**Supplementary table S4 - Critical appraisal summary by question**

| Study ID | Study design | NOS total score | NOS Q1 representative of population | NOS Q1 score | NOS Q8 adequacy of follow-up | NOS Q8 score | NOS Q3 Ascertainment of treatment exposure | NOS Q3 score | NOS Q2 Selection of non-exposed group | NOS Q2 score | NOS Q5 comparability of cohorts (part 1 - controls for key demographics; part 2 - controls for co-interventions) | NOS Q5 part 1 score | NOS Q5b part 2 score | NOS Q7 follow-up duration | NOS Q7 score | NOS Q6 assessment of outcome | NOS Q6 score | NOS Q4 Demonstration that outcome of interest not present at study start | NOS Q4 score |
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| **Cohort** | | | | | | | | | | | | | | | | | | | |
| Achille 2020 | Prospective cohort study | 4 | States that vast majority of eligible population entered study, but no values or percentages provided. Recruited from single clinic. | 0 | 116 participants entered study - 50 who completed questionnaires reported on. No information on those lost to follow-up. | 0 | Information in paper provides confidence that clinic data used. | 1 | Participants who had received puberty blockers were compared to participants who've received nothing at all or only cross sex-hormones. | 1 | Controlled for outcome at baseline, psychiatric medication and psychotherapy. Separate analysis by gender. Did not control for age or report differences between groups. Did not control for other hormone treatment. | 0.5 | 0.5 | Follow-up not linked to treatment duration. Exposure to treatment at any time used as variable - not duration. | 0 | Validated scales designed for self-completion. | 1 | N/A | |
| Akgul 2019 | Retrospective cohort study | 3 | Ten out of thirty participants excluded due to not being able to be matched with controls. | 0 | For most outcomes, no information given on follow-up rates. For the satisfaction outcome, the follow-up rate was less than 90%. | 0 | Procedure codes for LNG-IUS insertion used in medical records. | 1 | Matched with adolescents who received the 52 mg LNG-IUS primarily for noncontraceptive purposes (seen at the same subspecialty clinic by many of the same providers). | 0.5 | Participants were matched on age. Only participants assigned female at birth were included. Unadjusted analyses were used. | 1 | 0 | Insufficient information given to assess follow-up duration. | 0 | Mixture of clinical record data and Likert scales to measure satisfaction. | 0.5 | N/A | |
| Becker-Hebly 2020 | Retrospective cohort study | 3 | 434 children seen by clinic, 204 with baseline data and eligible, and invited to take part. Large proportion not included. Single clinic. | 0 | Response rate for follow-up 37% (n=75). | 0 | Self-reported treatment path then controlled via clinicians' reports. | 1 | Those not treated with hormones from same clinic sample. | 1 | Did not control for gender / sex, other treatments or outcome at baseline. Used age-adjusted population norms to compare outcomes. Did not control for distribution in intervention group. | 0 | 0 | Treatment started after baseline but duration and start of treatment not reported or included in analysis. | 0 | Validated scales - combination of self-report and clinician-report. | 1 | N/A | |
| Costa 2015 | Prospective cohort study | 5.5 | National clinic. Included all eligible adolescents. | 1 | None lost at 12 months, around half lost at 18 months - reasons not reported | 0.5 | Information in paper provides confidence that clinic data used. | 1 | Drawn from same source; plus comparison to adolescents without observed psychological / psychiatric symptoms. | 1 | Split analysis by delayed eligible and immediately eligible, presented some analysis re: natal sex differences but main analysis didn't control for this. | 0 | 0 | Sufficient follow-up period - 12 month follow-up was reported as 6 months of puberty suppression. | 1 | Validated measures used. | 1 | N/A | |
| de Nie 2022 | Retrospective cohort study | 5 | Single clinic population - only those who underwent bilateral orchiectomy combined with vaginoplasty were eligible - random sample taken for study. | 0 | Of the 263 sampled, 49 were then excluded due to no tissue being stored or no testicular parenchyma on slides. | 1 | Authors state data was collected from medical records. | 1 | Adults presenting to the same clinic who underwent bilateral orchiectomy combined with vaginoplasty. | 0.5 | Study participants are birth-registered males only, groups are split by puberty stage (Tanner stage 2-3; Tanner stage 4-5; Adult). Study does not control for use of medications such as contraceptive pill. | 1 | 0 | Information on follow-up period not explicitly given. Indications some participants would have had a duration of medical treatment longer than 12 months. | 0.5 | Detailed information on sample testing given. | 1 | N/A | |
| Grimstad 2021b | Retrospective cohort study | 3.5 | Single-clinic population, very small number excluded due to incomplete height data (6/195 eligible patients). | 0.5 | Only those with complete height data were included, those had not reached adult height by the end of the study were excluded. | 0.5 | Data obtained from medical records. | 1 | Drawn from same source. | 1 | Only participants who were assigned a female sex at birth were included. Unadjusted analyses were carried out. | 0.5 | 0 | No information provided on time between start of treatment and measurement of final height. | 0 | Height measured in triplicate at each clinic visit. Participants were defined as growing if they demonstrated a growth velocity of 0.5cm per year. | 0 | N/A | |
| Mejia-Otero 2021 | Retrospective cohort study | 4 | Single-clinic - only included patients who had undergone blood tests at baseline and 2-12 months. No information on number excluded. | 0 | Only those with blood test data were included. | 1 | Retrospective review of medical records. | 1 | Adolescents with central precocious puberty. Substantial differences between groups in age and sex. | 0 | Separate analyses for males and females were carried out. Unadjusted analyses were used. | 0.5 | 0 | Mean time between onset of therapy and follow-up was 5.9 months (SD2.9). Patients were eligible if they'd had a blood test 2-12 months after starting treatment. | 0.5 | Retrospective review of medical records. | 1 | N/A | |
| Pine-Twaddell 2022 | Retrospective cohort study | 5 | Two clinics. Participants without follow-up data were excluded. | 0 | Only participants with follow-up data were included. | 1 | Data was extracted from medical records. | 1 | Patients with central precocious puberty were selected from the same study clinics as the exposed group. | 0.5 | Separate analyses were carried out for males and females. No other covariates were adjusted for. | 0.5 | 0 | Baseline and single follow-up (17 to 65 months post-insertion). | 1 | All relevant study data were retrieved retrospectively from medical records. | 1 | N/A | |
| Schulmeister 2022 | Prospective cohort study | 5 | Four large clinics in the US (different localities). Aimed to recruit all treated. No information given on consent rates, exclusions. | 0.5 | 12 participants excluded from analysis due to not having a documented height at between 10-12 months of GnRHa treatment. | 0 | Information given on whether participant received implant or injection - medical records used. | 1 | Prepubertal adolescents (presumed not to have GD) not receiving hormonal intervention was drawn from the Bone Mineral Density in Childhood Study. | 0.5 | Analyses comparing exposed group to non-exposed group, stratified by sex and controlled for age. Other important covariates such as BMI, ethnicity and baseline hormones were used as covariates. | 1 | 0 | Follow-up carried out between 10-14 months post-treatment. | 1 | Anthropometric and laboratory data collected during clinical care were abstracted from the medical record. | 1 | N/A | |
| Tordoff 2022 | Prospective cohort study | 3.5 | Single-clinic study. 30% of eligible patients did not take part. | 0 | Follow-up rates less than 90% at each follow-up timepoint. | 0 | Data on puberty suppression collected via self-report. | 0 | Drawn from same source as exposed population. | 1 | Gender, but not sex was controlled for as a confounder. Ethnicity was also controlled for. The analysis controlled for receipt of mental health therapy. | 0.5 | 0.5 | 3, 6, 9, 12 month - follow-up not linked to treatment initiation but some participants with sufficient follow-up | 0.5 | Collected via validated scales. | 1 | N/A | |
| van de Grift 2020 | Retrospective cohort study | 5 | Single-clinic study. Patients lost to follow-up (n=68) were excluded. | 0 | Only participants with complete follow-up data were included. | 1 | Registry and patient record data collection used. | 1 | Drawn from same source as exposed group. | 1 | Males and females were analysed separately. Unadjusted analyses were used. | 0.5 | 0 | Initiation of different therapies in treatment protocol indicate most participants followed up for considerable duration. | 0.5 | Data collected as part of routine clinical practice. | 1 | N/A | |
| **Pre-post** | | | | | | | | | | | | | | | | | | | |
| Carmichael 2021 | Prospective pre-post single group study | 4.5 | Included sequentially eligible from single clinic. 44 out of 48 who discussed the study took part. | 0.5 | Very few lost to 12 month follow-up. However, around half lost at 24 months. | 0.5 | Recruitment to study was for treatment in clinic - medical records data. | 1 | N/A | | Sex / gender, puberty status at baseline controlled for in some analyses of continuous variable outcomes but not others. Co-interventions not controlled for. | 0.5 | 0 | Sufficient follow-up period. | 1 | Validated measures for psychosocial / mental health; validated approaches for physiologic measures. | 1 | N/A | |
| Chiniara 2018 | Retrospective pre-post single group study | 3.5 | Single-clinic study, 15/218 excluded due to missing data. | 0.5 | Low follow-up rates reported. | 0 | Retrospective review of medical records. | 1 | N/A | | Separate analyses were conducted by sex. | 0.5 | 0 | Repeat hormonal levels measured after 3.8 ± 1.9 months of initiation of GnRH-a therapy | 0.5 | Validated scales and clinical record data used. | 1 | N/A | |
| de Vries 2011 | Prospective pre-post single group study | 4 | National clinic. 111 prescribed GnRHa. Participants first 70 adolescents who subsequently started hormones. Unclear who excluded were. | 0.5 | Not all 70 provided data. Response across questionnaires: CBCL, YSR: 54; BDI, TPI, STAI, CGAS, and UGS: 41; BIS: 57. | 0 | Information presented on start of treatment - medical records data. | 1 | N/A | | Sex was controlled for. Study does not control for age/puberty stage or co-interventions. | 0.5 | 0 | Time between start of GnRHa and follow-up ranged between 0.42 and 5.06 years. | 1 | Validated measures used. | 1 | N/A | |
| de Vries 2014 | Prospective pre-post single group study | 3.5 | National clinic. 111 prescribed GnRHa. 70 participants approached one-year post-surgery - 55 took part. Large proportion of eligible population missing. | 0 | Only participants with data at all waves were included. Numbers: CGAS 32, BDI 32, TPI 32, STAI 32, CBCL-ABCL 40, YSR-ASR 43. UGDS 33, BIS 45. | 0 | Information presented on start of treatment - medical records data. | 1 | N/A | | Separate analyses were conducted by sex, and age was adjusted for. | 1 | 0 | Final follow-up took place one year after surgery. | 1 | All validated scales except 'self-constructed' objective measure of wellbeing. | 0.5 | N/A | |
| Delemarre-van de Waal 2006 | Prospective pre-post single group study | 2.5 | Single clinic, inadequate information on response rates given. | 0 | Inadequate information on follow-up given. | 0 | Follow-up protocol integrated into clinical practice - medical records data. | 1 | N/A | | No adjustment made for age, sex, co-interventions or sociodemographic confounders. | 0 | 0 | Participants were treated for two years or longer. | 1 | Clinical measurements presented, but no information given on how this information was obtained. | 0.5 | N/A | |
| Ghelani 2020 | Retrospective pre-post single group study | 4.5 | National clinic. Only those with complete data included and excluded some based on confounding lifestyle factors such as anorexia or bodybuilding. | 0 | Only those with complete data were included. | 1 | Data was collected as part of routine clinical practice - medical records data. | 1 | N/A | | Seprate analyses carried out by sex. No adjustment made for age or co-interventions or sociodemographic confounders. | 0.5 | 0 | Follow-up was from treatment and up until 12 months. | 1 | Whole-body impedance measured using Tanita Body Composition Analyzer. SDS for lean mass - UK reference data. Height, weight and BMI SDS - UK90 data. | 1 | N/A | |
| Hisle-Gorman 2021 | Retrospective pre-post single group study | 4 | All eligible participants were included from the Military Health System. | 0.5 | No information given on missing data. | 0 | Obtained from pharmacy records. | 1 | N/A | | Analyses adjusted for age and sex. Some important covariates such as parental rank adjusted for. | 1 | 0 | Median follow-up post-treatment was 1.5 years (IQR 0.7 to 2.7). | 0.5 | Outcome data collected from Military Healthcare Data Repository. | 1 | N/A | |
| Joseph 2019 | Retrospective pre-post single group study | 5 | National clinic, participants without complete data were excluded, with no information given on how many were excluded. | 0.5 | Only those with complete data were included in the study. | 1 | Data was collected as part of routine clinical practice. | 1 | N/A | | Separate analyses were carried out for sex. No other covariates were adjusted for. | 0.5 | 0 | All participants were followed up for at least one year post starting GnRHA treatment. | 1 | Assessed as part of clinical practice. | 1 | N/A | |
| Khatchadourian 2014 | Retrospective pre-post single group study | 3 | Single-clinic study, included all patients. | 0.5 | No information given on missing data. | 0 | Data obtained from clinical records. | 1 | N/A | | Descriptive summaries were presented separately for males and females. | 0.5 | 0 | No information given on time between start of treatment and assesment of outcomes. | 0 | Clinical outcomes assessed as part of routine medical care. | 1 | N/A | |
| Klaver 2018 | Retrospective pre-post single group study | 3 | Single-clinic study, participants without whole-body DXA excluded (n=5). 66 participants excluded on different treatment protocol - reason unclear. | 0 | No information given on follow-up rates. | 0 | Data collected from medical records. | 1 | N/A | | Analyses were carried out separately for sex. No other covariates were adjusted for. | 0.5 | 0 | Duration of GnRHA monotherapy median 2.1 years (IQR 1.0-2.8) for birth-registered males and median 1.0 (0.5-2.9) for birth-registered females. | 0.5 | Collected from medical records. | 1 | N/A | |
| Klaver 2020 | Retrospective pre-post single group study | 3.5 | Single-clinic study. Excluded those without whole-body DXA and with no consultation in early adulthood. No numbers reported. | 0 | No information given on follow-up timepoint. | 0 | Data collected from medical records. | 1 | N/A | | Separate analyses were carried out for males and females. No other covariates were adjusted for. | 0.5 | 0 | At addition of cross sex hormones - sufficient follow-up indicated by age at starting this. | 1 | Collected from medical records. | 1 | N/A | |
| Klink 2015 | Retrospective pre-post single group study | 4 | Single-clinic study. Only included participants with data available at each timepoint. Number of patients excluded not reported. | 0 | High follow-up rates at final timepoint. | 1 | Detailed information on timing of treatment given. | 1 | N/A | | Separate analyses were carried out for males and females. No other covariates were adjusted for. | 0.5 | 0 | At addition of cross sex hormones - sufficient follow-up for most participants but not all. | 0.5 | Collected from medical records. | 1 | N/A | |
| Kuper 2020 | Prospective pre-post single group study | 2.5 | Single-clinic study that excluded 22/209 patients due to missing follow-up. | 0.5 | Despite those with follow-up data being excluded, less than 90% of participants included in analysis of each outcome. | 0 | Clinician data were entered into a research database. | 1 | N/A | | Hypothesis testing (not separately by age or sex). Regression controlling for demographic and treatment variables planned, but no correlations found between change scores and demographic/treatment variables. | 0 | 0 | No information given on time between start of puberty suppresion and follow-up. | 0 | Validated scales used. | 1 | N/A | |
| Lynch 2015 | Retrospective pre-post single group study | 2.5 | Single-clinic study, not enough information given to ascertain proportion of eligible patients included in study. | 0 | Study makes reference to participants being lost to follow-up, but does not present information on follow-up rates. | 0 | Clinical data extracted from medical records. | 1 | N/A | | Narrative summary presented. | 0 | 0 | Baseline and relevant data from clinic follow-up at 1 and 6-monthly intervals (duration of follow-up not reported) | 0.5 | Extracted from medical records. | 1 | N/A | |
| Navabi 2021 | Retrospective pre-post single group study | 3 | Single-clinic study. Only participants with at least one DXA measurement were included. | 0 | Considerable number not included in analysis. | 0 | Retrospective review of medical records. | 1 | N/A | | Separate analyses carried out for males and females. Unadjusted analyses used. | 0.5 | 0 | Baseline and single follow-up (median 352.5 median days after GnRHa initiation, range 188-676 days) | 0.5 | Outcomes collected via DXA. | 1 | N/A | |
| Neyman 2019 | Retrospective pre-post single group study | 3 | Single-clinic study. No information given on eligibility. | 0 | Less than 90% follow-up for some outcomes. | 0 | Collected from medical records. | 1 | N/A | | Narrative summary presented. Only birth-registered males were included. | 0.5 | 0 | Time between baseline and first follow-up ranged from 2.18 to 8 months. | 0.5 | Extracted from medical records. | 1 | N/A | |
| Olson-Kennedy 2021 | Retrospective pre-post single group study | 4 | Small number of clinics. Participants excluded if they did not have data before and after histrelin implant placement. No information provided. | 0 | Only one participants excluded from one analysis. | 1 | Charts of existing patients who had a histrelin implant in place were reviewed. | 1 | N/A | | Stratified analyses by sex were carried out. No other covariates were adjusted for. | 0.5 | 0 | Baseline and single follow-up (2-12 months after treatment) | 0.5 | Abstracted from the medical record and from the larger study data pool. | 1 | N/A | |
| Peri 2020 | Retrospective pre-post single group study | 5 | Participants ecruited from a national clinic, only 3 participants were excluded due to missing BP data. | 1 | Those with missing data were excluded from the study. | 1 | Medical records data used to identify those on treatment. | 1 | N/A | | Only birth-registered females were included in the study. No information is given on adjustment for baseline variables. | 0.5 | 0 | Baseline, and follow-ups at end of GnRHa treatment (average 3 months SD 1). | 0.5 | Most measures extracted from medical records. BP measured during clinic visit using Welch Allyn Vital Signs Monitor VSM 300 (Welch Allyn, Inc., Beaverton, OR) | 1 | N/A | |

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| Perl 2021 | Retrospective pre-post single group study | 5 | Participants were recruited from national clinic, only 1 participant was excluded due to missing BP data. | 1 | Those with missing data were excluded from the study. | 1 | Data extracted from medical records. | 1 | N/A | | Only birth-registered males were included in the study. Unadjusted analyses were used. | 0.5 | 0 | Baseline, and follow-ups at end of GnRHa treatment (mean 9 months SD 6). | 0.5 | Most measures extracted from medical records. BP measured during clinic visit using Welch Allyn Vital Signs Monitor VSM 300 (Welch Allyn, Inc., Beaverton, OR) | 1 | N/A | | | | |
| Russell 2021 | Retrospective pre-post single group study | 5 | Two national clinics. Participants with incomplete outcome data were excluded (27/122). | 0.5 | Only participants with complete outcome data were included. | 1 | Details on GnRHa consent given. | 1 | N/A | | The analysis adjusted for sex. No other covariates were adjusted for. | 0.5 | 0 | Baseline and 12 month follow-up (plus / minus 3 months) | 1 | Validated scale used. | 1 | N/A | | | | |
| Schagen 2016 | Prospective pre-post single group study | 4.5 | National clinic. All eligible. | 1 | Low follow-up rates reported. | 0 | Participants excluded baised on treatment duration and receipt of medication, which implies access to medical records. | 1 | N/A | | Separate analyses carried out for males and females. Unadjusted analyses used. | 0.5 | 0 | Baseline, and 3, 6, 12, 24 and 36 months | 1 | Detailed information given on laboratory investigations and use DXA provided. | 1 | N/A | | | | |
| Schagen 2018 | Prospective pre-post single group study | 4 | National clinic. No information on consent rates but selected from all eligible. | 0.5 | No information given on follow-up rates. | 0 | Details on duration of treatment provided. | 1 | N/A | | Separate analyses carried out for males and females. No other covariates were adjusted for. | 0.5 | 0 | Analyses used data up to two years post-treatment. | 1 | Detailed information given on laboratory investigations. | 1 | N/A | | | | |
| Schagen 2020 | Prospective pre-post single group study | 5 | National clinic. Small number excluded due to DXA scans not being available at the start of GnRHa. | 1 | No information given on missing data rates at follow-up. | 0 | Detailed treatment protocol provided. | 1 | N/A | | Analyses adjusted for pubertal stage and sex. No other covariates were adjusted for. | 1 | 0 | Analyses presented up to 36 months of treatment. | 1 | Dual-energy x-ray absorptiometry (DXA) using Hologic QDR 4500. Markers of bone formation and resorption used fasting blood samples, drawn on day of DXA. | 1 | N/A | | | | |
| Segev-Becker 2020 | Retrospective pre-post single group study | 3 | National clinic. Consecutive participants recruited. | 1 | No information given on follow-up rates. | 0 | Information on treatment delivery presented. | 1 | N/A | | Some but not all descriptive summaries stratified by gender/sex. Participants were split into pre-pubertal and pubertal groups. | 0 | 0 | No information given on follow-up period. | 0 | Data collected retrospectively from clinical records. | 1 | N/A | | | | |
| Stoffers 2019 | Retrospective pre-post single group study | 4 | Single-clinic study. Only 2/64 participants declined to participate. | 0.5 | High rates of follow-up at 6 months post-treatment, but low rates at 12 and 24 months post-treatment. | 0.5 | Information provides confidence that medical data were used. | 1 | N/A | | Only birth-registered females were included. Unadjusted analyses were used. | 0.5 | 0 | The median duration of follow-up was 12 months (range 5-33 months). | 0.5 | Data collected via chart review. | 1 | N/A | | | | |
| Tack 2016 | Retrospective pre-post single group study | 4 | Single-centre study in country with three clinics. Small number (5 out of 43) excluded due to missing laboratory data. | 0.5 | No information given on follow-up rates at each timepoint. | 0 | Information provides confidence that medical data were used. | 1 | N/A | | Only birth-registered female adolescents were included. Unadjusted analyses were used. | 0.5 | 0 | Data collected 6 and 12 months after start of lynestrenol, | 1 | Data collected as part of clinical follow-up. | 1 | N/A | | | | |
| Tack 2017 | Retrospective pre-post single group study | 4.5 | Single-centre study in country with three clinics. All those who received CA for at least 6 months during study period were included. | 1 | No information given on follow-up rates at each timepoint. | 0 | Information provided on age at start of treatment - medical records data. | 1 | N/A | | Only birth-registered males were included in the study. Unadjusted analyses were used. | 0.5 | 0 | Baseline, 6 and 12 month follow-up with Cyproterone acetate. | 1 | Data collected as part of clinical follow-up. | 1 | N/A | | | | |
| Tack 2018 | Prospective pre-post single group study | 3 | Single-centre study in a country with three clinics. No information on eligibility or consent rates. | 0 | No information given on follow-up rates at each timepoint. | 0 | Mean age at start of treatment given - medical records data. | 1 | N/A | | Separate analyses were carried out for males and females. Unadjusted analyses were used. | 0.5 | 0 | The mean time interval between both examinations was 11.64 (4 to 40) months in birth-registered females and 10.57 (5 to 31) months in birth-registered males. | 0.5 | Detailed information on assessment of outcomes provided. | 1 | N/A | | | | |
| van der Loos 2021 | Retrospective pre-post single group study | 4.5 | Single-clinic study. 123 excluded due to DXA not being available. | 0 | Only participants who had a DXA were included. | 1 | Information presented on start of treatment - medical records data. | 1 | | | Separate analyses were carried out for males and females. Analyses were stratified by puberty stage. | 1 | 0 | Some participants received GnRHA alone for less than one year. | 0.5 | Detailed information on DXA testing given. | 1 | N/A | | | | |
| Vlot 2017 | Retrospective pre-post single group study | 3.5 | Single-clinic study. A large number of eligible participants were excluded due to incomplete data. | 0 | Data indicates that more than 10% were missing data for outcomes. | 0 | Data collection took place at point of treatment. | 1 | N/A | | Analysis stratified on sex and bone age. Unadjusted analyses were used. | 1 | 0 | Age ranges given at each timepoint indicate follow-up sufficient for some patients. | 0.5 | Detailed information on DXA testing provided. | 1 | N/A | | | | |
| Waldner 2022 | Retrospective pre-post single group study | 4.5 | 15 out of 48 patients excluded due to incomplete data. | 0 | Only participants with complete data were included. | 1 | Retrospective chart review of medical records. | 1 | N/A | | The mean post-Lupron QTc was presented separately for patients assigned male and assigned female at birth. | 0.5 | 0 | Stated that time between baseline and follow-up was at least 6 weeks, but no further information given. | 0 | Assessed as part of clinical practice. | 1 | Table 3 shows QTc range was 384-454ms. | 1 | | | | |
| **Cross-sectional** | | | | | | | | | | | | | | | | | | | | | | | |
| Arcelus 2016 | Cross-sectional study with controls | 3.5 | 299 eligible patients - 31 did not answer questions regarding NSSI and were excluded. National clinic. | 1 | More than 10% excluded from analysis - no information provided on those or explanation. | 0 | Self-reported data on treatments received prior to assessment at adult clinic. | 0 | Those not treated with hormones from same clinic sample. | 1 | Controlled for gender, self-esteem, transphobia, interpersonal problems, social support. | 0.5 | 0 | N/A | | Validated assessment tools used. | 1 | N/A | | | | |
| Burke 2020 | Cross-sectional study with controls | 5 | Single clinic population - no information provided about recruitment and response, or number of eligible individuals. | 0 | All participants included in analysis. | 1 | Clinic data used to select / categorise treatment groups. | 1 | Two control groups - treatment naive adolescents from same source and adolescent controls, which were appropriate for examining this outcome. | 1 | Controlled for puberty stage / age, sex assigned at birth but no other treatments. Cross-sectional so no baseline control. | 1 | 0 | N/A | | Standard assessment - equipment and procedure explained in full - same applied to all participants (treatments and controls). | 1 | N/A | | | | |
| Fontanari 2020 | Cross-sectional study with controls | 3 | Self-selecting survey. | 0 | All participants who completed survey were included in the analysis. | 1 | Self-report. | 0 | Non-exposed group from same survey sample. | 1 | No adjustment made for age, sex, co-interventions or sociodemographic confounders. | 0 | 0 | N/A | | Validated scales used. | 1 | N/A | | | | |
| Nokoff 2021 | Cross-sectional study with controls | 3.5 | Single-clinic study. No information provided on consent rate. | 0 | All participants included in analysis according to table data. | 1 | No information provided on ascertainment of treatment exposure. | 0 | Adolescents from Colorado RESistance to InSulin in Type 1 ANd Type 2 diabetes (RESISTANT) study and the Health Influences in Puberty (HIP) study. | 0.5 | Separate analyses were carried out for sex, and analyses matched on age. Analyses also matched on BMI. | 1 | 0 | N/A | | Body composition measured using DXA and detailed information on laboratory assays provided. | 1 | N/A | | | | |
| Staphorsius 2015 | Cross-sectional study with controls | 2.5 | Single-clinic study. No information given on consent rates. | 0 | Considerable number removed from analysis. | 0 | Information on treatment delivery presented. | 1 | Self-selective sample from friends and siblings of participants with GD. | 0 | ANOVA was used to examine differences in accuracy and reaction time. An analysis using ANCOVA examined the effect of IQ on group differences. | 0.5 | 0 | N/A | | The Tower of London Test was used. Detailed information is provided fMRI analysis. | 1 | N/A | | | | |
| Strang 2022 | Cross-sectional study with controls | 4 | Shared study protocol in two locations. No information given on consent rates. | 0 | Only those with complete report forms were included. | 1 | Collected through parent and self-report, and only verified when dates not fully recalled by families. | 0 | Drawn from same population as exposed group. | 1 | Analyses adjusted for assigned sex and age. Membership in the puberty suppression group included those who had ever taken it, including those in current receipt and those who were now taking cross-sex hormones. | 1 | 0 | N/A | | Validated scales and evaluations used. | 1 | N/A | | | | |
| Turban 2020 | Cross-sectional study with controls | 3 | National survey covering all 50 states in collaboration with 400+ lesbian, gay, bisexual and transgender organisations. | 1 | No information given on number of participants excluded from analyses due to missing data. | 0 | Self-reported by participants. | 0 | Drawn from same population as exposed group. | 1 | Age and sex were not adjusted for. Education level, employment status, and total household income were adjusted for. | 0.5 | 0 | N/A | | One validated scale used, the rest appear to be bespoke for the study. | 0.5 | N/A | | | | |
| van der Miesen 2020 | Cross-sectional study with controls | 5.5 | Nearly all patients included from a national service. | 1 | Only participants who completed the questionnaire were included. | 1 | Questionnaires were completed during clinical assessments. | 1 | Group with GD who had not received puberty suppresants drawn from same source as exposed group. | 1 | An analysis controling for gender and age confirmed the group effects. | 1 | 0 | N/A | | A validated scale was used (YSR). An ad hoc peer relations scale was created using 3 items of the YSR. | 0.5 | N/A | | | | |