 2020	Israel	To examine blood pressure changes in transgender male adolescents treated with GnRH <sub>a</sub> alone and after the addition of testosterone	Gender dysphoria clinic at children's hospital	Transgender male adolescents who were treated solely with GnRH <sub>a</sub> for at least 2 months	15 (mean age at initiation of GnRH <sub>a</sub> 14.4 SD 1.0)	Yes	Yes	GnRH <sub>a</sub> followed by addition of testosterone	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline, and follow-ups at end of GnRH <sub>a</sub> treatment (over age 3 months SD 1), initiation of testosterone, and mean 4 months (SD 2) after starting testosterone	Sought care between 2013 and 2018
Peri 2021	Israel	To examine blood pressure changes in transgender female adolescents treated with GnRH <sub>a</sub> alone and after the addition of estradiol	Gender dysphoria clinic at children's hospital	Transgender female adolescents who were treated solely with GnRH <sub>a</sub> for at least 2 months	19 (mean age at initiation of GnRH <sub>a</sub> 15.7 SD 1.6)	Yes	Yes	GnRH <sub>a</sub> and estradiol	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline, and follow-ups at end of GnRH <sub>a</sub> treatment (mean 9 months SD 0), initiation of estradiol, and 18.5 months (mean) after estradiol (range 3-63 months)	Sought care between 2013 and 2020
Schagen 2018	Netherlands	To assess the effects of GnRH <sub>a</sub> treatment and gender-affirming hormone treatment on adrenal androgen levels in adolescents with gender dysphoria	Center for Gender Dysphoria for all ages	Adolescents with gender identity disorder who fulfilled criteria for treatment according to Endocrine Society guideline	127 (73 brf mean age at GnRH <sub>a</sub> start 14.3 range 11.5-18.6, 54 brm age 14.0 range 11.6 to 17.9)	Yes	Yes	GnRH <sub>a</sub> treatment followed by GnRH <sub>a</sub> combined with estradiol or testosterone	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline and 6 monthly follow-up to 4 years	Treated between 1998 and 2009
Schagen 2020	Netherlands	To describe bone mass development in adolescents with gender dysphoria treated with GnRH <sub>a</sub> , subsequently combined with gender-affirming hormones	Center for Gender Dysphoria for all ages	Adolescents with gender identity disorder who fulfilled criteria for treatment according to existing guidelines	121 (51 brm mean age 14.1 SD 1.7, 70 brf mean age 14.5 SD 2.0)	Yes	Yes	GnRH <sub>a</sub> treatment followed by GnRH <sub>a</sub> combined with estradiol or testosterone	No comparator	No comparator	N/A	Prospective pre-post single group study	Baseline and 12-monthly follow-up to 5 years	Treated between 1998 and 2009
Segev-Becker 2020	Israel	To describe patient characteristics at presentation, management, and fertility preservation among a cohort of children with gender dysphoria	Multidisciplinary paediatric gender dysphoria clinic	All patients younger than 18 years who began GnRH <sub>a</sub> treatment	106 (median age at referral 15.5 range 4.6-18 years)	Yes	Yes	GnRH <sub>a</sub> followed by cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	All relevant data following initiation of treatment (follow-up period not reported)	Referred from Mar 2013 to Dec 2018
Sequeira 2019	US	To determine the effect of testosterone on body mass index (BMI) z-score in transmasculine adolescents at 6 and 12 months after initiation	Adolescent medicine clinic at large children's hospital	Transmasculine adolescents age 13 to 19 who received testosterone	46 (mean age not reported - criteria range 13-19)	Yes	No	Testosterone	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline, 6 and 12 month follow-up	Seen between Sep 2014 and May 2017

Stoffers 2019	Netherlands	To investigate the efficacy and safety of testosterone treatment in transgender adolescents	Clinic (no other information provided)	Adolescents diagnosed with gender dysphoria who had started GnRH and had subsequently received testosterone for more than 6 months	62 (median age at GnRH initiation 16.5 range 11.8-18.0)	Yes	Yes	GnRH followed by testosterone	No comparator	No comparator	N/A	Retrospective pre-post single group study	Median duration of follow-up 12 months (range 5-33 months).	Received treatment between Nov 2010 and Aug 2018
Tack 2016	Belgium	To analyse impact of consecutive treatment with lynestrol in combination with testosterone on physical characteristics, safety, metabolic parameters, and hormone levels in gender dysphoric adolescent transboys	Multi-disciplinary child gender team	Gender dysphoric transmale adolescents who received lynestrol for at least 6 months	38 (mean age at start of treatment 15 years 10 months)	Yes	Yes	Lynestrol - androgenic progestin (puberty suppressant) only, and in combination with testosterone	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline, 6 and 12 months follow-up with lynestrol plus testosterone	Treated from 2010 until Sep 2015
Tack 2017	Belgium	To assess the side effects and biochemical changes of Cyproterone acetate alone and in combination with estrogen in adolescent trans-girls	Multi-disciplinary child gender team	Trans-girls with gender dysphoria who received Cyproterone acetate for at least 6 months	27 (mean age at start of treatment 16 years 6 months)	Yes	Yes	Cyproterone acetate (puberty suppressant) only, and in combination with estrogen	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline, 6 and 12 month follow-up with Cyproterone acetate plus estrogen	Treated from 2008 to Oct 2016
van der Loos 2021	Netherlands	To investigate changes in bone geometry among transgender adolescents using GnRH and gender-affirming hormones	Center for Gender Dysphoria for all ages	Transgender adolescents treated with GnRH and subsequent gender-affirming hormones before the age of 18 years, min. duration 6 months GnRH, and for whom DXA scans were available	322 (106 brm median age 13.1 to 15.5 for sub-groups at GnRH start, 216 brf median age 11.9 to 15.7 for subgroups at GnRH)	Yes	Yes	GnRH and cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline (start of GnRH), and follow-ups at addition of cross-sex hormones, and 32 years after cross-sex hormones (median 3.1 4.3 years across six sub-groups)	Visited clinic between 1972 and Dec 2018
Vlot 2017	Netherlands	To investigate the effect of GnRH and cross-sex hormone treatment on bone turnover markers and bone mineral apparent density in transgender adolescents	Center for Gender Dysphoria for all ages	Adolescents diagnosed with gender dysphoria who were treated with GnRH and cross-sex hormone treatment, with available outcome data	70 (28 brm median age at GnRH start 13.5 range 11.5-18.3, 42 brf median age 15.1 range 11.7-18.6)	Yes	Yes	GnRH and cross-sex hormones	No comparator	No comparator	N/A	Retrospective pre-post single group study	Baseline (start of GnRH), and follow-ups at addition of cross-sex hormones, and 24 months after cross-sex hormones	Started treatment between 2001 and 2011
<b>Cross-sectional</b>														
Arcelus 2016	UK	To explore prevalence of non-suicidal self-injury (NSSI) in young trans people and to identify what factors can predict this	National gender clinic for adults (age 17+)	All individuals below the age of 25 years old who were referred for and offered an assessment	268 (mean age 19.9 SD 2.17; 121 brf, 136 brm, 11 no answer)	Yes	Yes	GnRH or cross-sex hormones	No hormone treatment	Non-exposed individuals from primary sample	N/A	Cross-sectional study with controls	Single time-point (initial assessment after referral to service)	Referred between Nov 2012 to June 2015
Burke 2020	Netherlands	To investigate whether hormonal interventions in adolescents diagnosed with gender dysphoria affect their click-evoked otoacoustic emissions compared to age- and sex-matched controls	Center for Gender Dysphoria for all ages	Children and adolescents diagnosed with gender dysphoria	105 (62 brf mean age 15.6 range 10.3-20.3, 43 brm mean age 15.9 range 11-20)	Yes	Yes	GnRH; cross-sex hormones and GnRH	No hormone treatment; Age- and sex-matched controls divided into early, mid- and late-adolescent groups.	Non-exposed individuals from primary sample; Other control group	Early (13 boys, mean age 12.8 (SD 1.9); 15 girls, 12.2 (1.7)); mid (18 boys, 13.9 (1.8); 10 girls, 15.1 (1.8)); late-adolescent (20 boys, 17.1 (0.8); 21 girls, 17.9 (0.4))	Cross-sectional study with controls	Single time-point	Not reported
Fontanari 2020	Brazil	To evaluate the impact of each domain of gender affirmation (social, legal, and medical/surgical) on the mental health of transgender and gender nonbinary youth.	Facebook	Transgender boys, transgender girls, and gender nonbinary Brazilian youth, age 16 to 24 years	350 (mean age 18.61 (CI 95% 18.34-18.88, 149 transgender boys, 85 transgender girls, 116 gender nonbinary)	Yes	Yes	Hormone therapy; 'any hormone or surgical treatment'	No hormone therapy; no hormone or surgical treatment	Non-exposed individuals from primary sample	N/A	Cross-sectional study with controls	Single time-point	Recruitment Feb to Apr 2018
Grannis 2021	US	To assess the effect of testosterone treatment on internalizing symptoms, body image dissatisfaction, and activation patterns within the amygdala-prefrontal cortex circuit in transgender adolescent boys	Gender development clinic at a large children's hospital	Adolescent transgender boys age 9-21 with a diagnosis of gender dysphoria receiving gender affirming medical care	47 (22 treated: mean age 17.03 SD 1.24; 25 untreated mean age 15.75 SD 1.47)	Yes	No	Testosterone	No testosterone	Non-exposed individuals from primary sample	N/A	Cross-sectional study with controls	Single time-point (around 1 year after treatment)	Recruited Dec 2018 to Mar 2020
Green 2022	US	To examine associations among access to gender-affirming hormone therapy with depression, thoughts of suicide, and attempted suicide among transgender and nonbinary youth	Community	Transgender or non-binary youth age 13-24 who reside in the US	11,914 (average age received GAHT 17.62, average age not received GAHT 17.30; transgender male 29%, transgender female 8%, nonbinary 63%)	Yes	No	Gender-affirming hormones	No hormones but wants to take them; no hormones and does not want to take them	Non-exposed individuals from primary sample	N/A	Cross-sectional study with controls	Single time-point	Data collected from Oct to Dec 2020
Millington 2021b	US	To examine lipoprotein subtype profiles in transmasculine adolescents treated with testosterone	Children's hospital (biobank)	Transmasculine adolescents age 12 to 23 treated with testosterone	17 (median age 18.4 IQR 17.6-19.5)	Yes	No	Testosterone	Two adolescent control groups (male and female) presumed no GD	Other control group	32 girls, mean age 17.6 (IQR 17.1-18.5); 33 boys, mean age 17.8 (IQR 17.0-19.4)	Cross-sectional study with controls	Single time-point (duration of treatment mean 1.2 months range 0.33 to 3.3 years)	Samples collected between Jan 2017 and Aug 2020
Nokoff 2020	US	To evaluate insulin sensitivity and body composition among transgender adolescents receiving cross-sex hormones compared with cisgender adolescents	Centre for gender diversity at children's hospital	Transgender adolescents (up to age 21) on either testosterone or estradiol for at least 3 months	35 (21 brf mean age 17.0 SD 1.4, 14 brm mean age 16.3 SD 1.4)	Yes	No	Testosterone, estradiol	Adolescents presumed no GD (matched on pubertal stage and BMI for brf, and age and BMI for brm)	Other control group	Controls for brf: 42 girls, mean age 15.2 (SD 1.9); 19 boys, 15.3 (SD 1.6) Controls for brm: 23 girls, 15.9 (SD 1.4); 24 boys, 15.7 (SD 1.4)	Cross-sectional study with controls	Single time-point (testosterone mean duration 11.2 SD 5.9 months, estradiol mean duration 12.9 SD 9.9 months)	Recruited from 2016 to 2018
Strang 2022	US	To explore the relationship between gender-affirming medical intervention status (i.e. pubertal suppression, gender-affirming hormones) and executive functioning in transgender youth	Community, gender services, gender and neurodiversity programme	Transgender youth age 11-21 enrolled in a study of cognition, mental health and neurodevelopment (all met criteria for gender dysphoria)	124 (mean age 16.67 range 11.65-21.56, female 41, male 81, non-binary 2)	Yes	Yes	Testosterone or estrogen (with or without puberty suppression)	No hormone treatment	Non-exposed individuals from primary sample	N/A	Cross-sectional study with controls	Single time-point	Enrolled in study between 2018 and 2020
Turban 2022	US	To examine associations between recalled access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults	Community	Transgender adults age 18 plus who reside in the US who reported ever desiring gender-affirming hormones	21,598 (accessed CSH: age 14-15 median age 21 IQR 18-35, age 16-17 median 19 IQR 18-22), age 18+ median 31 IQR 25-45, no access age not reported; 11,346 brf, 10,252 brm)	Yes	No	Cross-sex hormones	No cross-sex hormones; cross-sex hormones in adulthood	Non-exposed individuals from primary sample; Individuals receiving hormones in adulthood	N/A	Cross-sectional study with controls	Single time-point	Data collected Aug to Sep 2015

Abbreviations: BMI - body mass index; brf - birth-registered female; brm - birth-registered male; CSH - cross-sex hormones; GD - gender dysphoria; GnRH - Gonadotropin-releasing hormone analogue; NSSI - non-suicidal self-injury.

\* Terminology used in original paper retained for these columns to accurately reflect study aim and population selected