SBU BEREDER
PUBLIKATION NR: 307
PUBLICERAD: 20 DECEMBER 2019
NEDLADDAD: 11 NOVEMBER 2020

Könsdysfori hos barn och unga

En kunskapskartläggning

STATENS BEREDNING FÖR MEDICINSK OCH SOCIAL UTVÄRDERING

Innehåll

Sammanfattning 4

1. Inledning 6

2. Bakgrund 7

3. Frågeställningar och avgränsningar 8

PICO 8

Övriga avgränsningar 9

Studiedesign och språk 9

Projektprocessen 9

4. Epidemiologi 12

Förekomst hos barn och unga 12

Utveckling av barn som uttryckt könsdysfori 12

Antalet barn och unga som söker för könsdysfori ökar 13

Orsakerna till ökningen 13

Samsjuklighet 14

Flödet från remiss till behandling 14

5. Långtidseffekter på fysisk och psykisk hälsa 16

Förekomst av ånger efter könsbekräftande behandling 16

Psykosociala effekter 18

Kognitiva funktioner och hjärnstruktur 21

Cancerutveckling 22

Effekter på hjärta-kärl 22

Skeletthälsa 23

Behandling av barn och unga 25

6. Andra översikter 27

Pågående systematiskaöversikter 27

7. Diskussion 28

8. Ordlista 30

Terminologi i rapporten 30

9. Projektgrupp och externa granskare 32

Referensgrupp 32

SBU 32

Granskare från SBU:s vetenskapliga råd 32

Externa granskare 32
10. Referenser 34
Bilaga 1 Sökstrategier 43
Sökning Könsdysfori och barn och unga 43
Bilaga 2 Exkluderade studier 46
Gender dysphoria in children and adolescents 46
Tabeller med beskrivning av de ingående studierna 59

Observera att det är möjligt att ladda ner hela eller delar av en publikation. Denna pdf/utskrift behöver därför inte vara komplett. Hela publikationen och den senaste versionen hittar ni på www.sbu.se/307

ISBN 978-91-88437-49-5

Sammanfattning

SBU har fått regeringens uppdrag ((S2019/03053/FS) Socialdepartementet) att göra en systematisk kunskapsöversikt av könsdysfori hos barn och unga.

Detta är en systematisk sammanställning av litteraturen. Vi har inte bedömt studiernas kvalitét eller risk för bias och därför kan ingen sammanvägning av resultaten eller evidensbedömning göras. Sammanställningen kan ligga till grund för en senare utvärdering av evidensen.

- Vi har inte funnit någon vetenskaplig litteratur som förklarar det senaste decenniets ökning av antalet barn och unga som söker på grund av könsdysfori.
- Vi har inte kunnat identifiera någon studie som belyser om förekomsten (prevalensen) av könsdysfori har förändrats över tid och inte heller någon studie rörande eventuella förändringar av faktorer i samhället som kan förklara ökningen.
- Det finns få studier om könsbekräftande kirurgisk behandling av barn och unga och det är bara enstaka studier som omnämner genital kirurgi hos barn och unga.
- Vi har endast kunnat identifiera enstaka studier rörande effekter över längre tid av könsbekräftande behandling hos barn och unga, särskilt för de grupper som tillkommit under det senaste decenniet.
- Den vetenskapliga aktiviteten inom området är hög och en stor andel av de studier som identifierats i denna rapport är publicerade under 2019.
- Litteraturen består i huvudsak av observationsstudier av patientserier varav en mindre andel är före- och efterstudier. Likaså har en mindre andel av studierna jämförelsegrupper. Inga relevanta randomiserade kontrollerade studier har identifierats.
- Vi har inte hittat någon sammantagen nationell information om hur stor andel av de barn och unga som söker för könsdysfori
    - som får diagnosen transsexualism
    - som börjar pubertetsfördröjande behandling
    - som börjar könsbekräftande hormonbehandling
    - som genomgår könsbekräftande kirurgi av olika slag.

Innehållsdeklaration

- ~~Strukturerad litteratursökning~~
- ✔ Strukturerad och uttömmande litteratursökning
- ✔ Granskning av studiernas relevans
- ~~Bedömning av risk för snedvridning~~
- ~~Sammanvägning av resultaten~~
- ~~Tillförlitligheten i de sammanvägda resultaten bedömd av SBU~~
- ~~Tillförlitligheten i de sammanvägda resultaten bedömd av annan aktör än SBU~~
- ~~Granskning av andras systematiska översikter~~
- ~~Prioritering utförd med hjälp av konsensus~~
- ✔ Medverkan av ämnessakkunniga
- ~~Patient- eller brukarmedverkan~~
- ~~Etiska och sociala aspekter ingår~~
- ~~Ekonomiska aspekter ingår~~
- ✔ Granskning utförd av externa ämnessakkunniga
- ~~Granskning utförd av SBU:s kvalitetsgrupp~~
- ~~Granskning utförd av SBU:s vetenskapliga råd~~
- ~~Slutsatser godkända av SBU:s nämnd~~

1. Inledning

SBU har fått regeringens uppdrag ((S2019/03053/FS) Socialdepartementet) att göra en systematisk kunskapsöversikt av könsdysfori. SBU ska se över det vetenskapliga underlaget för utredning och behandling av barn och unga. Syftet är bland annat att öka kunskapen om långtidseffekter på både fysisk och psykisk hälsa. I uppdraget ingår också att samla kunskap om orsakerna till den ökning av barn och unga i Sverige och andra höginkomstländer som vänder sig till vården för utredning av könsdysfori. I uppdraget ingår även att identifiera kunskapsluckor på området.

SBU har i första hand systematiskt kartlagt den litteratur som tillkommit sedan Socialstyrelsens kunskapsstöd för vård och behandling av barn och unga med könsdysfori publicerades år 2015. I avsnitten om epidemiologin kring förekomsten av könsdysfori samt långtidseffekter efter behandling för könsdysfori, har vi gjort mer utförliga beskrivningar av de refererade artiklarna.

Detta är en sammanställning av den litteratur som avhandlar ämnena för denna rapport. Vi har inte bedömt studiernas kvalitét eller risk för bias och därför kan ingen sammanvägning av resultaten eller evidensbedömning göras. Sammanställningen kan dock ligga till grund för en senare utvärdering av evidensen.

2. Bakgrund

Antalet personer i alla åldrar som söker hälso- och sjukvården på grund av könsidentitetsstörningar (F64 (ICD-10-SE) [1]) ökar [2].

ICD-diagnosen **F64 Könsidentitetsstörningar** undergrupperas i ICD-10-SE som:

- **F64.0 Transsexualism** En önskan om att leva och bli accepterad som en medlem av det motsatta könet, ofta åtföljt av en känsla av obehag eller otillräcklighet med det egna anatomiska könet och en önskan om hormonell eller kirurgisk behandling för att kroppsligen likna det prefererade könet så mycket som möjligt.
- **F64.8 Andra specificerade könsidentitetsstörningar** Utesluter: Egodyston sexuell orientering (F66.1), Störning i sexuell mognad (F66.0).
- **F64.9 Könsidentitetsstörning** ospecificerad, Könsrollsstörning UNS.

Före år 2009 var det förhållandevis få barn och unga som utreddes för könsidentitetsstörningar, men under det senaste decenniet ses en tilltagande ökning. Det är oklart varför detta sker. Det korta tidsperspektivet gör att de studier som publicerats rörande de nya grupperna av barn och unga som söker för könsidentitetsstörning är betydligt färre än studier om vuxna. Studier med uppföljning mer än att par år av barn och unga som påbörjat behandling före 18 års ålder är sällsynta.

3. Frågeställningar och avgränsningar

I denna rapport behandlas enbart publikationer som rör personer som identifierar sig som man eller kvinna (binär).

Följande frågeställningar har belysts:

1. Vad finns det för vetenskapligt underlag rörande A) den epidemiologiska utvecklingen, B) effekter av behandling på lång sikt?
2. Vilken vetenskaplig litteratur har tillkommit om utredning och behandling sedan Socialstyrelsens kunskapsstöd för vård och behandling av barn och unga med könsdysfori publicerades år 2015?

PICO

Fråga 1A

Population: Barn och unga upp till 18 år med könsdysfori.

Insatser: Inte aktuellt.

Kontrollgrupp: Ingen begränsning.

Utfallsmått: Förekomst, incidens och prevalens av könsdysfori samt sökmönster.

Fråga 1B

Population: Personer med könsdysfori.

Insatser: Behandling av könsdysfori.

Kontrollgrupp: Ingen begränsning.

Utfallsmått: Långtidseffekter som mental ohälsa, självmordsförsök, självmord, hjärta–kärl, cancer, skeletthälsa och andel som ångrar sig.

Fråga 2

Population: Barn och unga upp till 18 år.

Insatser: Utredning och behandling av könsdysfori.

Kontrollgrupp: Ingen begränsning.

Utfallsmått: Relevanta studier.

Övriga avgränsningar

En bred litteratursökningen har gjorts över hela diagnosen. I den mån det gått har den övre åldersgränsen för barn och unga satts till 18 år.

Studiedesign och språk

Granskningen begränsas till primära studier med ”peer review” och systematiska översikter där sökning och urval följer PRISMA-riktlinjerna [3] Endast studier på engelska eller skandinaviska språk har beaktats. Fallstudier, mötesabstrakt och editorials har inte tagits med.

Projektprocessen

Litteratursökning

Projektets informationsspecialist utformade och genomförde litteratursökningarna i samråd med projektledaren och projektets sakkunniga. I sökstrategierna användes söktermer ur databasernas olika ämnesordslistor tillsammans med söktermer hämtade ur abstrakt och titlar. Sökstrategierna utvecklades genom att delvis återanvända sökstrategier och söktermer från andra systematiska översikter på området samt genom analys av ett antal nyckelartiklar. Nyckelartiklarna analyserades med hjälp av ordfrekvensanalysverktygen PubReminer samt AntConc. Sökstrategierna kompletterades med relevanta termer från projektgruppsmedlemmar. En testsökning gjordes för att se hur väl de fångat söktermer inom området.

De slutgiltiga litteratursökningarna gjordes i september 2019, och utfördes primärt i följande internationella databaser:

- CINAHL (EBSCO)
- Cochrane Library (Wiley)
- EMBASE (Embase.com)
- PsycINFO (EBSCO)
- PubMed (NLM)
- Scopus (Elsevier)
- SocINDEX (EBSCO)

Sökningen kompletterades med litteratur som identifierats via citeringssökningar i Scopus och i referenslistor från publicerade artiklar.

Litteratursökningen består i huvudsak av två sökningar:

Litteratursökning efter systematiska översikter

En sökning efter de systematiska översikter som tillkommit sedan 2013 (då Socialstyrelsen sökte till sin rapport). Utöver de databaser som nämns ovan,

söktes även följande databaser för att identifiera systematiska översikter: Campbell Library, Epistemonikos, Evidence Search, samt CRD:s databaser DARE, HTA och PROSPERO. Sökningen begränsades till att fånga studier av barn och unga.

Litteratursökning efter originalstudier

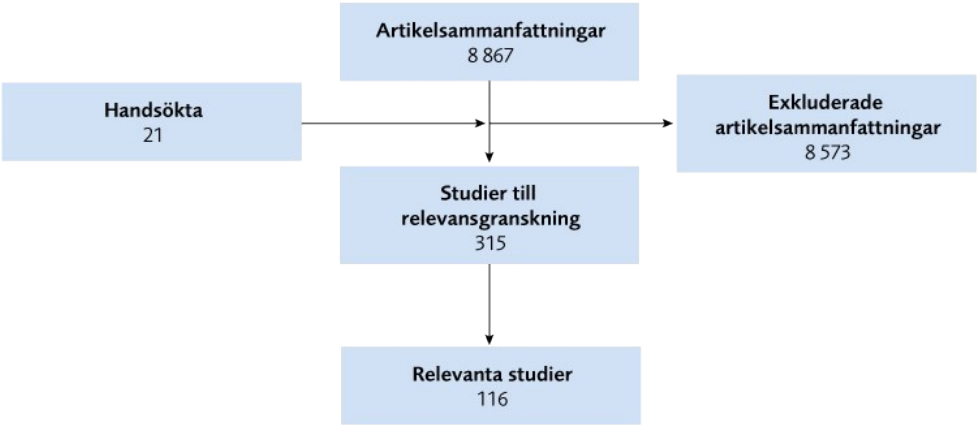
Det gjordes dessutom en sökning efter originalstudier som även begränsades till att fånga studier av barn och unga.

Kompletterande litteratursökningar

Dessutom gjordes en mer precis, kompletterande sökning efter studier med långtidsuppföljning efter påbörjad pubertetshämmande eller könsbekräftande behandling. För denna sökning sattes ingen begränsning i tid och ålderskategori, men sökningen begränsades i stället till uppföljningsstudier samt med termer för utfallsmått. Denna sökstrategi togs delvis fram med hjälp av en referensstandard (ibland benämnt gold standard) bestående av cirka 25 artiklar, identifierade genom huvudsökningen. Den kompletterande sökningen utfördes endast i databaserna PubMed, PsycINFO samt EMBASE.

En citeringssökning av centrala artiklar har gjorts i Scopus för att se i vilka artiklar som studierna citerats.

De använda sökstrategierna presenteras i Bilaga 1.



Figur 1 Flödesschema för ingående studier.

Urval av litteratur

Abstraktlistor har granskats och gallrats internt vid SBU:s kansli.

Studierna har granskats avseende relevans i fulltext av en eller två personer ur referensgruppen tillsammans med projektledaren. Referenspersonerna har inte bedömt artiklar i vilka de själva medverkar. Studiernas risk för bias har inte bedömts.

Tabellering

Relevanta studier har tabellerats efter frågeställning. Artiklar om utredning och behandling tabelleras med utgångspunkt från Socialstyrelsens kunskapsstöd [4].

Syntes

Ingen formell syntes eller evidensgradering av resultat har gjorts.

Artiklar rörande frågeställningarna om epidemiologi och långtidseffekter har redovisats narrativt.

4. Epidemiologi

Antalet barn och unga som söker hälso- och sjukvården på grund av en könsidentitetsstörning ökar. Det är oklart hur stor förekomsten i befolkningen är och om den ändrats över kalendertid. Det är oklart om det ökade antalet sökande beror på att fler i befolkningen upplever en könsidentitetsstörning eller om det är fler som upplever att samhället idag är mer öppet för detta och därmed söker.

Studierna nedan beskrivs i Tabell 1.

Förekomst hos barn och unga

I flera studier har man beskrivit förekomsten av könsdysfori vid en enstaka tidpunkt (prevalensstudier). De flesta av dessa studier rör vuxna [5] [6] [7].

Studier av barn och unga är färre.

Sumia och medförfattare [8] undersökte 719 finska ungdomar, 16–19 år gamla, med en enkät. Vid undersökningstillfället var det 2,2 procent av pojkarna och 0,5 procent av flickorna vars svar tydde på att man vid undersökningstillfället upplevde en könsdysfori.

Kaltiala-Heino och medförfattare [9] rapporterar från en enkätstudie att 3,6 procent pojkar och 2,3 procent flickor, 16–18 år, angav att man upplevde könsdysfori. Samma författargrupp diskuterade i en uppföljande studie tillförlitligheten av enkätdata i detta sammanhang, då man fann orimliga svar i en inte obetydlig utsträckning [10].

Utveckling av barn som uttryckt könsdysfori

Drummonds studie från 2008 [11] följde 25 flickor, 3–12 år, varav 15 hade fått diagnosen könsdysfori enligt Diagnostic and Statistical Manual of Mental Disorders (DSM) III/IV. Övriga hade en könsidentitetsstörning som inte uppfyllde dessa kriterier och hade därmed inte diagnosen könsdysfori. Uppföljning gjordes vid 15–36 års ålder och då bedömdes tre ha könsdysfori. Under perioden från diagnos till uppföljningen hade 18 personer fått någon form av psykologisk rådgivning.

Wallien och Cohen-Kettenis [12] följde 77 barn 5–12 år gamla som uttryckt könsdysfori. Av dem svarade 54 barn på en enkät cirka 10 år (16–28 år, medelålder 19 år) efter första kontakt. Tolv pojkar och 9 flickor angav då att de fortfarande hade en könsdysfori samtidigt som majoriteten, 28 pojkar och 5 flickor, inte upplevde könsdysfori längre. Om och i så fall hur de behandlats framgår inte.

Steensma och medförfattare [13] följde upp 127 ungdomar i åldrarna 15–17 år, som när de var 6–12 år gamla sökt för könsdysfori. Det var 47 stycken som återkommit med fortsatt könsdysfori i genomsnitt cirka 7 år efter första besöket.

De som inte återkommit (80 stycken) fick en enkät där drygt hälften svarade. Av de som lämnade uppgifter hade en del gjort en partiell social övergång (mest flickor) men ingen hade gjort en komplett övergång. En kvalitativ bakgrund till varför man inte behåller sin uppfattning beskrivs också. De som behöll sin upplevelse av fel könsidentitet upplevde en tilltagande dysfori i början av puberteten. Man uppgav att man i barndomen inte hade tänkt så mycket på saken och att man inte upplevt att det hade haft så stor betydelse då.

Strang och medförfattare [14] följde 22 ungdomar, 13–21 år gamla, med autismspektrumdiagnos (ASD) kombinerat med en upplevd könsidentitet som inte överensstämde med det vid födelsen tilldelade könet. Efter 22 månader hade sex stycken ökat sin transsexuella övertygelse, medan hos fyra hade graden av könsdysfori minskat. Övriga var stabila i sin upplevda könsidentitet.

Antalet barn och unga som söker för könsdysfori ökar

Antalet barn och unga som söker sig till hälso- och sjukvården på grund av könsidentitetsstörningar ökar i västvärlden [15] [16] [17] [18] [19] [20]. I Sverige har detta accentuerats det senaste decenniet [2]. I studier från Europa förefaller antalet flickor öka mer över tid än antalet pojkar [15] [17] [18] [19] [20] viket också överensstämmer med utvecklingen i Sverige [2].

De Graaf och medförfattare [21] beskriver 1 215 ungdomar som sökt vid Gender Identity Development Service i London under perioden 2000–2017. Man fann att andelen pojkar var större i åldersgruppen 3–9 år medan andelen flickor var större i åldersgruppen 10–12 år. Andelen flickor som sökt var signifikant högre under perioden 2007–2017 jämfört med åren 2000–2006. Pojkar har i några studier visat sig vara något yngre än flickor när man söker [21] [22].

Orsakerna till ökningen

Bakgrunden till ökningen av antalet barn och unga som söker för könsdysfori är oklar [2] [19]. Det finns inget i den vetenskapliga litteraturen som säkert förklarar ökningen. Studierna är få. Vi vet inte om förekomsten (prevalensen) av könsdysfori ökar i befolkningen eller om ökningen beror på faktorer i samhället som gör att en större andel av de som upplever könsdysfori söker för detta.

Arnoldussen och medförfattare [15] jämförde barn och unga som remitterats för könsdysfori år 2000 och 2016 i Nederländerna (Amsterdam). Samma instrument användes för utvärdering. År 2000 användes DSM-IV-TR och år 2016 DSM-5 för diagnossättning. Man fann en stor likhet mellan de som diagnostiserats år 2000 och 2016 i termer av andel som fick en klar diagnos, andel som fortsatte till pubertetshämmande eller könsbekräftande behandling, genomsnittsålder och grad av könsdysfori. Dock ökade andelen flickor. Eftersom individerna är till synes lika år 2000 och 2016 så kan ökningen bero på att fler upplever könsdysfori, det vill säga en ökad förekomst snarare än att individer med lägre

grad av könsdysfori söker vård.

Littman [23] beskriver ungdomar hos vilka könsdysforin debuterar mycket plötsligt och som av författarna kallades ”Rapid-Onset Gender Dysphoria”. Undersökningen gjordes genom att via tre webbsidor, där föräldrar tidigare lämnat inlägg om snabbt påkommande könsdysfori, erbjuda föräldrar att anonymt svara på ett frågeformulär. Föräldrarna rapporterade bland annat att ungdomarna ökat sitt användande av internet eller haft vänner som identifierat sig som transsexuella strax innan könsdysforin gavs till känna. Studien mötte metodologisk kritik och en uppföljande artikel publicerades där metodik och fynd förtydligades [24].

Acceptansen av transsexualism i samhället är troligen av betydelse. Landén och medförfattare [25] presenterade en enkätstudie gjord 1998 där 992 personer i Sverige tillfrågades om sin inställning till transsexuella personer. Man fann en relativt god acceptans och förhållandevis få var direkt mot. Till exempel uppgav 60 procent av de som svarade att man kunde tänka sig att ha en transperson som vän. Yngre personer och kvinnor hade bäst acceptans. Detta bekräftas i en IPSOS-undersökning från 2018 där man också ser stora skillnader mellan länder [26].

Samsjuklighet

Flera studier beskriver en ökad förekomst av ASD och annan psykiatrisk samsjuklighet hos barn och unga med könsdyfori [20] [27] [28] [29] [30] [31] [32] [33].

Omvänt, van der Miesen och medförfattare [34] undersökte 573 ungdomar (medelålder 16 år) med ASD och fann en högre förekomst könsidentitetsstörning hos dessa än i den omgivande befolkningen. Det var vanligare hos flickor än hos pojkar. Hilse-Gorman och medförfattare [27] genomförde en registerstudie i USA på drygt 48 000 barn 2–18 år (median ålder 12 år) med ASD (ICD-9). Till varje barn matchades fem kontroller ur den omgivande befolkningen. Totalt fann man 66 barn med diagnosen könsfysfori (ICD-9) och förkomsten var drygt 4 gånger högre (oddskvot 4,38 (95 % KI, 2,64 till 7,27), p<0,001) bland de med ASD.

Hur kopplingen mellan ASD och könsdysfori ser ut är dock oklart [35].

Flödet från remiss till behandling

Vi har inte hittat några sammantagna svenska data om hur stor andel av dem som söker för könsidentitetsstörning som får diagnosen transsexualism (F64.0 och F64.9), hur stor andel som börjar pubertetsfördröjande behandling, hur stor andel som börjar könsbekräftande hormonbehandling och hur stor andel som genomgår könsbekräftande kirurgi av olika slag. Bristen på information gäller allmänt och i synnerhet de barn och unga som idag söker vård. Det nationella kvalitetsregister som är under uppbyggnad kommer i framtiden att kunna ge svar

på dessa frågor.

Weipes och medförfattare [36] följde upp 5 433 vuxna med könsdysfori (gender dysphoria) i Nederländerna. Av transkvinnorna (MtF) startade 69 procent könsbekräftande hormonbehandling och av transmännen (FtM) 73 procent. Av de vuxna som sökte under åren 1972–1979 startade 90 procent könsbekräftande hormonbehandling, medan motsvarande andel för dem som sökte under åren 2010–2014 var 65 procent. Av de 812 personer som var mellan 8 och 12 år vid första besöket startade sedermera 29 procent av transkvinnorna (MtF) och 51 procent av transmännen (FtM) pubertetsfördröjande hormonbehandling medan 34 procent av transkvinnorna (MtF) och 31 procent av transmännen (FtM) startade könsbekräftande hormonbehandling utan föregående pubertetsfördröjande behandling. Detta skedde när de var 16 år eller äldre.

Bränström och medförfattare [37] presenterar en svensk registerstudie av de 2 679 personer som fått diagnosen könsidentitetsstörning i Sverige åren 2005–2015. Medelåldern var 31 år. Uppföljning gjordes 2015 år. Av dessa personer blev 70 procent förskrivna könsbekräftande hormonbehandling och 48 procent genomgick någon form av könsbekräftande kirurgi (av dessa 77 % kirurgi av bröst eller hud på bröstkorgen, 53 % genital kirurgi, 31 % hudkirurgi och 7 % kirurgi på struphuvudet).

5. Långtidseffekter på fysisk och psykisk hälsa

Vi har valt att inte definiera en ”lång uppföljningstid”. Istället anges uppföljningstiden i respektive studie i text och tabeller. De följder av den könsbekräftande behandlingen som vi undersökt är oönskade sådana. Effekter som är förväntade som till exempel förändringar i kroppskonstitution och fertilitet, har inte undersökts.

Ökningen av barn och unga (under 18 år) som söker för könsidentitetsstörningar har kommit under det senaste decenniet [2]. På grund av detta är det ännu få publikationer med uppföljning av denna grupp. Därför har vi valt att inkludera studier av och resultat från vuxna personer som underlag för effekter som kommer efter längre tid.

Förekomst av ånger efter könsbekräftande behandling

Studierna nedan beskrivs i Tabell 2.

Litteraturen består i huvudsak av observationsdata från kohorter som undersökts retrospektivt.

Begreppet ånger (regret) har olika innebörd i litteraturen, från att det uttrycks i journaler eller enkäter till att man ansöker om återkonvertering till ursprungligt kön. Besvikelse är också beskrivet, oftast på så vis att man inte är nöjd med någon del av den könsbekräftande behandlingen, till exempel det kosmetiska resultatet av olika typer av kirurgi, men utan att man för den skull ångrar sitt byte av kön.

Vi har inte funnit någon studie som beskriver utvecklingen av ånger över tid efter könsbekräftande behandling och inte heller över kalendertid.

Ånger hos barn och unga

Vi har inte kunnat identifiera några publikationer, som specifikt beskriver ånger/besvikelse efter könsbekräftande behandling i de grupper som tillkommit det senaste decenniet. Det finns studier som omfattar tiden från år 2009 och framåt men i dessa särskiljer författarna inte individer som påbörjat sin behandling som barn och unga från dem som startat behandlingen som vuxna.

Återkonvertering – vuxna

Dhejne och medförfattare [42] undersökte i en retrospektiv journalstudie de 767 personer som under perioden 1960–2010 ansökte om könsbekräftande kirurgi i Sverige. Av dem utfördes kirurgin hos 681 stycken. Man anger ingen uppföljningstid, men givet att man började med personer från 1960 och gjorde uppfölj-

ningen 2012–2013, så torde medianuppföljningstiden vara 20–25 år.

Landén och medförfattare [43] undersökte i en retrospektiv journalstudie de 218 personer som genomgått könsbekräftande kirurgi under perioden 1972–1992 i Sverige, med en uppföljningstid på mellan 4 och 24 år. De undersökta personerna torde också finnas med i den grupp som rapporterades av Dhejne och medförfattare [42].

Ånger uttryckt i enkäter eller journaler – vuxna

Könsbekräftande genital kirurgi

Blanchard och medförfattare [44] utvärderade 111 transsexuella från Kanada som genomgått könsbekräftande genital kirurgi med minst ett års uppföljningstid i en retrospektiv enkätundersökning.

Imbimbo och medförfattare [45] undersökte 163 transkvinnor (MtF) i Italien som genomgått könsbekräftande genital kirurgi 1992–2006 med en retrospektiv enkätundersökning. Uppföljning gjordes med en enkät eller telefonintervju 12–18 månader efter operation.

Johannsson och medförfattare [46] studerade 60 personer, som fått godkänt för könskorrigerande genital kirurgi med semi-strukturerade intervjuer. Undersökningen fullföljdes av 25 transkvinnor (MtF) och 17 transmän (FtM) fem år eller mer efter första besöket eller minimum två år efter könsbekräftande kirurgi.

Annan könsbekräftande kirurgi eller ej specificerat

Lawrence och medförfattare [47] studerade 232 transkvinnor som genomgått könsbekräftande kirurgi (sex reassignment surgery, ej närmare specificerat) mellan 1994 och 2000 i en retrospektiv enkätundersökning i USA. Uppföljningstiden var minst ett år.

Nelson och medförfattare [48] undersökte i en retrospektiv enkätundersökning 15 transmän (FtM), varav 12 svarade, som genomgått bröstreducerande kirurgi år 2000 till 2005. Uppföljning gjordes 2 till 23 månader efter operation.

Defrayne och medförfattare [49] redovisar en systematisk översikt av åtta studier om ånger med olika uttryck efter könsbekräftande kirurgi (bröst, genital, borttagande av testiklar eller äggstockar) hos transmän (FtM). Studierna spänner över tiden från 1960 till 2010. Studierna av Dhejne och medförfattare [42] och Landén och medförfattare [43] ovan är inkluderade i översikten.

Vi har identifierat ytterligare två studier som publicerats efter denna systematiska översikt.

Van de Grift och medförfattare [50] skickade en enkät till 546 personer, 17–63 år gamla (både transkvinnor (MtF) och -män (FtM)) som ansökt om könsbekräftande behandling år 2007 till 2009, 201 personer (37 %) svarade och

136 av dessa hade genomgått någon form av könsbekräftande kirurgi (genital, bröst, ansikte, stämband eller struphuvud).

Wiepjes och medförfattare [36] undersökte 6 793 personer (4 432 män och 2 361 kvinnor vid födelsen) (1 360 under 18 år vid första besök) i Nederländerna. De sökte vid en och samma klinik 1972 till 2015 och utvärderades retrospektivt i en journalstudie. Tiden från start av könsbekräftande hormonbehandling till uppföljning var 46 till 271 månader. Testiklar eller äggstockar hade tagits bort hos 2 627 personer (75 % av alla transkvinnor (MtF) och 84 % av alla transmän (FtM). Alla som ångrat borttagandet av könskörtlarna var mellan 25 och 54 år när de startade könsbekräftande hormonbehandling.

Psykosociala effekter

Studierna nedan beskrivs i Tabell 3.

Den litteratur som identifierats innehåller uteslutande observationsdata från tvärsnittsstudier, eller longitudinella studier före och efter könsbekräftande behandling, där de senare är få. I tvärsnittsstudierna använder man ibland kontroller ur den omgivande befolkningen som jämförelse. Då transsexuella personer redan från början uppvisar en ökad psykosocial problematik, blir dessa jämförelser mindre värdefulla när det gäller att utvärdera effekten av könsbekräftande behandling. Studier före och efter könsbekräftande behandling kan ge en bättre bild av hur behandling av könsdyfori påverkar psykosociala förhållanden, men dessa studier är få.

Barn och unga

Till följd av att könsdysfori hos barn och unga har kommit att öka under det senaste decenniet, är den möjliga uppföljningstiden kort. Det är få studier som konkret studerar psykosociala effekter av könsbekräftande behandling hos barn och unga. Det finns studier där barn och unga är inkluderade men där resultaten för dessa inte redovisas separat.

de Vries och medförfattare [52] följde 22 transflickor (MtF) och 33 transpojkar (FtM) vid tre tillfällen, innan start av pubertetsfördröjande hormonbehandling (medelålder 13,6 år), när könsbekräftande hormoner startades (medelålder 16,7 år) och minst ett år efter könsbekräftande genital kirurgi (medelålder 20,7 år). Personerna sökte könsbekräftande behandling mellan åren 2004 och 2011, inga kontroller förekom i denna studie. Man undersökte könsdysfori, kroppsuppfattning, övergripande funktion, depression, ångest, och beteendestörningar, social och professionell funktion samt upplevd livskvalitet och nöjdhet.

Vuxna eller ospecificerad ålder

Hormonbehandling eller ospecificerad behandling

Bränström och Pachankis ([37] presenterade nyligen en stor retrospektiv tvärsnittsstudie från Sverige. De 2 679 personer som fått diagnosen könsidentitetsstörning i Sverige åren 2005–2015 (medelålder 32 år) jämfördes med den totala svenska befolkningen (medelålder 41 år). Uppföljningen gjordes 2015 vilket betyder en uppskattad medianuppföljningstid på cirka 5 år. Utfallet mättes som förekomst av händelser tiden från 1 januari, 2015 till 31 december, 2015. Någon mätning före den könsbekräftande behandlingen gjordes inte.

Costa och medförfattare [39] presenterade en systematisk översikt utan metaanalys om effekten av könsbekräftande hormonbehandling. Studien baserades på litteraturen fram till år 2015. Man fann 17 observationsstudier varav 11 tvärsnittsstudier och 6 longitudinella studier.

Dhejne och medförfattare [53] publicerade en systematisk översikt med en begränsad sökning. Man fann 38 studier som uppfyllde kriterierna för översikten. I alla studierna var personerna över 18 år. Av dessa var majoriteten tvärsnittsstudier och 11 var studier med uppföljning över tid.

Gómez-Gil och medförfattare [54] undersökte ångest och depression i en tvärsnittsstudie av 120 vuxna spanska transsexuella (84 transkvinnor (MtF) och 36 transmän (FtM)) med könsbekräftande hormonbehandling (medelbehandlingstid sex år). Dessa jämfördes med 67 transpersoner (29 transkvinnor (MtF) och 38 transmän (FtM)) som var under utredning och ännu inte behandlats. Medelåldern var 33 år hos de behandlade och 26 år bland de obehandlade.

Keo-Meier och medförfattare [55] undersökte bland annat depression med ett frågeformulär hos 48 transmän (FtM), 16–54 år gamla, i USA. Man jämförde med 53 män (18–50 år) och 62 kvinnor (18–54 år) som matchades ur den omgivande befolkningen. Transmännen (FtM) svarade på frågorna strax innan och tre månader efter start av könsbekräftande hormonbehandling.

Millet och medförfattare [56] gjorde en systematisk översikt utan metaanalys av 17 tvärsnittsstudier och 8 longitudinella studier rörande ångest hos transsexuella. Behandling specificerades inte.

Murad och medförfattare [57] sammanfattar litteraturen fram till och med år 2007 i en systematisk översikt utan metaanalys. Man fann 28 studier varav åtta hade longitudinell uppföljning. Alla patienter i studierna var över 18 år och behandlades med könsbekräftande hormonbehandling.

Owen-Smith och medförfattare [58] rapporterar från en tvärsnittsstudie i USA där man sände en enkät till 2 136 vuxna transpersoner varav 697 svarade, 347 transmän (FtM) och 350 transkvinnor (MtF). Man undersökte ångest och depression i olika behandlingsgrupper. I studien fanns inga kontroller.

Rowiniak och medförfattare [59] rapporterar en systematisk översikt av studier om livskvalitet, ångest och depression efter könsbekräftande hormonbehandling, och utan åldersbegränsning. Sju studier inkluderades, tre tvärsnittsstudier och

fyra longitudinella studier, publicerade mellan åren 2008 och 2017.

Tomita och medförfattare [60] undersökte 868 transsexuella i USA, 363 transkvinnor (MtF) och 505 transmän (FtM) med en medelålder på 37 respektive 31 år. Alla var över 18 år. Man jämförde de som fått könsbekräftande behandling av något slag med dem som ännu inte behandlats.

Könsbekräftande kirurgi

Dhejne och medförfattare [61] undersökte självmord, självmordsförsök och andra psykiatriska tillstånd hos alla 324 (191 transkvinnor (MtF) och 133 transmän (FtM)) över 18 år som bytt legalt kön mellan 1973–2003. Till var och en av dessa matchades tio slumpmässigt utvalda personer ur den omgivande befolkningen. Två olika kontrollgrupper användes, en med samma kön som den transsexuelle haft vid födelsen och en grupp med det kön som man bytt till. Medeluppföljningstid anges inte men en del av gruppen kunde följas upp till 30 år.

Jellerstad och medförfattare [62] undersökte livskvalitet och depression i en tvärsnittsstudie med enkät hos 143 schweiziska transsexuella, alla äldre än 18 år. Flertalet hade genomgått könsbekräftande kirurgi varav 63 genital kirurgi. Resultaten jämfördes med standardresultat från den omgivande befolkningen.

Lindquist och medförfattare [63] undersökte livskvaliteten hos 190 transkvinnor (MtF) (medelålder 36 år, alla över 18 år) som genomgått könsbekräftande genital kirurgi år 2003–2015 vid en klinik. Man svarade på enkätfrågor före operation samt efter 1, 3 och 5 år. Antalet som svarade vid tidpunkterna var 146, 108, 64 respektive 43 stycken. Svaren jämfördes med standardvärden från befolkningen.

Ruppin och medförfattare [64] gjorde en longitudinell undersökning av 71 av totalt 140 möjliga transpersoner. Medelåldern var 47 år, 35 var transkvinnor (MtF) och 36 transmän (FtM) i Tyskland som alla bytt legalt kön. Alla hade genomgått könsbekräftande behandling och majoriteten genital kirurgi. Det frågeformulär som använts vid första besöket användes igen och intervjuer genomfördes. Uppföljningstiden var mellan 10 och 24 år (medeluppföljningstid 14 år).

Simonsen och medförfattare [65] undersökte ångest, depression, antal som haft någon psykiatrisk diagnos och dödsfall bland 56 transkvinnor (MtF) och 48 transmän (FtM), alla vuxna, i Danmark. Samtliga hade kastrerats och hade tillåtelse att genomgå könsbekräftande kirurgi. Undersökningen gjordes före och efter operation.

Weinforth och medförfattare [66] har publicerat en systematisk översikt om livskvalitet efter könsbekräftande genital kirurgi hos transkvinnor (MtF). Översikten omfattade 13 artiklar (under åren 2006–2017) som gav information om 1 101 individer med en medelålder på 40 år. De flesta studierna var tvärsnittsstudier och fyra var longitudinella. Sju olika frågeinstrument hade använts.

Wernick och medförfattare [67] har publicerat en systematisk översikt om psykologiska utfall av könsbekräftande kirurgi av olika typer. Beskrivningen är narrativ. Man fann 16 före- och efterstudier och 17 tvärsnittsstudier (under åren 1982–2018) med någon typ av kontrollgrupp. Sättet att mäta det psykologiska utfallet i de olika studierna varierade och en gemensam metodik för detta efterlystes.

Weyers och medförfattare [68] undersökte fysisk, mental och sexuell hälsa hos 50 transkvinnor (MtF) i Nederländerna i en enkätstudie. Medelåldern var 43 år. Alla hade genomgått könsbekräftande genital kirurgi och undersökningen gjordes i medeltal 75 månader efter operation. Studien hade ingen jämförelsegrupp.

Özata Yildizhan och medförfattare [69] intervjuade 20 transpersoner i Turkiet som genomgått könsbekräftande genital kirurgi 1–22 år tidigare och jämförde dem med 50 transpersoner som inte genomgått kirurgi. Medelåldern i grupperna var 33 respektive 27 år. Livskvaliteten utvärderades inte.

Kognitiva funktioner och hjärnstruktur

Studierna nedan beskrivs i Tabell 4.

Pubertetshämmande hormonbehandling av barn och unga

Staphorsius och medförfattare [70] jämförde åtta transflickor (MtF) och tolv transpojkar (FtM) som behandlades med pubertetshämmande hormonbehandling med tio transflickor (MtF) och tio transpojkar (FtM) som inte behandlats. Medelåldern i grupperna varierade från 14 till 16 år. Magnetskameraundersökning gjordes i medeltal 1,4 till 1,8 år efter start av den pubertetshämmande behandlingen.

Könsbekräftande hormon behandling hos vuxna

Schneider och medförfattare [71] undersökte Brain-derived neurotrophic factor (BNDF), bland annat kopplade till återhämtning efter hjärnkirurgi och psykiska reaktioner till omgivningsfaktorer, i serum hos 32 transkvinnor (MtF), alla äldre än 18 år. Undersökningarna gjordes före och efter könsbekräftande hormonell och kirurgisk behandling.

Nyugen och medförfattare [72] har i en systematisk översikt sammanställt artiklar som behandlar effekter av könsbekräftande hormonbehandling på hjärnans struktur, neuronal aktivering i hjärnan samt kognitiva funktioner hos vuxna. De ingående artiklarna var publicerade mellan åren 1994 och 2017. Åtta studier, två tvärsnittsstudier och sex longitudinella studier, beskriver MRI-detekterade förändringar i hjärnans struktur. Fem artiklar, två tvärsnittsstudier och tre longitudinella studier, alla med MRI av hjärnan, beskriver effekten på neuronal aktivering i hjärnan. Sex studier, två tvärsnittsstudier, tre longitudinella studier och en både tvärsnitts- och longitudinell studie, beskriver kognitiva effekter som

rumsuppfattning och verbal förmåga.

Cancerutveckling

Studierna nedan beskrivs i Tabell 5.

Det finns en teoretisk risk för uppkomst av hormonberoende cancertumörer efter den könsbekräftande hormonbehandling som ges över lång tid, testosteron till transmän (FtM) och östrogener till transkvinnor (MtF). I första hand är det frågan om bröstcancer och prostatacancer hos transkvinnor (MtF) och bröstcancer hos transmän (FtM). Övergripande finner man i studierna förhållandevis få fall av cancer och det är därmed svårt att dra säkra slutsatser i förhållande till den omgivande befolkningen och därmed bedöma risken med könsbekräftande östrogen- respektive testosteronbehandling.

Det finns enstaka publikationer om andra typer av tumörer.

Barn och unga

Vi har inte kunnat identifiera några studier som specifikt undersöker cancerutveckling hos barn och unga efter pubertetshämmande behandling.

Vuxna

Vi har identifierat två större systematiska översikter av cancerutveckling och könsbekräftande hormonbehandling [73] [74].

Vi har identifierat två studier som publicerats efter de två översikterna ovan.

De Blok och medförfattare [75] undersökte risken att få bröstcancer hos 2 260 transkvinnor (MtF) med en medelbehandlingstid av 18 år (7–37 år) efter insättande av östrogen. Man använde en befolkningsjämförelse för att räkna fram en standardiserad incidenskvot. Man undersökte också 1 229 transmän (FtM) med en medelbehandlingstid av 15 år (2–17 år).

Nota och medförfattare [76] undersökte förekomst av tumörer i skallen, särskilt meningiom och prolaktinom (båda tumörer i skallen men godartade) hos transkvinnor (MtF) och transmän (FtM) som man jämförde med kvinnor och män i den nederländska befolkningen.

Effekter på hjärta-kärl

Studierna nedan beskrivs i Tabell 5.

Det finns förhållandevis få aktuella studier. Det vetenskapliga underlaget är därför sparsamt. Sättet som hormoner administreras, som tabletter (peroralt), som injektioner (parenteralt) eller som plåster eller gel (transdermalt), är troligen av betydelse. Transdermala metoder (plåster, gel) har kommit i ett senare tidsskede och tidiga studier rör därför troligen behandling peroralt eller med injek-

tioner. Förekomsten av hjärt- och kärlsjukdomar måste också sättas i relation till andra riskfaktorer som rökning etc.

Barn och unga

Vi har inte kunnat identifiera några studier som specifikt undersöker effekter på hjärta och kärl hos barn och unga med könsdysfori som fått pubertetshämmande eller könsbekräftande hormonbehandling.

Vuxna eller ålder inte specificerad

Maraka och medförfattare [77] presenterade en systematisk översikt och meta-analys av litteraturen fram till april 2015 om blodfettsförändringar vid könsbekräftande hormonbehandling. Man fann 29 studier med en uppföljning på 3–24 månader.

van Velzen och medförfattare [78] undersökte blodtryck och blodfetter vid könsbekräftande hormonbehandling prospektivt. Data sammanställdes från verksamheter i Nederländerna, Belgien, Norge och Italien. Prover togs före och 12 månader efter insatt könsbekräftande hormonbehandling hos 242 transkvinnor (MtF) och 188 transmän (FtM) under åren 2010–2017.

Wierckx och medförfattare [51] undersökte venös trombos och lungemboli hos 214 transkvinnor (MtF) och 138 transmän (FtM) som jämfördes med matchade personer från en annan studie.

Getahun och medförfattare [79] undersökte ischemisk stroke och hjärtinfarkt samt venös trombos hos 2 842 transkvinnor (MtF) och 26 118 transmän (FtM) i en registerstudie i USA. Varje transperson matchades till 10 män och 10 kvinnor vardera ur den omgivande befolkningen. Uppföljning gjordes 2 och 8 år efter behandlingsstart. Medeluppföljningstid för transkvinnor (MtF) och transmän (FtM) var 4 respektive 3,6 år.

Dutra och medförfattare [80] redovisar 2019 en översikt av fall–kontroll- och tvärsnittsstudier om utveckling av metabola förändringar (blodfetter, etc) relaterade till hjärt- och kärlsjukdom och också hjärt- och kärlsjukdomar hos transkvinnor (MtF) och transmän (FtM). Sökningen gjordes enbart i PubMed.

Goldstien och medförfattare [81] redovisar 2019 en systematisk översikt av 13 observationsstudier publicerade 1989–2018 av östrogenbehandling hos transkvinnor (MtF).

Kahn och medförfattare [82] redovisar 2019 en systematisk översikt av 12 okontrollerade kohortsstudier av risk för venös tombos hos transkvinnor (MtF).

Skeletthälsa

Studierna nedan beskrivs i Tabell 5.

Pubertetshämmande hormonbehandling av barn och unga

Vi har inte identifierat någon publikation som rapporterar långsiktig effekt på benmassa/kvalitet vid pubertetshämmande GnRH-behandling av barn och unga med könsdysfori. Vi har heller inte funnit några studier som beroende på olika benmognadsgrad vid start av GnRH-behandling, följt upp effekten av östrogen- respektive testosteronbehandling förbi tidpunkten för uppnådd maximal benmassa (peak bone mass).

Vi har funnit två studier [83] [84] som beskriver benhälsa hos unga med kort uppföljning.

Benmassan ökar under puberteten under inflytande av framför allt könshormon, särskilt östrogen. Maximal benmassa uppnås vanligen i 20–25-årsåldern. Normalt minskar därefter benmassan med ökande ålder och sjunkande könshormonnivåer. Minskningstakten påverkas av livsstilsfaktorer såsom fysisk aktivitet, vikt, kalk och vitamin-D-intag, rökning med mera, samt halten av könshormon i blodet. En stor maximal benmassa minskar således risken för att i högre åldrar drabbas av skört skelett (osteoporos) med risk för invalidiserande frakturer och hög sjukvårdskonsumtion.

Nivån för uppnådd maximal benmassa för ungdomar med könsdysfori kan förväntas påverkas av graden av pubertetsutveckling och benmognad vid start av GnRH-behandling, hur länge den pågår och av efterföljande könsbekräftande hormonbehandling. En medicinskt viktig fråga är om en normal maximal benmassa kan uppnås efter könsbekräftande hormonbehandling, som påbörjas senare än den normala åldern för pubertet, och om tidpunkten för maximal benmassa senareläggs. Såväl administrationssätt (tablett eller plåster/gel/injektion), hormontyp, dosökningstempo och underhållsdosering/blodkoncentrationer för respektive könshormon har betydelse.

Joseph och medförfattare [83] studerade benmassan (bone mineral density, BMD) efter ett års pubertetshämmande hormonbehandling hos 70 transflickor (MtF) och transpojkar (FtM). Man studerade dels den absoluta benmassan, dels det relativa värdet (Z-score) i förhållande till värden från ungdomar ur den omgivande befolkningen med fysiologiskt ökande benmassa under puberteten.

Klink och medförfattare [84] följde 15 transkvinnor (MtF) och 17 transmän (FtM) upp till 22 års ålder vilka erhållit GnRH vid en medelålder av 15 år, samt från cirka 16 års ålder även könsbekräftande hormon.

Könsbekräftande hormonbehandling av vuxna

Tydligt är att kvinnor får en benskörhet och frakturbenägenhet efter klimakteriet. Män som kastrerats på grund av utbredd prostatacancer, och därigenom får en testosteron brist, har också en ökad risk för osteoporosrelaterade frakturer. Könshormoner är därmed av betydelsen för skeletthälsan.

Singh-Ospina och medförfattare [85] redovisar en systematisk översikt av 13

studier, alla okontrollerade kohorer, publicerade 1996–2015, av benhälsan hos 247 transmän (FtM) och 392 transkvinnor (MtF) före behandling med könskonträra hormoner, samt 12 och 24 månader efter behandlingsstart.

Fighera och medförfattare [86] redovisar 2019 en systematisk översikt av 19 publikationer av könskonträr hormonbehandling av transmän (FtM) (behandlingstid 12 månader till 18 år) eller transkvinnor (MtF) (behandlingstid 12 månader till 16 år). Bland transkvinnorna var den vanligaste kombinationen cyproteronacetat med peroralt estradiol. Fyra studier med 24 månaders före och efter design studerade effekten av GnRH med samtidig östrogenbehandling hos transkvinnor (MtF) med en medelålder på cirka 38 år. De vuxna transmännen (FtM) behandlades med parenteralt testosteron. Bedömning av BMD gjordes med dual-energy x-ray absorptiometry (DXA).

Efter dessa systematiska översikter har ytterliga tre studier identifierats.

Wiepjes och medförfattare [87] undersökte i journaldata benmassan och frakturrisk retrospektivt har vuxna, 1 089 transkvinnor (MtF) (medianuppföljningstid 8 år) och 1 036 transmän (FtM) (medianuppföljningstid 9 år) under 50 års ålder. Fem kvinnor och fem män ur den omgivande befolkningen matchades till varje fall, det vill säga tio kontroller till varje fall. Man undersökte också 934 transkvinnor (MtF) äldre än 50 år (medianuppföljningstid 19 år).

Wiepjes och medförfattare [88] undersökte retrospektivt i journaldata vuxna individer benmassa, 711 transkvinnor (MtF) och 543 transmän (FtM) som sökt åren 1998 till 2016 och som genomgått en DXA-mätning innan könskonträr hormonbehandling, vilken påbörjades efter tidigast 18 års ålder. För transkvinnor (MtF) kombinerades östrogenet med antiandrogen behandling till dess att orchidektomi utfördes, det vill säga i regel under 1–1,5 års tid. Uppföljande DXA-mätningar gjordes efter 2, 5 och 10 år av hormonbehandling.

Wiepjes och medförfattare [89] undersökte skelettstrukturen retrospektivt i journaldata vuxna, 535 transkvinnor (MtF) och 473 transmän (FtM) indelade efter ålder (20–29; 30–39; 40–59 år). Varje åldersgrupp delades in efter längd på hormonbehandling (5, 15, 25 år).

Behandling av barn och unga

Följande avsnitt bygger på Socialstyrelsens nationella kunskapsstöd ”God vård av barn och unga med könsdysfori” från år 2015. Vi redovisar här de studier som tillkommit sedan 2013 och bedömts vara relevanta för behandling av barn och unga med könsdysfori. Någon bedömning av risk för bias har inte gjorts och därmed heller ingen evidensbedömning. Samma studie kan förekomma i flera avsnitt om den innehåller flera relevanta frågeställningar. En del av studierna återfinns tidigare i denna rapport men redovisas också här för fullständighetens skull.

Det finns få studier av könsbekräftande kirurgi på barn och unga och då särskilt genital kirurgi. Vi har därför valt att inkludera studier som berör detta som är

publicerade tidigare än 2013.

Studierna beskrivs i Tabell 6.

6. Andra översikter

År 2018 publicerades en systematisk översikt från HTA-centrum i Västra Götalandsregionen om könsbekräftande kirurgi vid könsdysfori, risker och effekter [123]. Rapporten behandlar alla typer av könsbekräftande kirurgi utan några åldersavgränsningar. Sista litteratursökningen gjordes januari till april 2018. Man sammanfattar sina fynd med att antalet patienter diagnosticerade med könsdysfori ökar snabbt liksom antalet könsbekräftande kirurgiska ingrepp. Översikten visar att det vetenskapliga underlaget för könsbekräftande kirurgi är litet, litteraturen är begränsad till observationsstudier med generellt sett låg kvalitet, jämförande studier är mycket få och långtidsdata saknas varför evidensläget för nyttan av genitala, övriga kroppsliga ingrepp inklusive i ansiktet, generellt är otillräckligt, medan allvarliga komplikationer troligen är vanliga efter genital könsbekräftande kirurgi (GRADE ⨁⨁⨁◯). De flesta patienter värderar effekterna av ingreppen högt. Könsbekräftande kirurgiska ingrepp behöver utföras inom ramen för forskningsprojekt för att förbättra kunskapen om nytta och risker".

Pågående systematiskaöversikter

Vid sökningen i september 2019 fanns 23 systematiska översikter registrerade som pågående i PROSPERO-databasen där bland annat organisationer som SBU registrerar sina pågående projekt (se Tabell 7).

Status för dessa kontrollerades i oktober 2019 och då var ingen av dessa publicerad.

7. Diskussion

Vi har inte kunnat identifiera några studier som förklarar den ökning av barn och unga som under det senaste decenniet sökt för könsdysfori. Det finns inga studier om och i så fall hur förekomsten av könsdysfori i samhället förändrats över tid och inte heller på eventuella faktorer i samhället som kan förklara ökningen av dem som söker på grund av könsdysfori.

Studierna rörande effekter på längre sikt hos barn och unga är få. För att kunna bedöma detta är man därför hänvisad till studier på vuxna personer. Även här är studierna med lång uppföljning förhållandevis få. Sådana studier är angelägna att starta för alla ålderskategorier.

Den litteratur som kunnat identifieras rörande könsdysfori är generellt sparsam. Det är få studier som specifikt undersöker barn och unga. Det kan förklaras av att den stora ökningen av sökande till hälso- och sjukvården för utredning av könsdysfori har skett under det senast decenniet vilket medför att uppföljningstiden för dessa grupper är kort.

Den vetenskapliga aktiviteten inom området är hög. En stor andel av de artiklar som finns i vår systematiska sökning är publicerade under år 2019 och det finns ett stort antal planerade eller pågående systematiska översikter registrerade i PROSPERO-databasen. Man kan anta att kunskapsmassan inom området kommer att öka under de närmaste åren.

Det mesta av den identifierade litteraturen är observationsstudier av kohorter. En mindre andel av dessa beskriver förhållanden före och efter pubertetshämmande och könsbekräftande behandling. Få studier är på något sätt kontrollerade. Vanligen har man gjort jämförelser mot ett urval, ibland matchade på ålder, ur den omgivande befolkningen. Randomiserade studier torde vara svåra att göra bland annat av etiska skäl.

Vi har funnit ett antal nyligen publicerade systematiska översikter. Studier som ingår i dessa översikter har vi oftast inte kommenterat.

En stor andel av de studier som identifierats som relevanta kommer från Nederländerna och det centrum som finns i Amsterdam. Man har där lång erfarenhet och möjlighet till studier med lång uppföljning av många patienter. Studierna begränsas till den modell för utredning och behandling som man introducerat. Detta är också den modell som används i Sverige. Det finns andra förhållningsätt, exempelvis i USA där man till exempel inte använder pubertetshämmande behandling i lika stor utsträckning. Detta beror bland annat på vad försäkringsbolagen bedömer att man ska ersätta [110].

Det finns ingen sammantagen nationell information i Sverige om hur stor andel av dem som söker eller remitteras för könsidentitetsstörning som får diagnosen transsexualism. Inte heller den andel som påbörjar pubertetsfördröjande behandling, som börjar med könsbekräftande hormonbehandling och som genomgår

könsbekräftande kirurgi av olika slag. Bristen på information gäller allmänt och i synnerhet de barn och unga som idag söker vård. Vården av personer med könsdysfori sker inom ramen för olika verksamheter. Att på nationell nivå sammanställa data för hela behandlingsförloppet skulle kräva ett särskilt projekt över klinikgränser. Det nationella kvalitetsregister som är under uppbyggnad kommer i framtiden förhoppningsvis att kunna ge svar på dessa frågor.

8. Ordlista

ASD
Autismspektrumdiagnos (autism spectrum disorder)

BMD
Bone Mineral Density, bentäthet

DSM
Diagnostic and Statistical Manual of Mental Disorders

DXA
Dual-Energy X-ray Absorptiometry, metod att mäta bentäthet

GnRH
Gonadotropin Realeasing Hormone, gonadotropinfrisättande hormon som stimulerar testiklar och äggstockar att producera könshormoner

ICD
International Classification of Diseases

MRI
Magnetic Resonance Investigation, magnetkameraundersökning

PBM
Peak Bone Mass, maximalt uppnådd benmassa

Terminologi i rapporten

Transkvinna, tilldelat kön som man vid födseln som identifierar sig som kvinna (Male to Female, (MtF)).

Transman, tilldelat kön som kvinna vid födseln som identifierar sig som man (Female to Male, (FtM))

Könsbekräftande behandling, i litteraturen används vanligen ”gender affirming treatment” vilket kan översättas som könsbekräftande behandling. Begreppet används i rapporten i den meningen att det som bekräftas är den könsidentitet som personen upplever.

Könsbekräftande kirurgi, kirurgisk behandling av genitalia, yttre och inre, bröst, hud, ansikte, stämband och/eller struphuvud.

Könsbekräftande hormonbehandling: vanligen östrogener till transkvinnor (MtF) och testosteron till transmän (FtM), benämns också könskonträr hormonbehandling.

Pubertetshämmande behandling; Behandlingen kan inledas tidigast efter

pubertetsstart och stänger ned produktionen av könshormonfrisättande hormon (GnRH) vilket innebär att produktionen av östrogen respektive testosteron avstannar och därmed också pubertetsutvecklingen.

Könsdysfori: ett psykiskt lidande eller en försämrad förmåga att fungera i vardagen som orsakas av upplevelsen av sin könsidentitet relaterat till det vid födseln tilldelade könet.

9. Projektgrupp och externa granskare

Referensgrupp

- Jonas F. Ludvigsson, Professor i epidemiologi, Karolinska Institutet, barnläkare, Örebro Universitetssjukhus
- Berit Kriström, Docent, överläkare, barnendokrinolog, Umeå universitetssjukhus
- Mikael Landén, Professor i psykiatri, Sektionen för psykiatri och neurokemi, Institutionen för neurovetenskap och fysiologi, Sahlgrenska akademin, Göteborg
- Per-Anders Rydelius, Professor Emeritus, Barn- och Ungdomspsykiatri, Karolinska institutet

SBU

- Jan Adolfsson, projektledare
- Malin Höistad, utredare
- Kerstin Mothander, assistent
- Hanna Olofsson, informationsspecialist
- Anneth Syversson, projektadministratör

Granskare från SBU:s vetenskapliga råd

- Ulrik Kihlbom, Uppsala universitet
- Lars Sandman, Linköpings universitet
- Mussie Msghina, Örebro universitet

Externa granskare

- Anne Wæhre, Ph D, Overlege, Rikshospitalet, Oslo, Norge
- Maria Elfving, docent, överläkare, barnendokrinolog, Skånes universitetssjukhus

SBU anlitar externa granskare av sina rapporter. De har kommit med värdefulla kommentarer, som i hög grad bidragit till att förbättra rapporten. I slutversionen av rapporten är det möjligt att SBU inte kunnat tillgodose alla ändrings- eller tilläggsförslag från de externa granskarna, bland annat därför att de inte alltid varit samstämmiga. De externa granskarna står därför inte nödvändigtvis bakom

samtliga slutsatser eller andra texter i rapporten.

10. Referenser

1. Socialstyrelsen. Internationell statistisk klassifikation av sjukdomar och relaterade hälsoproblem. Systematisk förteckning. Svensk version 2019.https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/klassifikationer-och-koder/2019-1-12.pdf.
2. Landén M. [Dramatic increase in adolescent gender dysphoria requires careful consideration]. Läkartidningen 2019;116:FSMH.
3. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.
4. Socialstyrelsen. God vård av barn och ungdomar med könsdysfori. Nationellt kunskapsstöd. (https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/kunskapsstod/2015-4-6.pdf).
5. Åhs JW, Dhejne C, Magnusson C, Dal H, Lundin A, Arver S, et al. Proportion of adults in the general population of Stockholm County who want gender-affirming medical treatment. PLoS One 2018;13:e0204606.
6. Judge C, O'Donovan C, Callaghan G, Gaoatswe G, O'Shea D. Gender dysphoria - prevalence and co-morbidities in an irish adult population. Front Endocrinol (Lausanne) 2014;5:87.
7. Kuyper L, Wijsen C. Gender identities and gender dysphoria in the Netherlands. Arch Sex Behav 2014;43:377-85.
8. Sumia M, Lindberg N, Työläjärvi M, Kaltiala-Heino R. Current and recalled childhood gender identity in community youth in comparison to referred adolescents seeking sex reassignment. J Adolesc 2017;56:34-9.
9. Kaltiala-Heino R, Työläjärvi M, Lindberg N. Gender dysphoria in adolescent population: A 5-year replication study. Clin Child Psychol Psychiatry 2019;24:379-87.
10. Kaltiala-Heino R, Lindberg N. Gender identities in adolescent population: Methodological issues and prevalence across age groups. Eur Psychiatry 2019;55:61-6.
11. Drummond KD, Bradley SJ, Peterson-Badali M, Zucker KJ. A follow-up study of girls with gender identity disorder. Dev Psychol 2008;44:34-45.
12. Wallien MS, Cohen-Kettenis PT. Psychosexual outcome of gender-dysphoric children. J Am Acad Child Adolesc Psychiatry 2008;47:1413-23.
13. Steensma TD, McGuire JK, Kreukels BP, Beekman AJ, Cohen-Kettenis PT. Factors associated with desistence and persistence of childhood gender dysphoria: a quantitative follow-up study. J Am Acad Child Adolesc Psychiatry 2013;52:582-90.
14. Strang JF, Powers MD, Knauss M, Sibarium E, Leibowitz SF, Kenworthy L, et al. "They thought it was an obsession": Trajectories and perspectives of autistic transgender and gender-diverse Aadolescents. J Autism Dev Disord 2018;48:4039-55.

15. Arnoldussen M, Steensma TD, Popma A, van der Miesen AIR, Twisk JWR, de Vries ALC. Re-evaluation of the Dutch approach: are recently referred transgender youth different compared to earlier referrals? Eur Child Adolesc Psychiatry 2019. doi: 10.1007/s00787-019-01394-6 (Epub ahead of print).
16. Chen M, Fuqua J, Eugster EA. Characteristics of referrals for gender dysphoria over a 13-year period. J Adolesc Health 2016;58:369-71.
17. Chiniara LN, Bonifacio HJ, Palmert MR. Characteristics of adolescents referred to a gender clinic: Are youth seen now different from those in initial reports? Horm Res Paediatr 2018;89:434-41.
18. de Graaf NM, Giovanardi G, Zitz C, Carmichael P. Sex ratio in children and adolescents referred to the Gender Identity Development Service in the UK (2009–2016). Arch Sex Behav 2018;47:1301-4.
19. Kaltiala-Heino R, Bergman H, Carmichael P, de Graaf NM, Egebjerg Rischel K, Frisén L, et al. Time trends in referrals to child adolescent gender identity services: a study in four Nordic countries and in the UK. Nord J Psychiatry 2019;26:1-6 (Epub ahead of print).
20. Kaltiala-Heino R, Sumia M, Työläjärvi M, Lindberg N. Two years of gender identity service for minors: overrepresentation of natal girls with severe problems in adolescent development. Child Adolesc Psychiatry Ment Health 2015;9:9.
21. de Graaf NM, Carmichael P, Steensma TD, Zucker KJ. Evidence for a change in the sex ratio of children referred for gender dysphoria: Data from the Gender Identity Development Service in London (2000–2017). J Sex Med 2018;15:1381-3.
22. Becker-Hebly I, Gjergji V, Romer G, Möller B. Merkmale von kindern und jugendlichen mit geschlechtsdysphorie in der Hamburger Spezialsprechstunde [Characteristics of children and adolescents with gender dysphoria referred to the Hamburg Gender Identity Clinic]. Praxis der Kinderpsychologie und Kinderpsychiatrie 2014;63:486-509.
23. Littman L. Rapid-onset gender dysphoria in adolescents and young adults: A study of parental reports. PLoS One 2018;13(8).
24. Littman L. Correction: Parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria. PLoS One 2019;14(3):e0214157.
25. Landén M, Innala S. Attitudes toward transsexualism in a Swedish national survey. Arch Sex Behav 2000;29:375-88.
26. IPSOS. Global attitudes towards transgender people, 2018. https://www.ipsos.com/sites/default/files/ct/news/documents/2018-01/ipsos_report-transgender_global_data-2018.pdf
27. Hisle-Gorman E, Landis CA, Susi A, Schvey NA, Gorman GH, Nylund CM, et al. Gender dysphoria in children with autism spectrum disorder. LGBT Health 2019;6:95-100.
28. Nabbijohn AN, van der Miesen AIR, Santarossa A, Peragine D, de Vries ALC, Popma A, et al. Gender variance and the autism spectrum: An examination of children ages 6-12 years. J Autism Dev Disord

2019;49:1570-85.
29. Becerra-Culqui TA, Liu Y, Nash R, Cromwell L, Flanders WD, Getahun D, et al. Mental health of transgender and gender nonconforming youth compared with their peers. Pediatrics 2018;141. pii: e20173845. doi: 10.1542/peds.2017-3845.
30. Mann GE, Taylor A, Wren B, de Graaf N. Review of the literature on self-injurious thoughts and behaviours in gender-diverse children and young people in the United Kingdom. Clin Child Psychol Psychiatry 2019;24:304-21.
31. Nordahl-Hansen A, Cicchetti DV, Øien RA. A review update on gender dysphoria and ASD and response to corrections. J Autism Dev Disord 2019;49:1745-8.
32. Øien RA, Cicchetti DV, Nordahl-Hansen A. Gender dysphoria, sexuality and autism spectrum disorders: A systematic map review. J Autism Dev Disord 2018;48:4028-37.
33. Kuper LE, Mathews S, Lau M. Baseline mental health and psychosocial functioning of transgender adolescents seeking gender-affirming hormone therapy. J Dev Behav Pediatr 2019;40:589-96.
34. van der Miesen AIR, Hurley H, Bal AM, de Vries ALC. Prevalence of the wish to be of the opposite gender in adolescents and adults with autism spectrum disorder. Arch Sex Behav 2018;47:2307-17.
35. Turban JL, van Schalkwyk GI. 'Gender dysphoria' and autism spectrum disorder: Is the link real? J Am Acad Child Adolesc Psychiatry 2018;57:8-9.
36. Wiepjes CM, Nota NM, de Blok CJM, Klaver M, de Vries ALC, Wensing-Kruger SA, et al. The Amsterdam cohort of gender dysphoria study (1972-2015): Trends in prevalence, treatment, and regrets. J Sex Med 2018;15:582-90.
37. Bränström R, Pachankis JE. Reduction in mental health treatment utilization among transgender individuals after gender-affirming surgeries: A total population study. Am J Psychiatry 2019: https://doi.org/10.1176/appi.ajp.2019.19010080.
38. Connolly MD, Zervos MJ, Barone CJ, 2nd, Johnson CC, Joseph CL. The mental health of transgender youth: Advances in understanding. J Adolesc Health 2016;59:489-95.
39. Costa R, Colizzi M. The effect of cross-sex hormonal treatment on gender dysphoria individuals' mental health: a systematic review. Neuropsychiatr Dis Treat 2016;12:1953-66.
40. de Graaf NM, Manjra II, Hames A, Zitz C. Thinking about ethnicity and gender diversity in children and young people. Clin Child Psychol Psychiatry. 2019;24:291-303.
41. Zucker KJ. Epidemiology of gender dysphoria and transgender identity. Sex Health. 2017;14:404-11.
42. Dhejne C, Öberg K, Arver S, Landén M. An analysis of all applications for sex reassignment surgery in Sweden, 1960-2010: prevalence, incidence, and regrets. Arch Sex Behav 2014;43:1535-45.

43. Landén M, Wålinder J, Hambert G, Lundström B. Factors predictive of regret in sex reassignment. Acta Psychiatr Scand 1998;97:284-9.
44. Blanchard R, Steiner BW, Clemmensen LH, Dickey R. Prediction of regrets in postoperative transsexuals. Can J Psychiatry 1989;34:43-5.
45. Imbimbo C, Verze P, Palmieri A, Longo N, Fusco F, Arcaniolo D, et al. A report from a single institute's 14-year experience in treatment of male-to-female transsexuals. J Sex Med 2009;6:2736-45.
46. Johansson A, Sundbom E, Höjerback T, Bodlund O. A five-year follow-up study of Swedish adults with gender identity disorder. Arch Sex Behav 2010;39:1429-37.
47. Lawrence AA. Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. Arch Sex Behav 2003;32:299-315.
48. Nelson L, Whallett EJ, McGregor JC. Transgender patient satisfaction following reduction mammaplasty. J Plast Reconstr Aesthet Surg 2009;62:331-4.
49. Defreyne J, Motmans J, T'sjoen G. Healthcare costs and quality of life outcomes following gender affirming surgery in trans men: a review. Expert Rev Pharmacoecon Outcomes Res 2017;17:543-56.
50. van de Grift TC, Elaut E, Cerwenka SC, Cohen-Kettenis PT, Kreukels BPC. Surgical satisfaction, Quality of life, and their association after gender-affirming surgery: A follow-up study. J Sex Marital Ther 2018;44:138-48.
51. Wierckx K, Elaut E, Declercq E, Heylens G, De Cuypere G, Taes Y, et al. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. Eur J Endocrinol 2013;169:471-8.
52. de Vries AL, McGuire JK, Steensma TD, Wagenaar EC, Doreleijers TA, Cohen-Kettenis PT. Young adult psychological outcome after puberty suppression and gender reassignment. Pediatrics 2014;134:696-704.
53. Dhejne C, Van Vlerken R, Heylens G, Arcelus J. Mental health and gender dysphoria: A review of the literature. Int Rev Psychiatry 2016;28:44-57.
54. Gómez-Gil E, Zubiaurre-Elorza L, Esteva I, Guillamon A, Godás T, Cruz Almaraz M, et al. Hormone-treated transsexuals report less social distress, anxiety and depression. Psychoneuroendocrinology 2012;37:662-70.
55. Keo-Meier CL, Herman LI, Reisner SL, Pardo ST, Sharp C, Babcock JC. Testosterone treatment and MMPI-2 improvement in transgender men: a prospective controlled study. J Consult Clin Psychol 2015;83:143-56.
56. Millet N, Longworth J, Arcelus J. Prevalence of anxiety symptoms and disorders in the transgender population: A systematic review of the literature. Int J Transgenderism 2017;18:27-38.
57. Murad MH, Elamin MB, Garcia MZ, Mullan RJ, Murad A, Erwin PJ, et al. Hormonal therapy and sex reassignment: A systematic review and meta-analysis of quality of life and psychosocial outcomes. Clin Endocrinol 2010;72:214-31.
58. Owen-Smith AA, Gerth J, Sineath RC, Barzilay J, Becerra-Culqui TA, Getahun D, et al. Association between gender confirmation treatments and

perceived gender congruence, body image satisfaction, and mental health in a cohort of transgender individuals. J Sex Med 2018;15:591-600.
59. Rowniak S, Bolt L, Sharifi C. The effect of cross-sex hormones on the quality of life, depression and anxiety of transgender individuals: a quantitative systematic review. JBI Database of System Rev Implement Rep 2019;17:1826-54.
60. Tomita KK, Testa RJ, Balsam KF. Gender-affirming medical interventions and mental health in transgender adults. Psychology of Sexual Orientation and Gender Diversity 2019;6:182-93.
61. Dhejne C, Lichtenstein P, Boman M, Johansson ALV, Långström N, Landén M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: Cohort study in Sweden. PLoS One. 2011;6(2):e16885. doi: 10.1371/journal.pone.0016885.
62. Jellestad L, Jäggi T, Corbisiero S, Schaefer DJ, Jenewein J, Schneeberger A, et al. Quality of life in transitioned trans persons: A retrospective cross-sectional cohort study. BioMed Res Int 2018;2018:8684625.
63. Lindqvist EK, Sigurjonsson H, Möllermark C, Rinder J, Farnebo F, Lundgren TK. Quality of life improves early after gender reassignment surgery in transgender women. Eur J Plast Surg 2017;40:223-6.
64. Ruppin U, Pfäfflin F. Long-term follow-up of adults with gender identity disorder. Arch Sex Behav 2015;44:1321-9.
65. Simonsen RK, Giraldi A, Kristensen E, Hald GM. Long-term follow-up of individuals undergoing sex reassignment surgery: Psychiatric morbidity and mortality. Nord J Psychiatry 2016;70:241-7.
66. Weinforth G, Fakin R, Giovanoli P, Garcia Nuñez D. Quality of life following male-to-female sex reassignment surgery. Dtsch Arztebl Int 2019;116:253-60.
67. Wernick JA, Busa S, Matouk K, Nicholson J, Janssen A. A systematic review of the psychological benefits of gender-affirming surgery. Urol Clin North Am 2019;46:475-86.
68. Weyers S, Elaut E, De Sutter P, Gerris J, T'Sjoen G, Heylens G, et al. Long-term assessment of the physical, mental, and sexual health among transsexual women. J Sex Med 2009;6:752-60.
69. Özata Yildizhan B, Yüksel Ş, Avayu M, Noyan H, Yildizhan E. Effects of gender reassignment on quality of life and mental health in people with gender dysphoria. Türk Psikiyatri Derg 2018;29:1-10.
70. Staphorsius AS, Kreukels BP, Cohen-Kettenis PT, Veltman DJ, Burke SM, Schagen SE, et al. Puberty suppression and executive functioning: An fMRI-study in adolescents with gender dysphoria. Psychoneuroendocrinology 2015;56:190-9.
71. Schneider MA, Andreazza T, Fontanari AM, Costa AB, Silva DC, Aguiar BW, et al. Serum concentrations of brain-derived neurotrophic factor in patients diagnosed with gender dysphoria undergoing sex reassignment surgery. Trends Psychiatry Psychotheer 2017;39:43-7.
72. Nguyen HB, Loughead J, Lipner E, Hantsoo L, Kornfield SL, Epperson

CN. What has sex got to do with it? The role of hormones in the transgender brain. Neuropsychopharmacology 2019;44:22-37.
73. Joint R, Chen ZE, Cameron S. Breast and reproductive cancers in the transgender population: a systematic review. BJOG. 2018;125:1505-12.
74. McFarlane T, Zajac JD, Cheung AS. Gender-affirming hormone therapy and the risk of sex hormone-dependent tumours in transgender individuals - A systematic review. Clin Endocrinol 2018;89:700-11.
75. de Blok CJM, Wiepjes CM, Nota NM, Van Engelen K, Adank MA, Dreijerink KMA, et al. Breast cancer risk in transgender people receiving hormone treatment: Nationwide cohort study in the Netherlands. BMJ 2019;365:l1652. doi: 10.1136/bmj.l1652.
76. Nota NM, Wiepjes CM, de Blok CJM, Gooren LJG, Peerdeman SM, Kreukels BPC, et al. The occurrence of benign brain tumours in transgender individuals during cross-sex hormone treatment. Brain 2018;141:2047-54.
77. Maraka S, Singh Ospina N, Rodriguez-Gutierrez R, Davidge-Pitts CJ, Nippoldt TB, Prokop LJ, et al. Sex steroids and cardiovascular outcomes in transgender individuals: A systematic review and meta-analysis. J Clin Endocrinol Metab 2017;102:3914-23.
78. van Velzen DM, Paldino A, Klaver M, Nota NM, Defreyne J, Hovingh GK, et al. Cardiometabolic effects of testosterone in transmen and estrogen plus cyproterone acetate in transwomen. J Clin Endocrinol Metab 2019;104:1937-47.
79. Getahun D, Nash R, Flanders WD, Baird TC, Becerra-Culqui TA, Cromwell L, et al. Cross-sex hormones and acute cardiovascular events in transgender persons: A Cohort Study. Ann Intern Med 2018;169:205-13.
80. Dutra E, Lee J, Torbati T, Garcia M, Merz CNB, Shufelt C. Cardiovascular implications of gender-affirming hormone treatment in the transgender population. Maturitas 2019;129:45-9.
81. Goldstein Z, Khan M, Reisman T, Safer JD. Managing the risk of venous thromboembolism in transgender adults undergoing hormone therapy. J Blood Med 2019;10:209-16.
82. Khan J, Schmidt RL, Spittal MJ, Goldstein Z, Smock KJ, Greene DN. Venous thrombotic risk in transgender women undergoing estrogen therapy: A systematic review and metaanalysis. Clin Chem 2019;65:57-66.
83. Joseph T, Ting J, Butler G. The effect of GnRH analogue treatment on bone mineral density in young adolescents with gender dysphoria: findings from a large national cohort. J Pediatr Endocrinol Metab 2019;32:1077-81.
84. Klink D, Caris M, Heijboer A, van Trotsenburg M, Rotteveel J. Bone mass in young adulthood following gonadotropin-releasing hormone analog treatment and cross-sex hormone treatment in adolescents with gender dysphoria. J Clin Endocrinol Metab 2015;100:E270-5.
85. Singh-Ospina N, Maraka S, Rodriguez-Gutierrez R, Davidge-Pitts C, Nippoldt TB, Prokop LJ, et al. Effect of sex steroids on the bone health of transgender individuals: A systematic review and meta-analysis. J Clin Endocrinol Metabo 2017;102:3904-13.

86. Fighera TM, Ziegelmann PK, Da Silva TR, Spritzer PM. Bone mass effects of cross-sex hormone therapy in transgender people: Updated systematic review and meta-analysis. J Endocr Soc 2019;3:943-64.
87. Wiepjes CM, de Blok CJ, Staphorsius AS, Nota NM, Vlot MC, de Jongh RT, et al. Fracture risk in trans women and trans men using long-term gender-affirming hormonal treatment: a nationwide cohort study. J Bone Miner Res 2019 Sep 5. doi: 10.1002/jbmr.3862. [Epub ahead of print].
88. Wiepjes CM, de Jongh RT, de Blok CJ, Vlot MC, Lips P, Twisk JW, et al. Bone safety during the first ten years of gender-affirming hormonal treatment in transwomen and transmen. J Bone Miner Res 2019;34:447-54.
89. Wiepjes CM, Vlot MC, de Blok CJM, Nota NM, de Jongh RT, den Heijer M. Bone geometry and trabecular bone score in transgender people before and after short- and long-term hormonal treatment. Bone 2019;127:280-6.
90. van Kesteren P, Lips P, Gooren LJ, Asscheman H, Megens J. Long-term follow-up of bone mineral density and bone metabolism in transsexuals treated with cross-sex hormones. Clin Endocrinol (Oxf). 1998;48(3):347-54.
91. Alanko K, Lund H. Transgender youth and social support: A survey study on the effects of good relationships on well-being and mental health. Young 2019;1-8. https://journals.sagepub.com/doi/pdf/10.1177/1103308819850039
92. Bebes A, Samarova V, Shilo G, Diamond GM. Parental acceptance, parental psychological control and psychological symptoms among sexual minority adolescents. J Child Fam Stud 2015;24:882-90.
93. Costa R, Dunsford M, Skagerberg E, Holt V, Carmichael P, Colizzi M. Psychological support, puberty suppression, and psychosocial functioning in adolescents with gender dysphoria. J Sex Med 2015;12:2206-14.
94. de Vries AL, Steensma TD, Cohen-Kettenis PT, VanderLaan DP, Zucker KJ. Poor peer relations predict parent- and self-reported behavioral and emotional problems of adolescents with gender dysphoria: a cross-national, cross-clinic comparative analysis. Eur Child Adolesc Psychiatry 2016;25:579-88.
95. Johns MM, Beltran O, Armstrong HL, Jayne PE, Barrios LC. Protective factors among transgender and gender variant youth: A systematic review by socioecological level. J Prim Prev 2018;39:263-301.
96. Levitan N, Barkmann C, Richter-Appelt H, Schulte-Markwort M, Becker-Hebly I. Risk factors for psychological functioning in German adolescents with gender dysphoria: poor peer relations and general family functioning. Eur Child Adolesc Psychiatry 2019;28:1487-98.
97. Simons L, Schrager SM, Clark LF, Belzer M, Olson J. Parental support and mental health among transgender adolescents. J Adolesc Health 2013;53:791-3.
98. Thorne N, Witcomb GL, Nieder T, Nixon E, Yip A, Arcelus J. A comparison of mental health symptomatology and levels of social support in

young treatment seeking transgender individuals who identify as binary and non-binary. Int J Transgenderism 2019;20(2/3):241-50.
99. Weinhardt LS, Xie H, Wesp LM, Murray JR, Apchemengich I, Kioko D, et al. The Role of Family, Friend, and Significant Other Support in Well-Being Among Transgender and Non-Binary Youth. J GLBT Fam Stud 2019;15:311-25.
100. Wilson EC, Chen Y-H, Arayasirikul S, Raymond HF, McFarland W. The impact of discrimination on the mental health of transfemale youth and the protective effect of parental support. AIDS and Behavior 2016;20:2203-11.
101. Yadegarfard M, Meinhold-Bergmann ME, Ho R. Family rejection, social isolation, and loneliness as predictors of negative health outcomes (depression, suicidal ideation, and sexual risk behavior) among Thai male-to-female transgender adolescents. Journal of LGBT Youth 2014;11:347-63.
102. Grossman AH, Park JY, Russell ST. Transgender Youth and Suicidal Behaviors: Family rejection, social isolation, and loneliness as predictors of negative health outcomes (depression, suicidal ideation, and sexual risk behavior) among Thai male-to-female transgender adolescents. Journal of gay & lesbian mental health. 2016;20:329-49.
103. Turban JL, King D, Reisner SL, Keuroghlian AS. Psychological attempts to change a person's gender identity from transgender to cisgender: Estimated prevalence across US States, 2015. Am J Public Health 2019;109:1452-4.
104. Chew D, Anderson J, Williams K, May T, Pang K. Hormonal treatment in young people with gender dysphoria: A systematic review. Pediatrics 2018;141(4):1-18.
105. Klaver M, de Mutsert R, Wiepjes CM, Twisk JWR, den Heijer M, Rotteveel J, et al. Early hormonal treatment affects body composition and body shape in young transgender adolescents. J Sex Med 2018;15:251-60.
106. Kreukels BP, Cohen-Kettenis PT. Puberty suppression in gender identity disorder: the Amsterdam experience. Nat Rev Endocrinol 2011;7:466-72.
107. Lynch MM, Khandheria MM, Meyer Iii WJ. Retrospective study of the management of childhood and adolescent gender identity disorder using medroxyprogesterone acetate. Int J Transgenderism 2015;16:201-8.
108. Mahfouda S, Moore JK, Siafarikas A, Zepf FD, Lin A. Puberty suppression in transgender children and adolescents. Lancet Diabetes Endocrinol 2017;5:816-26.
109. Martinerie L, Condat A, Bargiacchi A, Bremont-Weill C, de Vries MC, Hannema SE. MANAGEMENT OF ENDOCRINE DISEASE: Approach to the management of children and adolescents with Gender Dysphoria. Eur J Endocrinol 2018;179:R219-r37.
110. Neyman A, Fuqua JS, Eugster EA. Bicalutamide as an androgen blocker with secondary effect of promoting feminization in male-to-female transgender adolescents. J Adolesc Health 2019;64:544-6.
111. Schagen SE, Cohen-Kettenis PT, Delemarre-van de Waal HA, Hannema SE. Efficacy and safety of gonadotropin-releasing hormone agonist treatment to suppress puberty in gender dysphoric adolescents. J Sex Med

2016;13:1125-32.
112. Schagen SEE, Lustenhouwer P, Cohen-Kettenis PT, Delemarre-van de Waal HA, Hannema SE. Changes in adrenal androgens during puberty suppression and gender-affirming hormone treatment in adolescents with gender dysphoria. J Sex Med 2018;15:1357-63.
113. Stoffers IE, de Vries MC, Hannema SE. Physical changes, laboratory parameters, and bone mineral density during testosterone treatment in adolescents with gender dysphoria. J Sex Med 2019;16:1459-68.
114. Tack LJW, Craen M, Lapauw B, Goemaere S, Toye K, Kaufman JM, et al. Proandrogenic and antiandrogenic progestins in transgender youth: Differential effects on body composition and bone metabolism. J Clin Endocrinol Metab 2018;103:2147-56.
115. Vlot MC, Klink DT, den Heijer M, Blankenstein MA, Rotteveel J, Heijboer AC. Effect of pubertal suppression and cross-sex hormone therapy on bone turnover markers and bone mineral apparent density (BMAD) in transgender adolescents. Bone 2017;95:11-9.
116. Hahn A, Kranz GS, Sladky R, Kaufmann U, Ganger S, Hummer A, et al. Testosterone affects language areas of the adult human brain. Hum Brain Mapp 2016;37:1738-48.
117. Sequeira GM, Kidd K, El Nokali NE, Rothenberger SD, Levine MD, Montano GT, et al. Early effects of testosterone initiation on body mass index in transmasculine adolescents. J Adolesc Health 2019;65:818-20.
118. Marinkovic M, Newfield RS. Chest reconstructive surgeries in transmasculine youth: Experience from one pediatric center. Int J Transgenderism 2017;18:376-81.
119. Olson-Kennedy J, Warus J, Okonta V, Belzer M, Clark LF. Chest reconstruction and chest dysphoria in transmasculine minors and young adults: Comparisons of nonsurgical and postsurgical cohorts. JAMA pediatrics 2018;172:431-6.
120. Cohen-Kettenis PT, van Goozen SH. Sex reassignment of adolescent transsexuals: a follow-up study. J Am Acad Child Adolesc Psychiatry 1997;36:263-71.
121. Smith YL, van Goozen SH, Cohen-Kettenis PT. Adolescents with gender identity disorder who were accepted or rejected for sex reassignment surgery: a prospective follow-up study. J Am Acad Child Adolesc Psychiatry 2001;40:472-81.
122. Smith YL, Cohen L, Cohen-Kettenis PT. Postoperative psychological functioning of adolescent transsexuals: a Rorschach study. Arch Sex Behav 2002;31:255-61.
123. Georgas K, Beckman U, Bryman I, Elander A, Jivegård L, Mattelin E, et al. Gender affirmation surgery for gender dysphoria - effects and risks. [Könskonfirmerande kirurgi vid könsdysfori - effekter och risker]. Göteborg: Västra Götalandsregionen, Sahlgrenska University Hospital, HTA-centrum: 2018. Regional activity based HTA 2018:102.

Bilaga 1 Sökstrategier

Sökning Könsdysfori och barn och unga

PubMed via NLM 6 September 2019

Title: Gender dysphoria & children/adolescence

Search terms		Items found
Population: persons with gender dysphoria		
1.	"Gender Dysphoria"[Mesh]	338
2.	"Transsexualism"[Mesh]	3545
3.	"Sex Reassignment Procedures"[Mesh]	671
4.	"Transgender Persons"[Mesh]	2444
5.	"Health Services for Transgender Persons"[Mesh]	116
6.	(agender[ti] OR "assigned female"[ti] OR "assigned females"[ti] OR "assigned male" [ti] OR "assigned males"[ti] OR bigender[ti] OR bi-gender[ti] OR "confirmation surgery"[ti] OR female-born[ti] OR "gender change"[ti] OR gender confirm*[ti] OR "gender dysphoria"[ti] OR "gender fluid"[ti] OR "gender identity disorder"[ti] OR "gender reassignment"[ti] OR "gender transition"[ti] OR "gender transitioning"[ti] OR gender-affirming[ti] OR gender affirmative[ti] OR gender incongru*[ti] OR gender non-binary[ti] OR gender nonbinary[ti] OR gender non-conform*[ti] OR transfeminine[ti] OR transgender*[ti] OR trans-gender[ti]OR trans-man[ti] OR transmasculine[ti] OR transpeople[ti] OR trans-people[ti] OR transpopulation[ti] OR trans-population[ti] OR transsex*[ti] OR trans-sex*[ti] OR trans-wom*[ti] OR transwom*[ti])	5265
7.	(agender[tiab] OR "assigned female"[tiab] OR "assigned females"[tiab] OR "assigned male"[tiab] OR "assigned males"[tiab] OR bigender[tiab] OR bi-gender[tiab] OR "confirmation surgery"[tiab] OR female-born[tiab] OR "gender change"[tiab] OR gender confirm*[tiab] OR "gender dysphoria"[tiab] OR "gender fluid"[tiab] OR "gender identity disorder"[tiab] OR "gender reassignment"[tiab] OR "gender transition"[tiab] OR "gender transitioning"[tiab] OR gender-affirming[tiab] OR gender affirmative[tiab] OR gender incongru*[tiab] OR gender non-binary[tiab] OR gender nonbinary[tiab] OR gender non-conform*[tiab] OR transfeminine[tiab] OR transgender*[tiab] OR trans-gender[tiab]OR trans-man[tiab] OR transmasculine[tiab] OR transpeople[tiab] OR trans-people[tiab] OR transpopulation[tiab] OR trans-population[tiab] OR transsex*[tiab] OR trans-sex*[tiab] OR trans-wom*[tiab] OR transwom*[tiab]) NOT medline[SB]	1932
8.	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7	8168
Population: children and adolescents		
9.	("Child"[Mesh] OR "child"[tw] OR "children"[tw] OR "Infant"[Mesh] OR "infant"[tw] OR "infants"[tw] OR "infancy"[tw] OR "newborn"[tw] OR "newborns"[tw] OR "new-born"[tw] OR "new-borns"[tw] OR "neonate"[tw] OR "neonates"[tw] OR "neonatal" [tw] OR "neo-nate"[tw] OR "neo-nates"[tw] OR "neo-natal"[tw] OR "neonatology"[tw] OR "NICU"[ti] OR "premature"[tw] OR "prematures"[tw] OR "pre-mature"[tw] OR "pre-matures"[tw] OR "preterm"[tw] OR "pre-term"[tw] OR "postnatal"[tw] OR "post-natal"[tw] OR "baby"[tw] OR "babies"[tw] OR "suckling"[tw] OR "sucklings"[tw] OR "toddler"[tw] OR "toddlers"[tw] OR "childhood"[tw] OR "schoolchild"[tw] OR "schoolchildren"[tw] OR "childcare"[tw] OR "child-care"[tw] OR "young"[ti] OR "youngster"[tw] OR "youngsters"[tw] OR "preschool"[tw] OR "pre-school"[tw] OR "kid"[tw] OR "kids"[tw] OR "boy"[tw] OR "boys"[tw] OR "girl"[tw] OR "girls"[tw] OR	4781542

	"Adolescent"[Mesh] OR "adolescent"[tw] OR "adolescents"[tw] OR "adolescence" [tw] OR "pre-adolescent"[tw] OR "pre-adolescents"[tw] OR "pre-adolescence"[tw] OR "schoolage"[tw] OR "schoolboy"[tw] OR "schoolboys"[tw] OR "schoolgirl"[tw] OR "schoolgirls"[tw] OR "pre-puber"[tw] OR "pre-pubers"[tw] OR "pre-puberty"[tw] OR "prepuber"[tw] OR "prepubers"[tw] OR "prepuberty"[tw] OR "puber"[tw] OR "pubers" [tw] OR "puberty"[tw] OR "puberal"[tw] OR "teenager"[tw] OR "teenagers"[tw] OR "teens"[tw] OR "youth"[tw] OR "youths"[tw] OR "underaged"[tw] OR "under-aged"[tw] OR "Pediatrics"[Mesh] OR "Pediatric"[tw] OR "Pediatrics"[tw] OR "Paediatric"[tw] OR "Paediatrics"[tw] OR "PICU"[ti] OR ("child"[all fields] NOT child[au]) OR children*[all fields] OR schoolchild*[all fields] OR "infant"[all fields] OR "infants"[all fields] OR "infancy"[all fields] OR adolesc*[all fields] OR pediat*[all fields] OR paediat*[all fields] OR neonat*[all fields] OR toddler*[all fields] OR "teen"[all fields] OR "teens" [all fields] OR teenager*[all fields] OR preteen*[all fields] OR newborn*[all fields] OR postneonat*[all fields] OR postnatal*[all fields] OR "puberty"[all fields] OR preschool*[all fields] OR suckling*[all fields] OR "juvenile"[all fields] OR "new born" [all fields] OR "new borns"[all fields] OR new-born*[all fields] OR neo-nat*[all fields] OR neonat*[all fields] OR perinat*[all fields] OR underag*[all fields] OR "under age"[all fields] OR "under aged"[all fields] OR youth*[all fields] OR kinder* [all fields] OR pubescen*[all fields] OR prepubescen*[all fields] OR "prepuberty"[all fields] OR "school age"[all fields] OR "schoolage"[all fields] OR "school ages"[all fields] OR schoolage*[all fields] OR "one year old"[ti] OR "two year old"[ti] OR "three year old"[ti] OR "four year old"[ti] OR "five year old"[ti] OR "six year old"[ti] OR "seven year old"[ti] OR "eight year old"[ti] OR "nine year old"[ti] OR "ten year old"[ti] OR "eleven year old"[ti] OR "twelve year old"[ti] OR "thirteen year old"[ti] OR "fourteen year old"[ti] OR "fifteen year old"[ti] OR "sixteen year old"[ti] OR "seventeen year old"[ti] OR "eighteen year old"[ti] OR "1 year old"[ti] OR "2 year old" [ti] OR "3 year old"[ti] OR "4 year old"[ti] OR "5 year old"[ti] OR "6 year old"[ti] OR "7 year old"[ti] OR "8 year old"[ti] OR "9 year old"[ti] OR "10 year old"[ti] OR "11 year old"[ti] OR "12 year old"[ti] OR "13 year old"[ti] OR "14 year old"[ti] OR "15 year old"[ti] OR "16 year old"[ti] OR "17 year old"[ti] OR "18 year old"[ti] OR "two years old"[ti] OR "three years old"[ti] OR "four years old"[ti] OR "five years old"[ti] OR "six years old"[ti] OR "seven years old"[ti] OR "eight years old"[ti] OR "nine years old"[ti] OR "ten years old"[ti] OR "eleven years old"[ti] OR "twelve years old" [ti] OR "thirteen years old"[ti] OR "fourteen years old"[ti] OR "fifteen years old"[ti] OR "sixteen years old"[ti] OR "seventeen years old"[ti] OR "eighteen years old"[ti] OR "2 years old"[ti] OR "3 years old"[ti] OR "4 years old"[ti] OR "5 years old"[ti] OR "6 years old"[ti] OR "7 years old"[ti] OR "8 years old"[ti] OR "9 years old"[ti] OR "10 years old"[ti] OR "11 years old"[ti] OR "12 years old"[ti] OR "13 years old"[ti] OR "14 years old"[ti] OR "15 years old"[ti] OR "16 years old"[ti] OR "17 years old"[ti] OR "18 years old"[ti])	
Combined sets		
10.	8 AND 9	2729
Combined sets, limited to study types: systematic reviews and meta-analysis (filter: PubMed[1], with modifications, broad)		
11.	(systematic review [ti] OR meta-analysis [pt] OR systematic review[pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR(reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR	420344

	publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT(letter [pt] OR newspaper article [pt])	
12.	10 AND 11	97
13.	12 ANDFilters activated: Publication date from 2013/08/01.	81
14.	10 NOT 13	2648
15.	14 NOT (letter [pt] OR newspaper article [pt] OR "Editorial" [Publication Type] OR "Comment" [Publication Type]) AND (english[la] OR swedish[la] OR danish[la] OR norwegian[la])	2327

[1] https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/filters-to-identify-systematic-reviews/-pubmed-search-strategy
* = Truncation
The search result, usually found at the end of the documentation, forms the list of abstracts.
[AU] = Author; [MAJR] = MeSH Major Topic; [MeSH] = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy; [MeSH:NoExp] = Does not include terms found below this term in the MeSH hierarchy; [OT] = Other term; [SB] = Filter for retrieving systematic reviews; [TW] = Text Word; Systematic; [TI] = Title; [TIAB] = Title or abstract

Bilaga 2 Exkluderade studier

Gender dysphoria in children and adolescents

Studies considered not relevant

Study	Reason for exclusion
Abel BS. Hormone treatment of children and adolescents with gender dysphoria: an ethical analysis. The Hastings Center report. 2014;44 Suppl 4:S23-7.	Ethics
Adams N, Hitomi M, Moody C. Varied Reports of Adult Transgender Suicidality: Synthesizing and Describing the Peer-Reviewed and Gray Literature. Transgender health. 2017;2(1):60-75.	Mix of literature
Aitken M, Steensma TD, Blanchard R, VanderLaan DP, Wood H, Fuentes A, et al. Evidence for an altered sex ratio in clinic-referred adolescents with gender dysphoria. The journal of sexual medicine. 2015;12(3):756-63.	Age
Alessandrin A. The notion of regret in the clinical approach to gender reassignment. Evolution Psychiatrique. 2019;84(2):277-84.	Review
Allen LR, Watson LB, Egan AM, Moser CN. Well-being and suicidality among transgender youth after gender-affirming hormones. Clinical Practice in Pediatric Psychology. 2019;7(3):302-11.	Short term follow-up
Angus L, Leemaqz S, Ooi O, Cundill P, Silberstein N, Locke P, et al. Cyproterone acetate or spironolactone in lowering testosterone concentrations for transgender individuals receiving oestradiol therapy. Endocr Connect. 2019;8(7):935-40.	Cyproterone acetate not used in Sweden
Aranda G, Fernandez-Rebollo E, Pradas-Juni M, Hanzu FA, Kalko SG, Halperin I, et al. Effects of sex steroids on the pattern of methylation and expression of the promoter region of estrogen and androgen receptors in people with gender dysphoria under cross-sex hormone treatment. The Journal of steroid biochemistry and molecular biology. 2017;172:20-8.	Non-clinical
Aranda G, Mora M, Hanzu FA, Vera J, Ortega E, Halperin I. Effects of sex steroids on cardiovascular risk profile in transgender men under gender affirming hormone therapy. Endocrinol Diabetes Nutricion. 2019;66(6):385-92.	Short term follow-up
Arcelus J, Bouman WP, Van Den Noortgate W, Claes L, Witcomb G, Fernandez-Aranda F. Systematic review and meta-analysis of prevalence studies in transsexualism. European Psychiatry. 2015;30(6):807-15.	Data from before rise in numbers seeking care
Armuand G, Dhejne C, Olofsson JI, Rodriguez-Wallberg KA. Transgender men's experiences of fertility preservation: A qualitative study. Hum Reprod. 2017;32(2):383-90.	Fertility
Arnold JD, Sarkodie EP, Coleman ME, Goldstein DA. Incidence of Venous Thromboembolism in Transgender Women Receiving Oral Estradiol. The journal of sexual medicine. 2016;13(11):1773-7.	Oral oestrogens not relevant in Sweden
Ascha M, Massie JP, Morrison SD, Crane CN, Chen ML. Outcomes of Single Stage Phalloplasty by Pedicled Anterolateral Thigh Flap versus Radial Forearm Free Flap in Gender Confirming Surgery. The Journal of urology. 2018;199(1):206-14.	Age
Asscheman H, T'Sjoen G, Lemaire A, Mas M, Meriggiola MC, Mueller A, et al. Venous thrombo-embolism as a complication of cross-sex hormone treatment of male-to-female transsexual subjects: a review. Andrologia.	Old data

2014;46(7):791-5.	
Auer MK, Fuss J, Nieder TO, Briken P, Biedermann SV, Stalla GK, et al. Desire to Have Children Among Transgender People in Germany: A Cross-Sectional Multi-Center Study. The journal of sexual medicine. 2018;15(5):757-67.	Fertility
Aydin D, Buk LJ, Partoft S, Bonde C, Thomsen MV, Tos T. Transgender Surgery in Denmark from 1994 to 2015: 20-Year Follow-Up Study. The journal of sexual medicine. 2016;13(4):720-5.	Trends in surgery in Denmark
Bailey L, Ellis SJ, McNeil J. Suicide risk in the UK trans population and the role of gender transition in decreasing suicidal ideation and suicide attempt. Mental Health Review Journal. 2014;19(4):209-20.	Fertility
Barnard EP, Dhar CP, Rothenberg SS, Menke MN, Witchel SF, Montano GT, et al. Fertility Preservation Outcomes in Adolescent and Young Adult Feminizing Transgender Patients. Pediatrics. 2019;144(3).	Fertility
Bartholomaeus C, Riggs DW. Transgender and non-binary Australians' experiences with healthcare professionals in relation to fertility preservation. Culture, health & sexuality. 2019:1-17.	Fertility
Becerra Fernández A. Gender identity disorders: Guidelines for their diagnosis and treatment. Endocrinol Nutr. 2003;50(1):19-33.	Guide lines
Becerra-Fernández A, Rodríguez-Molina JM, Asenjo-Araque N, Lucio-Pérez MJ, Cuchí-Alfaro M, García-Camba E, et al. Prevalence, Incidence, and Sex Ratio of Transsexualism in the Autonomous Region of Madrid (Spain) According to Healthcare Demand. Archives of Sexual Behavior. 2017;46(5):1307-12.	Regional
Bechard M, VanderLaan DP, Wood H, Wasserman L, Zucker KJ. Psychosocial and Psychological Vulnerability in Adolescents with Gender Dysphoria: A "Proof of Principle" Study. Journal of sex & marital therapy. 2017;43(7):678-88.	Short-term follow-up
Bennett CM, Dillman Taylor D. Acting as yourself: Implementing acceptance and commitment therapy for transgender adolescents through a developmental lens. Journal of Child and Adolescent Counseling. 2019.	Implementation
Bertrand B, Perchenet AS, Colson TR, Drai D, Casanova D. [Female-to-male transgender chest reconstruction: A retrospective study of patient satisfaction]. Annales de chirurgie plastique et esthetique. 2017;62(4):303-7.	Language
Bizic MR, Jeftovic M, Pusica S, Stojanovic B, Duisin D, Vujovic S, et al. Gender Dysphoria: Bioethical Aspects of Medical Treatment. BioMed Research International. 2018;2018.	Ethics
Blanchard R, Steiner BW, Clemmensen LH, Dickey R. Prediction of regrets in postoperative transsexuals. Canadian journal of psychiatry Revue canadienne de psychiatrie. 1989;34(1):43-5.	Old data, sexuality
Bockting WO. Vulnerability and resilience among gender-nonconforming children and adolescents: Mental health professionals have a key role to play. Journal of the American Academy of Child & Adolescent Psychiatry. 2016;55(6):441-3.	Editorial
Boos MD, Yeung H, Inwards-Breland D. Dermatologic care of sexual and gender minority/LGBTQIA youth, part I: An update for the dermatologist on providing inclusive care. Pediatric dermatology. 2019.	Guide-lines
Bouman MB, van Zeijl MC, Buncamper ME, Meijerink WJ, van Bodegraven AA, Mullender MG. Intestinal vaginoplasty revisited: a review of surgical techniques, complications, and sexual function. The journal of sexual medicine. 2014;11(7):1835-47.	Non-systematic review
Bouman WP, Richards C, Addinall RM, Arango de Montis I, Arcelus J, Duisin D, et al. Yes and yes again: Are standards of care which require two referrals for genital reconstructive surgery ethical? Sexual and Relationship	Ethics, position paper

Therapy. 2014;29(4):377-89.	
Braun H, Nash R, Tangpricha V, Brockman J, Ward K, Goodman M. Cancer in transgender people: Evidence and methodological considerations. Epidemiologic Reviews. 2017;39(1):93-107.	Review, methods
Brik T, Vrouenraets L, Schagen SEE, Meissner A, de Vries MC, Hannema SE. Use of Fertility Preservation Among a Cohort of Transgirls in the Netherlands. The Journal of adolescent health: official publication of the Society for Adolescent Medicine. 2019;64(5):589-93.	Fertility
Brown GR, Jones KT. Incidence of breast cancer in a cohort of 5,135 transgender veterans. Breast cancer research and treatment. 2015;149(1):191-8.	Included in systematic reviews ref 73 och 74 in the report
Bryson C, Honig SC. Genitourinary Complications of Gender-Affirming Surgery. Current Urology Reports. 2019;20(6).	Review
Burke SM, Manzouri AH, Dhejne C, Bergstrom K, Arver S, Feusner JD, et al. Testosterone Effects on the Brain in Transgender Men. Cerebral cortex (New York, NY : 1991). 2018;28(5):1582-96.	Included in ref 72 in the report
Burke SM, Manzouri AH, Savic I. Structural connections in the brain in relation to gender identity and sexual orientation. Scientific reports. 2017;7(1):17954	Not specifically gender dysphoria
Butler G, De Graaf N, Wren B, Carmichael P. Assessment and support of children and adolescents with gender dysphoria. Archives of disease in childhood. 2018;103(7):631-6.	Review
Campo-Engelstein L, Chen D, Baratz AB, Johnson EK, Finlayson C. The Ethics of Fertility Preservation for Pediatric Patients with Differences (Disorders) of Sex Development. Journal of the Endocrine Society. 2017;1(6):638-45.	Fertility
Cartaya J, Lopez X. Gender dysphoria in youth: a review of recent literature. Current opinion in endocrinology, diabetes, and obesity. 2018;25(1):44-8.	Review
Casado JC, Rodriguez-Parra MJ, Adrian JA. Voice feminization in male-to-female transgendered clients after Wendler's glottoplasty with vs. without voice therapy support. European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2017;274(4):2049-58.	Age
Castellano E, Crespi C, Dell'Aquila C, Rosato R, Catalano C, Mineccia V, et al. Quality of life and hormones after sex reassignment surgery. J Endocrinol Invest. 2015;38(12):1373-81.	Short-term follow-up
Chen D, Kyweluk MA, Sajwani A, Gordon EJ, Johnson EK, Finlayson CA, et al. Factors Affecting Fertility Decision-Making Among Transgender Adolescents and Young Adults. LGBT Health. 2019;6(3):107-15.	Fertility
Chen D, Matson M, Macapagal K, Johnson EK, Rosoklija I, Finlayson C, et al. Attitudes Toward Fertility and Reproductive Health Among Transgender and Gender-Nonconforming Adolescents. The Journal of adolescent health: official publication of the Society for Adolescent Medicine. 2018;63(1):62-8.	Fertility
Chen D, Simons L, Johnson EK, Lockart BA, Finlayson C. Fertility Preservation for Transgender Adolescents. The Journal of adolescent health: official publication of the Society for Adolescent Medicine. 2017;61(1):120-3.	Fertility
Cheng PJ, Pastuszak AW, Myers JB, Goodwin IA, Hotaling JM. Fertility concerns of the transgender patient. Translational andrology and urology. 2019;8(3):209-18.	Fertility
Chiniara LN, Viner C, Palmert M, Bonifacio H. Perspectives on fertility preservation and parenthood among transgender youth and their parents. Archives of disease in childhood. 2019;104(8):739-44.	Fertility

Churcher Clarke A, Spiliadis A. 'Taking the lid off the box': The value of extended clinical assessment for adolescents presenting with gender identity difficulties. Clinical child psychology and psychiatry. 2019;24(2):338-52.	Case description
Claes KEY, Pattyn P, D'Arpa S, Robbens C, Monstrey SJ. Male-to-Female Gender Confirmation Surgery: Intestinal Vaginoplasty. Clinics in plastic surgery. 2018;45(3):351-60.	Methods description
Colizzi M, Costa R, Scaramuzzi F, Palumbo C, Tyropani M, Pace V, et al. Concomitant psychiatric problems and hormonal treatment induced metabolic syndrome in gender dysphoria individuals: a 2-year follow-up study. Journal of psychosomatic research. 2015;78(4):399-406.	Age
Colizzi M, Costa R, Todarello O. Transsexual patients' psychiatric comorbidity and positive effect of cross-sex hormonal treatment on mental health: Results from a longitudinal study. Psychoneuroendocrinology. 2014;39:65-73.	Short-term follow-up
Cristofari S, Bertrand B, Leuzzi S, Rem K, Rausky J, Revol M, et al. Postoperative complications of male to female sex reassignment surgery: A 10-year French retrospective study. Annales de chirurgie plastique et esthetique. 2019;64(1):24-32.	Surgical complications
Cuccolo NG, Kang CO, Boskey ER, Ibrahim AMS, Blankensteijn LL, Taghinia A, et al. Masculinizing Chest Reconstruction in Transgender and Nonbinary Individuals: An Analysis of Epidemiology, Surgical Technique, and Postoperative Outcomes. Aesthetic plastic surgery. 2019.	Method, complications
D'Angelo R. Psychiatry's ethical involvement in gender-affirming care. Australasian Psychiatry. 2018;26(5):460-3.	Ethics
Davidge-Pitts C, Clarke BL. Transgender bone health. Maturitas. 2019;127:35-42.	Review
de Vries ALC, Roehle R, Marshall L, Frisen L, van de Grift TC, Kreukels BPC, et al. Mental Health of a Large Group of Adults with Disorders of Sex Development in Six European Countries. Psychosomatic medicine. 2019;81(7):629-40.	Different sex development disorders
de Vries ALC, Steensma TD, Doreleijers TAH, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. Journal of Sexual Medicine. 2011;8(8):2276-83.	See ref 52 in the report
Deebel NA, Morin JP, Autorino R, Vince R, Grob B, Hampton LJ. Prostate Cancer in Transgender Women: Incidence, Etiopathogenesis, and Management Challenges. Urology. 2017;110:166-71.	Non-systematic review
Deuster D, Matulat P, Knief A, Zitzmann M, Rosslau K, Szukaj M, et al. Voice deepening under testosterone treatment in female-to-male gender dysphoric individuals. Eur Arch Oto-Rhino-Laryngol. 2016;273(4):959-65.	Age
Djordjevic ML, Bizic MR, Duisin D, Bouman MB, Buncamper M. Reversal surgery in regretful male-to-female transsexuals after sex reassignment surgery. Journal of Sexual Medicine. 2016;13(6):1000-7.	Surgical method
Djordjevic ML, Bizic MR. Comparison of two different methods for urethral lengthening in female to male (metoidioplasty) surgery. The journal of sexual medicine. 2013;10(5):1431-8.	Surgical method
Dy GW, Nolan IT, Hotaling J, Myers JB. Patient reported outcome measures and quality of life assessment in genital gender confirming surgery. Translational andrology and urology. 2019;8(3):228-40.	Review
Eldh J, Berg A, Gustafsson M. Long-term follow up after sex reassignment surgery. Scandinavian journal of plastic and reconstructive surgery and hand surgery. 1997;31(1):39-45.	Age, surgical outcome
Fakin RM, Zimmermann S, Kaye K, Lunger L, Weinforth G, Giovanoli P. Long-Term Outcomes in Breast Augmentation in Trans-Women: A 20-Year Experience. Aesthetic surgery journal. 2019;39(4):381-90.	Surgical outcome

Falcone M, Garaffa G, Gillo A, Dente D, Christopher AN, Ralph DJ. Outcomes of inflatable penile prosthesis insertion in 247 patients completing female to male gender reassignment surgery. BJU international. 2018;121(1):139-44.	Surgical outcome
Ferlatte O, Salway T, Rice SM, Oliffe JL, Knight R, Ogrodniczuk JS. Inequities in depression within a population of sexual and gender minorities. Journal of mental health (Abingdon, England). 2019:1-8.	Not specifically gender dysphoria
Fernandez JD, Tannock LR. Metabolic effects of hormone therapy in transgender patients. Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2016;22(4):383-8.	Review
Fighera TM, da Silva E, Lindenau JD, Spritzer PM. Impact of cross-sex hormone therapy on bone mineral density and body composition in transwomen. Clinical endocrinology. 2018;88(6):856-62.	Included in ref 86 in the report
Fisher AD, Castellini G, Bandini E, Casale H, Fanni E, Benni L, et al. Cross-Sex Hormonal Treatment and Body Uneasiness in Individuals with Gender Dysphoria. Journal of Sexual Medicine. 2014;11(3):709-19.	Satisfaction
Frederick MJ, Berhanu AE, Bartlett R. Chest Surgery in Female to Male Transgender Individuals. Annals of plastic surgery. 2017;78(3):249-53.	Age, cannot differ younger pts.
Frisen L, Soder O, Rydelius PA. [Dramatic increase of gender dysphoria in youth]. Lakartidningen. 2017;114.	Review
Gaither TW, Awad MA, Osterberg EC, Murphy GP, Romero A, Bowers ML, et al. Postoperative Complications following Primary Penile Inversion Vaginoplasty among 330 Male-to-Female Transgender Patients. The Journal of urology. 2018;199(3):760-5.	Surgical method
Gava G, Cerpolini S, Martelli V, Battista G, Seracchioli R, Meriggiola MC. Cyproterone acetate vs leuprolide acetate in combination with transdermal oestradiol in transwomen: a comparison of safety and effectiveness. Clinical endocrinology. 2016;85(2):239-46.	Cyproterone acetate nor used in Sweden
Gijs L, Brewaeys A. Surgical Treatment of Gender Dysphoria in Adults and Adolescents: Recent Developments, Effectiveness, and Challenges. Annual Review of Sex Research. 2007;18(1):178-224.	Review
Gooren L, Morgentaler A. Prostate cancer incidence in orchidectomised male-to-female transsexual persons treated with oestrogens. Andrologia. 2014;46(10):1156-60.	Included in ref 74 in the report
Gooren LJ, van Trotsenburg MA, Giltay EJ, van Diest PJ. Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. The journal of sexual medicine. 2013;10(12):3129-34.	Included in ref 73 and 74 in the report
Gurney K. Sex and the surgeon's knife: The family court's dilemma… informed consent and the specter of iatrogenic harm to children with intersex characteristics. Am J Law Med. 2007;33(4):625-61.	Ethics
Hamidi O, Davidge-Pitts CJ. Transfeminine Hormone Therapy. Endocrinol Metab Clin North Am. 2019;48(2):341-55.	Review
Hancock AB. An ICF Perspective on Voice-related Quality of Life of American Transgender Women. Journal of Voice. 2017;31(1):115.e1-.e8.	Method, age
Harris RM, Tishelman AC, Quinn GP, Nahata L. Decision Making and the Long-Term Impact of Puberty Blockade in Transgender Children. American Journal of Bioethics. 2019;19(2):67-9.	Ethics
Hartley RL, Stone JP, Temple-Oberle C. Breast cancer in transgender patients: A systematic review. Part 1: Male to female. European journal of surgical oncology: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2018;44(10):1455-62.	Same as ref 73 and 74 in the report
Hess J, Neto RR, Panic L, Rübben H, Senf W. Satisfaction with male-to-	Surgery, satisfaction

female gender reassignment surgery: Results of a retrospective analysis. Deutsches Ärzteblatt International. 2014;111(47):795-801.	
Hirsch S, Pickering J, Adler R. Meeting the Needs of Trans and Gender Diverse Youth: The Varied, Ubiquitous Role of the Speech-Language Pathologist in Voice and Communication Therapy/Training. Perspectives of the ASHA Special Interest Groups. 2019;4(1):111-7.	Review
Horbach SE, Bouman MB, Smit JM, Ozer M, Buncamper ME, Mullender MG. Outcome of Vaginoplasty in Male-to-Female Transgenders: A Systematic Review of Surgical Techniques. The journal of sexual medicine. 2015;12(6):1499-512.	Surgical method
Houk CP, Lee PA. The diagnosis and care of transsexual children and adolescents: a pediatric endocrinologists' perspective. Journal of pediatric endocrinology & metabolism: JPEM. 2006;19(2):103-9.	Review
Irwin JA, Coleman JD, Fisher CM, Marasco VM. Correlates of Suicide Ideation Among LGBT Nebraskans. Journal of Homosexuality. 2014;61(8):1172-91.	Nor gender dysphoria specifically
Jacobsson J, Andréasson M, Kölby L, Elander A, Selvaggi G. Patients' Priorities Regarding Female-to-Male Gender Affirmation Surgery of the Genitalia—A Pilot Study of 47 Patients in Sweden. Journal of Sexual Medicine. 2017;14(6):857-64.	Surgery, attitudes
Jain J, Kwan D, Forcier M. Medroxyprogesterone Acetate in Gender-Affirming Therapy for Transwomen: Results from a Retrospective Study. The Journal of clinical endocrinology and metabolism. 2019.	Medroxyprogesterone acetate nor used in Sweden
Jeftovic M, Stojanovic B, Bizic M, Stanojevic D, Kisic J, Bencic M, et al. Hysterectomy with Bilateral Salpingo-Oophorectomy in Female-to-Male Gender Affirmation Surgery: Comparison of Two Methods. BioMed research international. 2018;2018:3472471.	Surgery, method, age
Kääriäinen M, Salonen K, Helminen M, Karhunen-Enckell U. Chest-wall contouring surgery in female-to-male transgender patients: A one-center retrospective analysis of applied surgical techniques and results. Scand J Surg. 2017;106(1):74-9.	Surgery, method, age
Kang A, Aizen JM, Cohen AJ, Bales GT, Pariser JJ. Techniques and considerations of prosthetic surgery after phalloplasty in the transgender male. Translational andrology and urology. 2019;8(3):273-82.	Surgery, method, age
Karpel L, Gardel B, Revol M, Brémont-Weil C, Ayoubi JM, Cordier B. Psychological and sexual well being of 207 transsexuals after sex reassignment in France. Annales Medico-Psychologiques. 2015;173(6):511-9.	Language
Kjölhede A, Cornelius F, Huss F, Kratz G. Metoidioplasty and groin flap phalloplasty as two surgical methods for the creation of a neophallus in female-to-male gender-confirming surgery: A retrospective study comprising 123 operated patients. JPRAS Open. 2019;22:1-8.	Surgery, method
Klein C, Gorzalka BB. Sexual functioning in transsexuals following hormone therapy and genital surgery: A review. Journal of Sexual Medicine. 2009;6(11):2922-39.	Review
Knox ADC, Ho AL, Leung L, Hynes S, Tashakkor AY, Park YS, et al. A Review of 101 Consecutive Subcutaneous Mastectomies and Male Chest Contouring Using the Concentric Circular and Free Nipple Graft Techniques in Female-to-Male Transgender Patients. Plastic and reconstructive surgery. 2017;139(6):1260e-72e.	Surgery, method
Kosche C, Mansh M, Luskus M, Nguyen A, Martinez-Diaz G, Inwards-Breland D, et al. Dermatologic care of sexual and gender minority/LGBTQIA youth, Part 2: Recognition and management of the unique dermatologic needs of SGM adolescents. Pediatric dermatology. 2019.	Not gender dysphoria specifically
Lamm B, Gernhardt A, Rübeling H. How Societal Changes Have Influenced	Scientific method

German Children's Gender Representations as Expressed in Human Figure Drawings in 1977 and 2015. Sex Roles. 2019;81(1/2):118-25.	
Landén M, Bodlund O, Ekselius L, Hambert G, Lundström B. Done is done - and gone is gone; sex change presently the best remedy for transsexuals. Lakartidningen. 2001;98(30-31):3322-6.	Review
Levy JA, Edwards DC, Cutruzzula-Dreher P, McGreen BH, Akanda S, Tarry S, et al. Male-to-Female Gender Reassignment Surgery: An Institutional Analysis of Outcomes, Short-term Complications, and Risk Factors for 240 Patients Undergoing Penile-Inversion Vaginoplasty. Urology. 2019;131:228-33.	Surgery. method, age
Lundgren KC, Koudstaal MJ. Midfacial Bony Remodeling. Facial plastic surgery clinics of North America. 2019;27(2):221-6.	Surgery, method
Mahfouda S, Moore JK, Siafarikas A, Hewitt T, Ganti U, Lin A, et al. Gender-affirming hormones and surgery in transgender children and adolescents. The lancet Diabetes & endocrinology. 2019;7(6):484-98.	Review
Marchand JB, Pelladeau E, Pommier F. Transsexualism/transgenderism: Psychotherapy and sex/gender reassignment therapy. Annales Medico-Psychologiques. 2017;175(3):210-6.	Language
Mattawanon N, Spencer JB, Schirmer DA, 3rd, Tangpricha V. Fertility preservation options in transgender people: A review. Reviews in endocrine & metabolic disorders. 2018;19(3):231-42.	Ethics
McDonald K. Social support and mental health in LGBTQ adolescents: A review of the literature. Issues in Mental Health Nursing. 2018;39(1):16-29.	Review
McEvenue G, Xu FZ, Cai R, McLean H. Female-to-Male Gender Affirming Top Surgery: A Single Surgeon's 15-Year Retrospective Review and Treatment Algorithm. Aesthetic surgery journal. 2017;38(1):49-57.	Surgery, method
McQueen P. Authenticity, intersubjectivity and the ethics of changing sex. Journal of Gender Studies. 2016;25(5):557-70.	Ethics
McQueen P. The Role of Regret in Medical Decision-making. Ethical Theory Moral Pract. 2017;20(5):1051-65.	Ethics
Meerwijk EL, Sevelius JM. Transgender Population Size in the United States: a Meta-Regression of Population-Based Probability Samples. American Journal of Public Health. 2017;107(2):e1-e8.	Review
Meister J, Kuhn H, Shehata-Dieler W, Hagen R, Kleinsasser N. Perceptual analysis of the male-to-female transgender voice after glottoplasty-the telephone test. Laryngoscope. 2017;127(4):875-81.	Surgery
Meriggiola MC, Gava G. Endocrine care of transpeople part II. A review of cross-sex hormonal treatments, outcomes and adverse effects in transwomen. Clinical endocrinology. 2015;83(5):607-15.	Review
Miller TJ, Wilson SC, Massie JP, Morrison SD, Satterwhite T. Breast augmentation in male-to-female transgender patients: Technical considerations and outcomes. JPRAS Open. 2019;21:63-74.	Surgery, method
Milrod C, Karasic DH. Age Is Just a Number: WPATH-Affiliated Surgeons' Experiences and Attitudes Toward Vaginoplasty in Transgender Females Under 18 Years of Age in the United States. The journal of sexual medicine. 2017;14(4):624-34.	Ethics
Milrod C. How young is too young: Ethical concerns in genital surgery of the transgender MTF adolescent. Journal of Sexual Medicine. 2014;11(2):338-46.	Ethics
Moravek MB. Fertility preservation options for transgender and gender-nonconforming individuals. Current opinion in obstetrics & gynecology. 2019;31(3):170-6.	Fertility
Morrison SD, Satterwhite T. Lower Jaw Recontouring in Facial Gender-	Surgery, method

Affirming Surgery. Facial Plastic Surgery Clinics of North America. 2019;27(2):233-42.	
Nahata L, Tishelman AC, Caltabellotta NM, Quinn GP. Low Fertility Preservation Utilization Among Transgender Youth. The Journal of adolescent health: official publication of the Society for Adolescent Medicine. 2017;61(1):40-4.	Fertility
Neblett MF, 2nd, Hipp HS. Fertility Considerations in Transgender Persons. Endocrinology and metabolism clinics of North America. 2019;48(2):391-402.	Fertility
Neuville P, Morel-Journel N, Maucourt-Boulch D, Ruffion A, Paparel P, Terrier JE. Surgical Outcomes of Erectile Implants After Phalloplasty: Retrospective Analysis of 95 Procedures. Journal of Sexual Medicine. 2016;13(11):1758-64.	Surgery, method
Nikolic D, Granic M, Ivanovic N, Zdravkovic D, Nikolic A, Stanimirovic V, et al. Breast cancer and its impact in male transsexuals. Breast cancer research and treatment. 2018;171(3):565-9.	Review
Nolan IT, Morrison SD, Arowojolu O, Crowe CS, Massie JP, Adler RK, et al. The Role of Voice Therapy and Phonosurgery in Transgender Vocal Feminization. The Journal of craniofacial surgery. 2019;30(5):1368-75.	Age
Nota NM, Dekker MJHJ, Klaver M, Wiepjes CM, van Trotsenburg MA, Heijboer AC, et al. Prolactin levels during short- and long-term cross-sex hormone treatment: an observational study in transgender persons. Andrologia. 2017;49(6).	Metabolism
Notini L, McDougall R, Pang KC. Should Parental Refusal of Puberty-Blocking Treatment be Overridden? The Role of the Harm Principle. American Journal of Bioethics. 2019;19(2):69-72.	Ethics
Nygren U, Nordenskjöld A, Arver S, Södersten M. Effects on Voice Fundamental Frequency and Satisfaction with Voice in Trans Men during Testosterone Treatment—A Longitudinal Study. Journal of Voice. 2016;30(6):766.e23-.e34.	Treatment outcome, age
Olson KR. Prepubescent transgender children: What we do and do not know. Journal of the American Academy of Child & Adolescent Psychiatry. 2016;55(3):155-6.	Review
Olsson SE, Möller A. Regret after sex reassignment surgery in a male-to-female transsexual: A long-term follow-up. Archives of Sexual Behavior. 2006;35(4):501-6.	Case description
Özkan O, Ozkan O, Cinpolat A, Dogan NU, Bektas G, Dolay K, et al. Vaginal reconstruction with the modified rectosigmoid colon: surgical technique, long-term results and sexual outcomes. Journal of plastic surgery and hand surgery. 2018;52(4):210-6.	Surgery, method
Papadopulos NA, Lelle JD, Zavlin D, Herschbach P, Henrich G, Kovacs L, et al. Quality of Life and Patient Satisfaction Following Male-to-Female Sex Reassignment Surgery. The journal of sexual medicine. 2017;14(5):721-30.	Surgery, method
Papadopulos NA, Zavlin D, Lelle JD, Herschbach P, Henrich G, Kovacs L, et al. Combined vaginoplasty technique for male-to-female sex reassignment surgery: Operative approach and outcomes. Journal of plastic, reconstructive & aesthetic surgery : JPRAS. 2017;70(10):1483-92.	Surgery, method
Pariser JJ, Kim N. Transgender vaginoplasty: Techniques and outcomes. Translational andrology and urology. 2019;8(3):241-7.	Surgery, method
Peitzmeier S, Gardner I, Weinand J, Corbet A, Acevedo K. Health impact of chest binding among transgender adults: a community-engaged, cross-sectional study. Cult Health Sexual. 2017;19(1):64-75.	Age
Perry DG, Pauletti RE, Cooper PJ. Gender identity in childhood: A review of the literature. International Journal of Behavioral Development. 2019;43(4):289-304	Review

Postuvan V, Podlogar T, Zadravec Sedivy N, De Leo D. Suicidal behaviour among sexual-minority youth: a review of the role of acceptance and support. The Lancet Child & adolescent health. 2019;3(3):190-8.	Review
Poudrier G, Nolan IT, Cook TE, Saia W, Motosko CC, Stranix JT, et al. Assessing Quality of Life and Patient-Reported Satisfaction with Masculinizing Top Surgery: A Mixed-Methods Descriptive Survey Study. Plastic and reconstructive surgery. 2019;143(1):272-9.	Age
Priest M. Transgender Children and the Right to Transition: Medical Ethics When Parents Mean Well but Cause Harm. The American journal of bioethics: AJOB. 2019;19(2):45-59.	Ethics
Priest MM. Response to Commentaries on "Transgender Children and the Right to Transition". American Journal of Bioethics. 2019;19(6):W10-W5.	Ethics
Proulx CN, Coulter RWS, Egan JE, Matthews DD, Mair C. Associations of lesbian, gay, bisexual, transgender, and questioning–inclusive sex education with mental health outcomes and school-based victimization in US high school students. Journal of Adolescent Health. 2019;64(5):608-14.	Not only gender dysphoria.
Puckett JA, Matsuno E, Dyar C, Mustanski B, Newcomb ME. Mental health and resilience in transgender individuals: What type of support makes a difference? Journal of Family Psychology. 2019.	Age, 16-73 yrs, adolescents cannot be distinguished
Puszczyk M, Czajeczny D. Gender dysphoria and gender variance in children – Diagnostic and therapeutic controversies. Archives of Psychiatry and Psychotherapy. 2017;19(3):34-42.	Review
Radix A, Davis AM. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons. JAMA: Journal of the American Medical Association. 2017;318(15):1491-2.	Synopsis
Raigosa M, Avvedimento S, Yoon TS, Cruz-Gimeno J, Rodriguez G, Fontdevila J. Male-to-female genital reassignment surgery: A retrospective review of surgical technique and complications in 60 patients. Journal of Sexual Medicine. 2015;12(8):1837-45.	Surgery, method
Reisner SL, Hughto JMW. Comparing the health of non-binary and binary transgender adults in a statewide non-probability sample. PLoS One. 2019;14(8):e0221583.	Age, short-term follow-up
Remington AC, Morrison SD, Massie JP, Crowe CS, Shakir A, Wilson SC, et al. Outcomes after Phalloplasty: Do Transgender Patients and Multiple Urethral Procedures Carry a Higher Rate of Complication? Plastic and reconstructive surgery. 2018;141(2):220e-9e.	Surgery, method
Rider GN, McMorris BJ, Gower AL, Coleman E, Eisenberg ME. Gambling Behaviors and Problem Gambling: A Population-Based Comparison of Transgender/Gender Diverse and Cisgender Adolescents. Journal of gambling studies. 2019;35(1):79-92	Gambling
Rosenthal SM. Approach to the patient: transgender youth: endocrine considerations. The Journal of clinical endocrinology and metabolism. 2014;99(12):4379-89	Cases, review
Rothman MS, Iwamoto SJ. Bone Health in the Transgender Population. Clinical reviews in bone and mineral metabolism. 2019;17(2):77-85.	Review
Rowlands S, Amy JJ. Preserving the reproductive potential of transgender and intersex people. The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception. 2018;23(1):58-63.	Fertility
Sanchez Lorenzo I, Mora Mesa JJ, Oviedo de Lucas O. Psychomedical care in gender identity dysphoria during adolescence. Revista de psiquiatria y salud mental. 2017;10(2):96-103.	Language
Schwarz K, Fontanari AMV, Schneider MA, Borba Soll BM, da Silva DC, Spritzer PM, et al. Laryngeal surgical treatment in transgender women: A	Systematic review, age adolescents

systematic review and meta-analysis. Laryngoscope. 2017;127(11):2596-603.	cannot be distinguished.
Seal LJ. A review of the physical and metabolic effects of cross-sex hormonal therapy in the treatment of gender dysphoria. Annals of clinical biochemistry. 2016;53(Pt 1):10-20.	Review
Seyed-Forootan K, Karimi H, Seyed-Forootan NS. Autologous Fibroblast-Seeded Amnion for Reconstruction of Neo-vagina in Male-to-Female Reassignment Surgery. Aesthetic plastic surgery. 2018;42(2):491-7.	Surgery, experimental
Shatzel JJ, Connelly KJ, DeLoughery TG. Thrombotic issues in transgender medicine: A review. American journal of hematology. 2017;92(2):204-8.	Systematic review, overlap with ref 82 (later) in the report
Sherer I. Social transition: Supporting our youngest transgender children. Pediatrics. 2016;137(3):1-2.	Commentary
Shulman GP, Holt NR, Hope DA, Eyer J, Mocarski R, Woodruff N. A review of contemporary assessment tools for use with transgender and gender nonconforming adults. Psychology of Sexual Orientation and Gender Diversity. 2017;4(3):304-13.	Review
Sigurjonsson H, Rinder J, Möllermark C, Farnebo F, Lundgren TK. Male to female gender reassignment surgery: Surgical outcomes of consecutive patients during 14 years. JPRAS Open. 2015;6:69-73.	Surgery, method
Slater MW, Vinaja X, Aly I, Loukas M, Terrell M, Schober J. Neovaginal Construction with Pelvic Peritoneum: Reviewing an Old Approach for a New Application. Clinical anatomy (New York, NY). 2018;31(2):175-80.	Surgery, method
Smith KP, Madison CM, Milne NM. Gonadal suppressive and cross-sex hormone therapy for gender dysphoria in adolescents and adults. Pharmacotherapy. 2014;34(12):1282-97.	Review
Song TE, Jiang N. Transgender Phonosurgery: A Systematic Review and Meta-analysis. Otolaryngology--head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2017;156(5):803-8.	Surgery, method, age
Spivey LA, Edwards-Leeper L. Future Directions in Affirmative Psychological Interventions with Transgender Children and Adolescents. Journal of clinical child and adolescent psychology: the official journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53. 2019;48(2):343-56.	Review/editorial
Stanfors M, Goldscheider F. The forest and the trees: Industrialization, demographic change, and the ongoing gender revolution in Sweden and the United States, 1870-2010. Demographic Research. 2017;36:173-226.	Review
Stevenson MO, Tangpricha V. Osteoporosis and Bone Health in Transgender Persons. Endocrinology and metabolism clinics of North America. 2019;48(2):421-7.	Review
Streed CG, Harfouch O, Marvel F, Blumenthal RS, Martin SS, Mukherjee M. Cardiovascular disease among transgender adults receiving hormone therapy: A narrative review. Annals of Internal Medicine. 2017;167(4):256-67.	Systematic review, overlap with ref 80 and 81 in the report
Sutcliffe PA, Dixon S, Akehurst RL, Wilkinson A, Shippam A, White S, et al. Evaluation of surgical procedures for sex reassignment: a systematic review. J Plast Reconstr Aesthetic Surg. 2009;62(3):294-306.	Surgery, method
Syed IA, Afridi MI, Dars JA. An artistic inquiry into gender identity disorder/ gender dysphoria: A silent distress. Asian journal of psychiatry. 2019;44:86-9.	Method
Tebbens M, Nota NM, Liberton NPTJ, Meijer BA, Kreukels BPC, Forouzanfar T, et al. Gender-affirming hormone treatment induces facial feminization in transwomen and masculinization in transmen: Quantification by 3D scanning and patient-reported outcome measures. Journal of Sexual	Treatment effect

Medicine. 2019;16(5):746-54.	
Tellier P-P, Wren B. Ethical issues arising in the provision of medical interventions for gender diverse children and adolescents. Clinical Child Psychology & Psychiatry. 2019;24(2):203-22.	Ethics
Tellier P-P, Wren B. Reflections on 'Thinking an Ethics of Gender Exploration: Against Delaying Transition for Transgender and Gender Variant Youth'. Clinical Child Psychology & Psychiatry. 2019;24(2):237-40.	Ethics
Terrier JE, Courtois F, Ruffion A, Morel Journel N. Surgical outcomes and patients' satisfaction with suprapubic phalloplasty. The journal of sexual medicine. 2014;11(1):288-98.	Surgery, method
Thijs P, Te Grotenhuis M, Scheepers P. The relationship between societal change and rising support for gender egalitarianism among men and women: Results from counterfactual analyses in the Netherlands, 1979–2012. Social Science Research. 2017;68:176-94.	Review
Thomas TN, Unger CA. Vaginoplasty for the Transgender Woman. Current Obstetrics and Gynecology Reports. 2017;6(2):133-9.	Surgery, method
Top H, Balta S. Transsexual Mastectomy: Selection of Appropriate Technique According to Breast Characteristics. Balkan medical journal. 2017;34(2):147-55.	Surgery, method
Traish AM, Gooren LJ. Safety of physiological testosterone therapy in women: lessons from female-to-male transsexuals (FMT) treated with pharmacological testosterone therapy. The journal of sexual medicine. 2010;7(11):3758-64.	Review
T'Sjoen G, Arcelus J, Gooren L, Klink DT, Tangpricha V. Endocrinology of Transgender Medicine. Endocrine reviews. 2019;40(1):97-117.	Review
T'Sjoen G, Van Caenegem E, Wierckx K. Transgenderism and reproduction. Current opinion in endocrinology, diabetes, and obesity. 2013;20(6):575-9.	Review
Twist J, de Graaf NM, Tellier P-P. Gender diversity and non-binary presentations in young people attending the United Kingdom's National Gender Identity Development Service. Clinical Child Psychology & Psychiatry. 2019;24(2):277-90.	Inventory of gender identity
Walls NE, Atteberry-Ash B, Kattari SK, Peitzmeier S, Kattari L, Langenderfer-Magruder L. Gender Identity, Sexual Orientation, Mental Health, and Bullying as Predictors of Partner Violence in a Representative Sample of Youth. The Journal of adolescent health: official publication of the Society for Adolescent Medicine. 2019;64(1):86-92	Short-term, bullying
Van Boerum MS, Salibian AA, Bluebond-Langner R, Agarwal C. Chest and facial surgery for the transgender patient. Translational andrology and urology. 2019;8(3):219-27.	Surgery, method
Van Caenegem E, Wierckx K, Taes Y, Dedecker D, Van de Peer F, Toye K, et al. Bone mass, bone geometry, and body composition in female-to-male transsexual persons after long-term cross-sex hormonal therapy. The Journal of clinical endocrinology and metabolism. 2012;97(7):2503-11.	Include in ref 86 in the report
Van Caenegem E, Wierckx K, Taes Y, Schreiner T, Vandewalle S, Toye K, et al. Preservation of volumetric bone density and geometry in trans women during cross-sex hormonal therapy: a prospective observational study. Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2015;26(1):35-47.	Included in ref 85 in the report
Van Damme S, Cosyns M, Deman S, Van den Eede Z, Van Borsel J. The Effectiveness of Pitch-raising Surgery in Male-to-Female Transsexuals: A Systematic Review. Journal of voice: official journal of the Voice Foundation. 2017;31(2):244.e1-.e5.	Systematic review, surgery, method age,
van de Grift TC, Pigot GLS, Boudhan S, Elfering L, Kreukels BPC, Gijs L, et al. A Longitudinal Study of Motivations Before and Psychosexual Outcomes	Surgery, motivation

After Genital Gender-Confirming Surgery in Transmen. The journal of sexual medicine. 2017;14(12):1621-8.	
van der Sluis WB, Bouman MB, de Boer NKH, Buncamper ME, van Bodegraven AA, Neefjes-Borst EA, et al. Long-Term Follow-Up of Transgender Women After Secondary Intestinal Vaginoplasty. Journal of Sexual Medicine. 2016;13(4):702-10.	Surgery, method
van der Sluis WB, Pavan N, Liguori G, Bucci S, Bizic MR, Kojovic V, et al. Ileal vaginoplasty as vaginal reconstruction in transgender women and patients with disorders of sex development: an international, multicentre, retrospective study on surgical characteristics and outcomes. BJU international. 2018;121(6):952-8.	Surgery, method
van der Sluis WB, Smit JM, Pigot GLS, Buncamper ME, Winters HAH, Mullender MG, et al. Double flap phalloplasty in transgender men: Surgical technique and outcome of pedicled anterolateral thigh flap phalloplasty combined with radial forearm free flap urethral reconstruction. Microsurgery. 2017;37(8):917-23.	Surgery, method
Vaughan SC. Suicidality in LGBTQ+ Youth. Psychoanal Study Child. 2018;71(1):40-54	Review
Vrouenraets LJ, Fredriks AM, Hannema SE, Cohen-Kettenis PT, de Vries MC. Early Medical Treatment of Children and Adolescents With Gender Dysphoria: An Empirical Ethical Study. The Journal of adolescent health: official publication of the Society for Adolescent Medicine. 2015;57(4):367-73.	Ethics
Weigert R, Frison E, Sessiecq Q, Al Mutairi K, Casoli V. Patient satisfaction with breasts and psychosocial, sexual, and physical well-being after breast augmentation in male-to-female transsexuals. Plastic and reconstructive surgery. 2013;132(6):1421-9.	Age
Wiepjes CM, Vlot MC, Klaver M, Nota NM, de Blok CJM, de Jongh RT, et al. Bone Mineral Density Increases in Trans Persons After 1 Year of Hormonal Treatment: A Multicenter Prospective Observational Study. J Bone Miner Res. 2017;32(6):1252-60.	Short-term follow-up
Wierckx K, Elaut E, Declercq E, Heylens G, De Cuypere G, Taes Y, et al. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. European journal of endocrinology. 2013;169(4):471-8.	Included in ref 77 in the report
Wilson SC, Morrison SD, Anzai L, Massie JP, Poudrier G, Motosko CC, et al. Masculinizing Top Surgery: A Systematic Review of Techniques and Outcomes. Annals of plastic surgery. 2018;80(6):679-83.	Surgery, method
Wirthmann AE, Majenka P, Kaufmann MC, Wellenbrock SV, Kasper L, Hüttinger S, et al. Phalloplasty in Female-to-Male Transsexuals by Gottlieb and Levine's Free Radial Forearm Flap Technique--A Long-Term Single-Center Experience over More than Two Decades. J Reconstr Microsurg. 2018;34(4):235-41.	Surgery, method
Witcomb GL, Claes L, Bouman WP, Nixon E, Motmans J, Arcelus J. Experiences and Psychological Wellbeing Outcomes Associated with Bullying in Treatment-Seeking Transgender and Gender-Diverse Youth. LGBT Health. 2019;6(5):216-26	Short-term, bullying
Wolter A, Scholz T, Pluto N, Diedrichson J, Arens-Landwehr A, Liebau J. Subcutaneous mastectomy in female-to-male transsexuals: Optimizing perioperative and operative management in 8 years clinical experience. Journal of plastic, reconstructive & aesthetic surgery: JPRAS. 2018;71(3):344-52.	Surgery, method
Wood H, Sasaki S, Bradley S, Singh D, Fantus S, Owen-Anderson A, et al. Patterns of Referral to a Gender Identity Service for Children and Adolescents (1976–2011): Age, Sex Ratio, and Sexual Orientation. Journal of Sex & Marital Therapy. 2013;39(1):1-6.	Letter

Wright T, Candy B, King M. Conversion therapies and access to transition-related healthcare in transgender people: a narrative systematic review. BMJ Open. 2018;8(12):e022425.	Review
Yilmaz T, Kuscu O, Sozen T, Suslu AE. Anterior Glottic Web Formation for Voice Feminization: Experience of 27 Patients. Journal of voice : official journal of the Voice Foundation. 2017;31(6):757-62.	Surgery, method
Zaheer U, Granger A, Ortiz A, Terrell M, Loukas M, Schober J. The anatomy of free fibula osteoseptocutaneous flap in neophalloplasty in transgender surgery. Clinical anatomy (New York, NY). 2018;31(2):169-74.	Surgery, method
Zavlin D, Schaff J, Lellé JD, Jubbal KT, Herschbach P, Henrich G, et al. Male-to-Female Sex Reassignment Surgery using the Combined Vaginoplasty Technique: Satisfaction of Transgender Patients with Aesthetic, Functional, and Sexual Outcomes. Aesthet Plast Surg. 2018;42(1):178-87.	Surgery, method
Zeluf G, Dhejne C, Orre C, Mannheimer LN, Deogan C, Hoijer J, et al. Erratum to: Health, disability and quality of life among trans people in Sweden-a web-based survey. BMC Public Health. 2016;16(1):1085.	Erratum
Zeluf G, Dhejne C, Orre C, Mannheimer LN, Deogan C, Höijer J, et al. Health, disability and quality of life among trans people in Sweden-a web-based survey. BMC Public Health. 2016;16(1):1-15.	Not only gender dysphoria.
Zhang YF, Liu CY, Qu CY, Lu LX, Liu AT, Zhu L, et al. Is vaginal mucosal graft the excellent substitute material for urethral reconstruction in female-to-male transsexuals? World J Urol. 2015;33(12):2115-23.	Surgery, method
Zimlich R. LGBT teens and suicide risk: How you can help. Contemporary Pediatrics. 2019;36(3):34-5	Review
Zucker KJ. Adolescents with Gender Dysphoria: Reflections on Some Contemporary Clinical and Research Issues. Archives of sexual behavior. 2019	Review

Tabeller med beskrivning av de ingående studierna

Tabeller med beskrivning av de ingående studierna (PDF)

Table 1 Articles on the epidemiology of gender dysphoria in children and adolescents.

Author **Year** **Ref** **Country**	**Age**	**Study design** **n**	**Aims/ Research question(s)**	**Outcome measures**
Arnoldussen et al 2019 [15] The Netherlands	**Mean** 14.6 years **Range** 10.1–18.1 years	Prevalence 2000–2016 N=1 072 (n=668 females)	To examine whether consecutively transgender clinic-referred adolescents between 2000 and 2016 differ over time in demographic, psychological, diagnostic, and treatment characteristics	Demographics. Intelligence: measured by Dutch version of the Wechsler Intelligence Scale for Children, or the Wechsler Adult Intelligence Scale. Psychological functioning: measured by the Child Behaviour Check List Gender dysphoria intensity: Youth Self-Report, intensity of gender dysphoria measured by the Utrecht Gender Dysphoria Scale. Percentage of referrals diagnosed with gender dysphoria Percentage of diagnosed adolescents that started with affirmative medical treatment (puberty suppression and/or gender-affirming hormones)
Becerra-Culqui et al 2018 [29] USA	**Range** 3–17 years	Electronic medical record (EMR) – based retrospective and prospective cohort study n=588 transfeminine n=745 transmasculine children 10 male and 10 female referent cisgender enrolees matched to each TGNC individual	To estimate the prevalence of mental health diagnoses among transfeminine and transmasculine children and adolescents at the time of their initial presentation (index date) and compare their mental health status to that of their cisgender counterparts.	Prevalence ratios of: Anxiety disorders attention deficit disorders Autism spectrum disorders Conduct and/or disruptive disorders Depressive disorders Eating disorders Self-inflicted injury Suicidal ideation

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Bränström et al 2019 [37] Sweden	**Mean** 31.5 years	Registry study, 3 linked registries 2005 -2015 n=2 679 Legal gender: n=1 284 male n=1 395 female Swedish Total Population Register National Patient Register Prescribed Drug Register.	To ascertain the prevalence of mood and anxiety disorder health care visits and antidepressant and anxiolytic prescriptions in 2015 as a function of gender incongruence diagnosis and gender affirming hormone and surgical treatment in the entire Swedish population.	Epidemiology **Mental health treatment** Mood disorder Anxiety disorder Health care visits, Antidepressant prescriptions Anxiolytic prescriptions Hospitalization after a suicide attempt. **Hormone treatment** Oestrogen or progesterone Androgen Androgen-suppressing or -blocking medication **Surgical treatment** Breast or dermatological chest surgery Surgery of the reproductive organs Dermatological surgery Laryngeal surgery
Chen et al 2016 [16] USA	**Mean** 14.4 ± 3.2 years	Retrospective chart review of referrals 2002–2015 n=38 n=22 natal females **Follow-up** 13 years	Frequency and characteristics of referrals	Numbers of referrals per year Timing of referral Comorbid conditions Hormonal therapy Eligibility for treatment. Pubertal status at presentation, Psychological evaluation for GD, History of RLE (real-life experience of living full-time in the identified gender). **Concurrent diagnoses** (depression, attention deficit/hyperactivity disorder, autism spectrum disorder, suicidality and/or self-harm, psychotropic medications)

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Chiniara et al 2018 [17] Canada	**Range** 12–18 years **Mean** 16 years	Retrospective review 2014–2016 n=203 n=156 natal females	Examine characteristics, including mental health comorbidities, among adolescents presenting to a transgender clinic	Demographic data: AFAB - assigned female at birth; AMAB - assigned male at birth; social transition; age at referral Clinical characteristics, Tanner stage, Bone age Utrecht Gender Dysphoria Scale Mental health comorbidities (depression, anxiety, autism spectrum disorder, suicidal ideation, self-harm, medication for mood disorder) Blood work
Connolly et al 2016 [38]		Review		
Costa and Colizzi 2016 [39] United Kingdom	**Range** 18–58 years	Systematic review up to 2016 17 included studies (cross-sectional studies and longitudinal studies)	Systematic review of all studies examining the effect of cross-sex hormonal treatment on mental health and well-being in gender dysphoria.	
de Graaf et al 2018 [18] United Kingdom	**Age at referral** **Mean** 8.72 years (SD 2.30) natal boys **Mean** 9.78 years (SD 2.15) natal girls	Extraction of health records 2000–2017 n=1 215 n=681 natal boys n=534 natal girls	Examine the sex ratio of children, age at referral and year of referral, for children referred to the Gender Identity Development Service in the UK.	Birth assigned gender Year of referral Age at assessment

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
de Graaf et al 2018 [21] United Kingdom	**Range** 1–18 years	Retrospective review of referrals 2009–2016. N=4 506	Examine the sex ratio in the number of children and adolescents referred over the past 7 years.	Age at referral Birth assigned gender Sex ratio Psychological functioning (internalizing and externalizing problems: Child Behaviour Checklist)
de Graaf et al 2019 [40] United Kingdom	Under 18 years	Referrals between 2012–2014 N=995	Identify the ethnicities of children and young people referred to the UK Gender Identity Development Service.	Ethnicity
Drummond et al 2008 [11] Canada	**Age at assessment** Mean: 8.88 years Range: 3–12 years **Age at follow-up** Mean: 23.24 years Range: 15–36 years	Cohort 1975–2004 n=25 girls	This study provided information on the natural histories of 25 girls with gender identity disorder.	Cognitive functioning: assessed by Wechsler Adult Intelligence Scale Sex-typed behaviour Recalled childhood gender identity and gender role behaviour Concurrent gender identity. Sexual orientation in behaviour. Sexual identity self-labelling. Social desirability
Hisle-Gorman et al 2019 [27) USA	**Range** 2–18 years **Median** 11.6 years	Retrospective case-cohort study of GD diagnoses with and without ASD Health care records 2000–2013. n=48 762 diagnosed with ASD **Follow-up** 3 years	We investigated diagnosed GD in patients formally diagnosed with ASD in the Military Health System	Diagnosis of GD

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Kaltiala-Heino et al 2019 [10] Finland	**Mean** 15.7 years	Prevalence Data from a School Health Promotion Study 2017. N=135 760	To explore the susceptibility of gender identity to mischievous responding, and prevalence of cis-gender, opposite-sex and other/ non-binary gender identities as corrected for likely mischievous responding among Finnish adolescents.	Sex Perceived gender Disability Factitious responses (implausible, likely mischievous responding). The School Health Promotion Study (SHPS) by the National Institute for Health and Welfare is a school-based survey designed to examine the health, health behaviours and school experiences of teenagers.
Kaltiala-Heino et al. 2015 [20] Finland	**Mean** 16 years	Structured quantitative retrospective chart review of all Sex Reassignment applicants (2011–2013). N=47 n=41 natal girls n=6 natal boys	To describe the adolescent applicants for legal and medical sex reassignment during the first two years of adolescent gender identity team in Finland, in terms of sociodemographic, psychiatric and gender identity related factors and adolescent development.	Signs of gender dysphoria/ gender incongruence in childhood (< age 12) Age of onset of gender concerns Age convinced of being transsexual. Duration of living in desired gender role. Psychiatric history prior to entering gender identity service (anxiety, depression, suicidal behaviours, conduct problems, autism spectrum related problems, substance abuse, psychotic symptoms, other) Peer-related difficulties (bullying, isolation, before or after onset of gender dysphoria) Sociodemographic variables (age, natal sex, family structure, parental education)

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Kaltiala-Heino et al 2019 [9] Finland	**Range** 16–18 years	Survey on gender experience among junior high school students, during the 2012–2013 and 2017 school years. n=1 746 survey responders n=644 male n=1 102 female	Explore whether there has been an increase in prevalence and changes in sex ratio in feelings of gender dysphoria (GD) in an adolescent population in Northern Europe	Gender identity/Gender Dysphoria: measured with GIDYQ-A. Age
Landen and Innala 2000 [25] Sweden	**Range** 18–70 years	Questionnaire 1998 n=992 randomly selected national sample of Swedish residents (lay people) n=668 respondents	A general inventory of the ethical views on sex reassignment and attitudes toward transsexuals in Sweden.	Demographic Characteristics Possibility to undergo sex reassignment Bearing of expenses Right to get married in their new sex Right to work with children Right to adopt and raise children
Littman 2018 [23] Littman 2019 correction [24] USA	**At announced transgender identification** Mean age of 15.2 **At survey** Mean: 16.4 years	Descriptive, exploratory study, survey n=256 parent-completed surveys (82.8% natal females)	To collect data about parents' observations, experiences, and perspectives about their adolescent and young adult children showing signs of an apparent sudden or rapid onset of gender dysphoria that began during or after puberty, and develop hypotheses about factors that may contribute to the onset and/or expression of gender dysphoria among this demographic group.	Non-heterosexual sexual orientation Rapid onset gender dysphoria Pre-existing diagnosis of mental health disorder Pre-existing diagnosis of Neurodevelopmental disability Parent-child relationships Behaviours (distrust, asocial, isolation, social media/internet use)
Mann et al 2019 [30] United Kingdom	Up to 25 years	Systematic Review, 2000–2017 n=7 included studies	To investigate the prevalence of self-injurious thoughts and behaviours among children and young people in the UK identifying as a gender not typically associated with the sex they were assigned at birth and, further, to examine relevant prevalence rates of self-injurious thoughts and behaviours reported.	Prevalence of self-injurious thoughts and behaviours: Self-harm/ self-injurious behaviour Thoughts of self-harm Suicidal ideation Suicide attempt

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Nabbijohn et al 2019 [28] Canada	**Range** 6–12 years	Parent-report online questionnaire (anonymous survey) June to Dec 2016. n=2 445 n=441 clinical subgroup (mental health/ developmental diagnoses) n=2004 nonclinical (not seeking health care) subgroup	Gender variance in association with Autism Spectrum Disorder characteristics in nonclinical children and in children with developmental/ mental health diagnoses.	Gender Variance (GV): measured by Gender Identity Questionnaire for Children. Subdomains of ASD characteristics: measured by the Children's Social Behaviour Questionnaire. Clinical diagnoses: Autism Spectrum Disorder (ASD), Attention-deficit/hyperactivity disorder (ADHD), Obsessive–compulsive disorder (OCD), Sensory processing disorder (SPD), Oppositional defiant disorder (ODD), Mood and anxiety disorders, Learning disabilities, Neurodevelopmental conditions. Among nonclinical children: Parent-reported difficulties orienting socially, Stereotyped behaviours
Nordahl-Hansen et al 2019 [31]	Review update of Oien et al 2018 [32]		Update of previous review: Systematic map review on Gender Dysphoria, sexuality and Autism spectrum disorder (Øien et al. 2018)	
Øien et al 2018 [32]		**Systematic map review,** overview of systematic reviews, up to 2018 n=28 included quantitative studies n=19 included qualitative studies	To map the current empirical research on the co-occurrence of GD and ASD	Gender dysphoria Autism spectrum disorder

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Steensma et al 2013 [13] The Netherlands	**Age at referral and first diagnosis** Range: 6–12 years **Age at follow-up** Range: 15–17 years	Referrals 2000 and 2008 n=127 adolescents n=79 boys n=48 girls **Follow-up** 4-year period between 2008 and 2012	To assess Childhood Predictors of Persistence of GDiInto Adolescence	Demographics: natal sex, age at assessment, diagnosis (DSM-IV-TR GID), social role transition, parents' marital status, parents' social class, and Full-Scale IQ. Gender Identity and Gender Dysphoria: The Dutch version of the Gender Identity Interview for Children (GIIC). The Dutch version of the Gender Identity Questionnaire (GIQ) Psychological Functioning: assed through parental report, by the Dutch version of the Child Behaviour Checklist/ 4-18 (CBCL), and teacher report, by the Dutch version of the Teacher's Report Form (TRF). Quality of Peer Relations. Adolescence: Gender Identity: The Gender Identity Interview for Adolescents and Adults (GIAA) Gender Dysphoria: The Utrecht Gender Dysphoria Scale (UGDS) Body Image: The Body Image Scale (BIS) Sexual Orientation Parent Report.
Strang et al 2018 [14] USA	**Range** 13–21 years **Mean** 16.6 (SD 1.9) years	Interviews n=22 autistic gender-diverse adolescents **Follow-up** 12 and 22 months	To characterize the short-term gender trajectories of adolescents with the co-occurrence [autistic gender-diverse adolescents who have diagnostically-confirmed ASD); To identify salient themes in these young people's lives	Pre-pubertal gender nonconformity Gender dysphoria Social gender affirmation

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Sumia et al 2017 [8] Finland	**Mean** 17 years	Anonymously classroom questionnaire on current and childhood gender experience. n=719 n=401 girls n=318 boys	We studied current and recalled childhood gender identity	Dimensions of identity: Current gender identity: assessed with the Gender Identity/Gender Dysphoria Questionnaire for adolescents (GIDYQ-A) Recalled gender identity: assessed with the Recalled Childhood Gender Identity scale (RCGI)
Wallien et al 2008 [12] The Netherlands	**At referral** Mean: 8.4 years Range: 5–12 years **At follow-up** Mean: 18.9 years Range: 16–28 years	Retrospective 1989 and 2005 n=77 children n=59 boys n=18 girls **Follow-up** 10.4 ± 3.4 years	To establish the psychosexual outcome of gender-dysphoric children at 16 years or older and to examine childhood characteristics related to psychosexual outcome	Cross-gender identification Discomfort with their own sex Gender roles Gender dysphoria Sexual orientation
Van der Miesen et al 2018 [34] The Netherlands	**Mean** 16 years adolescents 32 years adults	Prevalence 2010–2014 n=573 adolescents with ASD n=807 adults with ASD n=1 862 controls	The self-reported wish to be of the opposite gender of adolescents and adults with ASD	Emotional and behavioural problems: measured by DSM-oriented scales of the Youth Self-Report and the Adult Self-Report. Subdomains of the ASD spectrum: measured by Children's Social Behaviour Questionnaire and the Adult Social Behaviour Questionnaire.
Wiepjes et al 2018 [36] The Netherlands www.sbu.se/307	**Range** 7–81 years **Three age groups** <12 years 12–18 years >18 years	Retrospective review of medical files, 1972–2015 n=6 793 n=2 361 natal females n=4 432 natal males **Follow-up** 46–271 months after initiation of hormone treatment	To study the current prevalence of gender dysphoria, how frequently gender-affirming treatments are performed, and the number of people experiencing regret of this treatment.	Number who applied for transgender health care, Percentage starting with gender-affirming hormonal treatment (HT) Prevalence of transgender people receiving gender-affirming treatment Percentage who underwent gonadectomy Percentage who regretted gonadectomy

Author Year Ref Country	Age	Study design n	Aims/ Research question(s)	Outcome measures
Zucker KJ 2017 [41]		Review		

ASD = autism spectrum disorder, GD= Gender dysphoria.

Table 2 Articles on regret of gender affirmative treatment.

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Blanchard et al. 1989 [44] Canada	**At surgery** **Range** 29–41 years	Questionnaire 1981–1985 n=111 postoperative **Follow-up** >1 year after surgery	Whether heterosexual males are more likely to regret sex reassignment surgery than homosexual males or females.	Regret
Defreyne et al 2017 [49] Belgium www.sbu.se/307	Not reported	Systematic Review 1960–2017 29 articles included	The impact and outcomes of gender affirming hormonal treatment and gender affirming surgery on the quality of life of trans men.	Regret Hormonal therapy: quality of life, sexual functioning; Gender affirming surgery: Chest reconstructive surgery Hysterectomy and oophorectomy Gender affirming genital surgery Fertility; Effects of gender affirming surgery: Satisfaction, Regret, quality of life, sexual functioning

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Dhejne et al. 2014 [42] Sweden	**Age at application** **Range** 16–75 years **Median** 27 years FtM 32 years MtF	Review of application files 1960–2010 n=767 n=289 natal females n=478 natal males **Follow-up** 50 years	Incidence and prevalence of applications in Sweden for legal and surgical sex reassignment examined over a 50-year period (1960–2010), including the legal and surgical reversal applications.	Regret, for surgical conversion to original sex Assigned sex at birth, Date of first visit to a healthcare provider with a documentation of gender dysphoria, Date and outcome of the decision (with reasons if refused), Date of new legal gender, Sex reassignment abroad (if applicable). Age of the applicants calculated based on the date of the first application.
Imbimbo et al 2009 [45] Italy	**Range** 21–59 years **Mean** 31.36 ± 5.1 years	Questionnaire 1992–2006 n=163 MtF patients who had undergone gender-transforming surgery **Follow-up** 12–18 months after surgery	Clinical and psychosocial profile of male-to-female transsexuals in Italy, personal and clinical experience and evaluation of their postsurgical satisfaction levels.	Regret Suicidal ideation/suicide before SRS Emotional support Presurgical preparation Surgical procedure Postsurgical discomfort Postsurgical sex life Overall satisfaction. General demographic data (employment status, family status, personal relationships)

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Johansson et al 2010 [46] Sweden	**Age at index** **Male-to-female** Range: 21–60 years Mean: 37.3 **Female-to-male** Range: 18–46 Mean: 27.8 **Age at SRS** **Male-to-female** Range: 22–57 Mean: 38.2 **Female-to-male** Range: 22–49 Mean: 31.4	Follow-up study, semi-structured interview. Prospective and longitudinal n=60 patients approved for sex reassignment n=25 MtF (5) n=17 FtM (51) **At follow-up** n=32 completed sex reassignment surgery n=5 in process n=abstained from genital surgery **Follow-up** >5 years in the process, or >2 years after sex reassignment surgery	Evaluation of the process of sex reassignment	Regret Early-onset transsexualism Late-onset transsexualism Global outcome of sex reassignment Satisfaction with the sex reassignment process Work, partner relationships, and sex life
Landen et al 1998 [43] Sweden	**At request for intervention** Mean: 24–25 years	Retrospective review of inception cohort, 1972–1992 n=218 **Follow-up** 4–24 years from application to evaluation	Evaluate the features and calculate the frequency of sex-reassigned subjects who had applied for reversal to their biological sex, and to compare these with non-regretful subjects.	Regret Applications for surgical conversion to original sex
Lawrence et al 2003 [47] USA.	**Age at SRS** **Mean** 44 years (SD 9) **Range** 18–70 years	Questionnaire, 2000–2000 n=232 MtF **Follow-up** >1-year postoperative	This study examined factors associated with satisfaction or regret following sex reassignment surgery (SRS), operated by one surgeon using a consistent technique.	Regret Preoperative Predictor Variables Related to Transsexual Typology Preoperative Predictor Variables Related to Compliance with Established Treatment Regimens Mental, Physical, and Social Factors Satisfaction

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Nelson et al 2009 [48] United Kingdom	**Range** 20–45 years **Mean** 31 years	Retrospective review, postal questionnaire n=17 FtM **Follow-up** **Range:** 2–23 months **Mean:** 10 months	Intervention: Reduction mammaplasty	Regret Patient satisfaction Surgical outcome Psychological morbidity Complications (haematomas, wound infection, wound dehiscence, hypertrophic scars) Secondary surgery (scar revision, nipple reduction/realignment, dog-ear correction, nipple tattooing)
van de Grift et al 2018 [50] The Netherlands	**Range** 17–63 years **Mean** 36.3 years	Multi-centre, cross-sectional follow-up study, applications for medical interventions 2007–2009 n=201 responded n=136 had undergone GAS **Follow-up** 4 to 6 years after first clinical contact	We assessed the outcomes of gender-affirming surgery (GAS, or sex-reassignment surgery) and the associations between postoperative (dis)satisfaction and quality of life. **Intervention** Genital, chest, facial, vocal cord and/or thyroid cartilage surgery	Regret Procedure performed, self-reported complications, satisfaction with surgical outcomes (standardized questionnaires), quality of life (Satisfaction with Life Scale, Subjective Happiness Scale, Cantril Ladder), gender dysphoria (Utrecht Gender Dysphoria Scale), psychological symptoms (Symptom Checklist-90)
Wiepjes et al. 2018 [36] The Netherlands www.sbu.se/307	**Range** 7–81 years **Three age groups** <12 years 12–18 years >18 years	Retrospective review of medical files 1972–2015 n=6 793 people n=4 432 birth-assigned male n=2 361 birth-assigned female **Follow-up** 46–271 months after initiation of hormone treatment	To study the current prevalence of gender dysphoria, how frequently gender-affirming treatments are performed, and the number of people experiencing regret of this treatment.	Regret of gonadectomy Number applied for transgender health care, Number starting with gender-affirming hormonal treatment Number receiving gender-affirming treatment Number undergone gonadectomy (all 25 years or older)

Table 3 Articles on psychosocial effects of puberty suppression and gender affirming hormonal treatment.

Author **Year** **Ref** **Country**	**Age**	**Study design** **n** **Follow-up**	**Aims/ Research question(s)** **Intervention/Exposure**	**Outcome measures**
Bränström et a 2019 [37] Sweden	**Mean** 31.5 years	Registry study, 3 linked registries 2005 and 2015 n=2 679 Legal gender: n=1 284 male n=1 395 female Swedish Total Population Register National Patient Register Prescribed Drug Register.	To ascertain the prevalence of mood and anxiety disorder health care visits and antidepressant and anxiolytic prescriptions in 2015 as a function of gender incongruence diagnosis and gender affirming hormone and surgical treatment in the entire Swedish population.	Epidemiology: Mental health treatment: Mood disorder Anxiety disorder health care visits, antidepressant prescriptions anxiolytic prescriptions hospitalization after a suicide attempt.
Costa et al 2016 [39]		Systematic review		
de Vries et al. 2014 [52] The Netherlands	**Range** 13.6–20.7 years **Before the start of puberty suppression** Mean: 13.6 years; **When cross-sex hormones were introduced** Mean: 16.7 years; **>1 year after gender reassignment surgery** Mean: 20.7 year	Follow-up study. Individuals receiving puberty suppression during adolescence 2004–2011 n=55 n=22 natal males, n=33 natal females **Follow-up** >1 year after gender reassignment surgery	Longer-term longitudinal evaluation of puberty suppression by means of gonadotropin-releasing hormone analogues	Psychological functioning: gender dysphoria, body image, global functioning, depression, anxiety, emotional problems behavioural problems; Objective wellbeing: social and educational/ professional functioning; Subjective wellbeing: quality of life, satisfaction with life happiness

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s) Intervention/Exposure	Outcome measures
Dhejne et al 2011 [61] Sweden	At study entry **Female at birth** Range: 20–62 years Mean: 33.3 (SD 8.7) **Male at birth** Range: 21–69 years Mean: 36.3 (SD 10.1)	Population-based matched cohort study, 1973–2003 n=324 sex-reassigned persons n=191 MtF n=133 FtM **Follow-up** Mean: 10.4 years (risk of being hospitalized for any psychiatric disorder); Mean: 11.4 years (all-cause mortality) Linkage of Swedish national registers used: Hospital Discharge Register Total Population Register Medical Birth Register Cause of Death Register Crime Register	To estimate mortality, morbidity, and criminal rate after surgical sex reassignment of transsexual persons.	**Mortality** All-cause mortality Death by definite/uncertain suicide Death by cardiovascular disease Death by tumour **Psychiatric morbidity** Any psychiatric disorder (gender identity disorders excluded) Alcohol/drug misuse and dependence Definite/uncertain suicide attempt Accidents Crime
Dhejne et al 2016 [53] Sweden	>18 years	Systematic Review n=38 included studies Included study designs: 27cross-sectional studies 11 longitudinal studies	To systematically review the prevalence of psychiatric disorders and psychopathology among trans people, and the psychiatric outcome following gender-confirming medical interventions (GCMI), either cross-sex hormone treatment (CHT) and/or gender-confirming genital surgery (GCGS)	Prevalence rates of psychiatric disorders and/or psychopathology Psychiatric outcome of post gender-confirming medical interventions

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s) Intervention/Exposure	Outcome measures
Gómez-Gil et al 2012 [54] Spain	**Range** 15–61 years **Mean** 29.87 (SD 9.15)	Questionnaires n=187 transsexual patients n=120 hormonal treatment n=84 MtF n=36 FtM n=67 no hormonal treatment n=29 MtF n=38 FtM	To evaluate the presence of symptoms of current social distress, anxiety and depression in transsexuals. **Previous intervention** Hormonal treatment w/o SRS **Duration** **Hormone Treatment** MtF patients: mean 11.0 years (SD: 9.9), range 1–46 years FtM patients: mean 4.7 years (SD 5.2), range 1–22 years	Social anxiety: assessed with Social Anxiety and Distress Scale (SADS) Depression and anxiety: assessed with Hospital Anxiety and Depression Scale (HADS)
Jellestad et al 2018 [62] Switzerland	**Range** 18–75 years **Mean** Transfeminine: 51.51 (SD 17.06) Transmasculine: 35.95 (SD 12.79)	Retrospective Cross-sectional cohort study N=143 individuals n=77 transfeminine n=41 transmasculine n=25 nonbinary gender	Examine associations between GAI and quality of life in transitioned trans individuals. **Previous intervention** Hormonal treatment w/o SRS Duration: Hormone Treatment: 0 to >20 years	Quality of Life: assessed with Short Form Health Survey questionnaire (SF-36) Depressive Symptoms: Allgemeine Depressionsskala (ADS-K), a validated German short form adaptation of the Centre for Epidemiologic Studies Depressions Scale (CES-D)
Keo-Meier et al 2015 [55] USA www.sbu.se/307	**Mean** 26.6 years **Range** 16–51 years transgender men **Range** 18–50 years non-transgender male **Range** 18–54 years non-transgender female	Prospective Controlled Study n=48 transgender men **Matched controls** n=53 non-transgender male n=62 non-transgender female **Follow-up** 3 months after testosterone initiation	Investigate the short-term effects of testosterone treatment on psychological functioning in transgender men. Intervention: Testosterone treatment:	Psychological functioning: assessed with Minnesota Multiphasic Personality Inventory (MMPI–2) The MMPI–2 is the most commonly utilized assessment of psychopathology Personality profiles and 10 clinical scales: "Hypochondriasis, Depression, Hysteria, Psychopathic- Deviate, Masculinity- Femininity, Paranoia, Psychasthenia, Schizophrenia, Hypomania, and Social Introversion”

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s) Intervention/Exposure	Outcome measures
Lindqvist et al 2017 [63] Sweden	**Range** 19–76 years **Mean** 36 years	Prospective cohort study 2003–2015 n=190 patients undergoing male-to-female GRS **Follow-up** 1, 3 and 5 years post-operatively	Examine the quality of life of transgender women undergoing gender reassignment surgery (GRS).	Quality of Life: Swedish version of the Short Form-36 Health Survey (SF-36)
Millet et al 2017 [56] United Kingdom	**Range** 7–65 years	Systematic Review 25 articles included (17 cross-sectional studies, 8 longitudinal studies) **Follow-up** At different stages of transition	To collect and critically appraise the information from the available studies describing prevalence rates of anxiety disorders and symptoms.	Anxiety disorder: Generalized Anxiety Disorder Panic disorder, Social phobia, Specific phobia, Agoraphobia, Obsessive Compulsive Disorder Measurement tools: Structured clinical interview for DSM (SCID-I) Short interview (MINI-Plus) Symptom Checklist Revised (SCL-90-R) Brief Symptom Inventory (BSI) Hospital Anxiety and Depression Scale (HADS) Speilberger State and Trait Anxiety Inventory (STAI)
Murad et al 2010 [57] USA www.sbu.se/307	**Mean** 38 years MF 31 years FM	Systematic Review 28 included studies whereof 20 cross-sectional and 8 longitudinal n=1 833 participants n=1 093 MtF n= 801 FtM **Follow-up** Mean 6 years	Prognosis of individuals with gender identity disorder receiving hormonal therapy as a part of sex reassignment in terms of quality of life and other self-reported psychosocial outcomes. **Previous intervention** Hormonal therapy (self-reported) Sex reassignment surgery	Resolution of Gender dysphoria Psychiatric comorbidity (depression, anxiety, suicide, suicidal thoughts) Sexual function Quality of life (employment, social situation)

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s) Intervention/Exposure	Outcome measures
Owen-Smith et al 2018 [58] USA	**At time of survey** **Range** 18–55+ years +	Cohort study, Survey 2015–2017. n=697 subjects n=347 FtM n=350 MtF n=234 Hormone treatment without any surgery n=404 surgery (any)	Examine the degree to which individuals' body-gender congruence, body image satisfaction, depression and anxiety differed by gender confirmation treatments (GCT) groups in cohorts of transmasculine and transfeminine individuals. **Previous intervention** Hormone therapy, "top" surgery, "bottom" surgery	Body-gender congruence Body image satisfaction Depression Anxiety
Özata Yildizhan et al 2018 [69] Turkey	**Mean** 32.60 ± 7.16 years GRT group **Mean** 27.04 ± 7.56 years NR group	Interviews n= 20 gender reassigned transsexuals n=50 new referrals Follow-up: 1–22 years post- surgery.	Family and social relationships (social adaptation) and the quality of life in people with gender dysphoria with and without history of sex reassignment surgery.	Mental Health Disorders: Major Depression, Anxiety Disorders, Alcohol/Substance Abuse, Any Psychiatric Diagnosis, Suicide Attempts. Assessments made with: Structured Clinical Interview for DSM-IV TR Axis I Disorders (SCID-I), Family Assessment Device (FAD), Multidimensional Scale for Perceived Social Support (MSPSS), World Health Organization Quality of Life Scale (WHOQOL- BREF)
Rowniak et al 2019 [59] USA	>15 years	Systematic Review up to 2017 7 included studies n=552 individuals Includes evidence grading using GRADE. Critically appraised JBI critical appraisal tools	**Review question** What are the effects of cross-sex hormone treatment on the quality of life, depression and anxiety of transgender persons? **Periods intervention** Oestrogen or testosterone	Quality of life: assessed with SF-36, SQUALA, WHOQOL-100; Depression: assessed with BDI, SDS, SCL-90, SCL-90-R, MMPI, MMPI-2; Anxiety: assessed with: SAS, SCL-90, SCL-90-R.

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s) Intervention/Exposure	Outcome measures
Ruppin and Pfafflin 2015 [64] Germany	**Mean** 47.0 years (SD 10.42) **MtF** 52.9 years (SD 10.82) **FtM** 41.2 years (SD 5.78)	Interviews & Questionnaires n=71 participants with legal name change n=35 MtF n=36 FtM **Follow-up** 10–24 years **Mean** 13.8 years (SD2.78) Inclusion criteria: the legal recognition of participants' gender change via a legal name change had to date back at least 10 years	Long-term follow-up of former patients with gender identity disorder whose aim it was to re-examine these patients from a psychosocial perspective after as long a period of time as possible after their name change and legal transition into their desired gender role	Positive and desired changes, wellbeing and social integration. Psychological problems: assessed with the Symptom Checklist (SCL-90-R Interpersonal difficulties: assessed with the Inventory of Interpersonal Problems (IIP) Gender role stereotypes: measured using the Bem Sex Role Inventory (BSRI) Personality: assessed with Freiburg Personality Inventory (FPI-R)
Simonsen et al 2016 [65] Denmark	**At referral** **Mean** 30.3 years MtF 27.0 years FtM **At initiating cross-sex hormones** **Mean** 32.0 years MtF 29.8 years FtM **At permission for SRS:** **Mean** 37.1 years MtF 32.6 years FtM	Retrospective register study 1978–2010 n =104 sex reassigned individuals n=56 MtF n=48 FtM **Follow-up** up to 16 years after SRS: **Register** Danish Psychiatric Central Research Register, Cause of Death Register	To investigate psychiatric morbidity before and after sex reassignment surgery among Danish individuals To investigate mortality among Danish individuals who underwent sex reassignment surgery during the period of 1978–2010.	Mortality Psychiatric morbidity: Depression Anxiety Abuse Personality disorder Neurotica personalis Psychosis Any psychiatric diagnosis

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s) Intervention/Exposure	Outcome measures
Tomita et al 2019 [60] USA	**Mean** 33.3 years	Survey 2013 n=868 participants n=363 trans feminine n=505 trans masculine Data collected as part of the Trans Health Survey, a national U.S. web-based health survey	Examine relationships between hormone therapy, chest surgery, and genital surgery—and the mental health outcomes of suicidality, depression, social anxiety, generalized anxiety, PTSD, alcohol use, and drug use. **Previous intervention** Hormone therapy w/o surgery	Depression Social anxiety Generalized anxiety Post traumatic stress disorder Suicidality Alcohol abuse Drug abuse
Weinforth et al 2019 [66] Germany	**Range** 18–76 years **Mean** 39.9 years	Systematic Review 13 articles included (11 quantitative, 2 mixed quantitative/ qualitative studies) N=1 101 transwomen **Follow-up** 3 months – 30 years	Overview of the currently available data on quality of life after male-to-female sex reassignment surgery.	Postoperative quality of life Life satisfaction Emotional wellbeing Sexuality Urinary incontinence
Wernick et al 2019 [67] USA	**Range of means** 17–51 years	Systematic Review 33 articles included (16 pre- postoperative studies 17 cross-sectional studies)	Understand the impact of gender-affirming surgeries on the psychological well-being of individuals with gender dysphoria. **Previous interventions** Breast augmentation, mastectomy, chest reconstruction, surgical voice feminization, craniofacial reconstructive surgery, vaginoplasty, or phalloplasty.	Gender Dysphoria, Quality of life: Satisfaction with Life Scale (SWLS), and the World Health Organization Quality of Life Assessment (WHOQOL-100); Body image/satisfaction: Body Image Scale (BIS) and the BREAST-Q General psychological functioning: Rosenberg Self-Esteem Scale (RSES), Hospital Anxiety and Depression Scale (HADS), and the Symptom Checklist-90 (SCL-90). Depression Anxiety Psychosocial outcomes

Table 4 Articles on effects on cognition and brain function by puberty suppressive and gender affirming hormonal treatment.

Author **Year** **Country**	**Age**	**Study design** **n** **FU**	**Aims/ Research question(s)** **Intervention**	**Outcome measures**
Nguyen et al 2019 [72] USA		Systematic review		
Schneider et al 2017 [71] Brazil	**Mean** 28.75 ± 6.53 years	Before- and -after study 2009–2015 n=32 male-to-female who underwent surgery and hormonal treatment **Follow-up** At least 6 months post-SRS (mean 279.28 ± 190.34 days after SRS	To measure preoperative and postoperative serum BDNF levels in transsexual individuals as a biomarker of alleviation of stress related to gender incongruence after SRS. **Previous intervention** Hormone treatment Penile inversion vaginoplasty	BDNF serum levels Time elapsed between the pre-SRS and post-SRS blood collections
Staphorsius et al 2015 [70] The Netherlands	**Range** 14–16 years	MRI n=41 adolescents n=22 female-to-males: (n=12 using GnRHa) (n=10 untreated FM) n=18 male-to-females: (n=8 using GnRHa) (n=10 untreated MF) n=45 age-matched controls n=24 girls (F) n=21 boys (M)	Determine whether the performance on the Tower of London task (ToL), a commonly used (executive functiontask, was altered in adolescents with GD when treated with GnRHa. Determine whether untreated adolescents with GD showed sex-atypical brain activation during Tower of London performance. **Intervention** triptorelin (Decapeptyl-CR®) every 4 weeks, s.c. or i.m Treatment duration: mean 1.6 ± SD 1.0 years	Tower of London performance scores (reaction times, accuracy) Region-of-interest (ROI) analyses (left DLPFC, bilateral RLPFC, praecuneus) CBCL: Child Behaviour Checklist IQ (measured with Wechsler Intelligence Scales)

GD = Gender dysphoria; GnRHa = Gonadotropin releasing hormone analogue; SRS = Sex reassignment surgery

Table 5 Articles on cancer development, cardiac disease and bone health after puberty suppression and gender affirming hormone treatment.

Author **Year** **Ref** **Country**	**Age**	**Study design** **n** **Follow-up**	**Aims/ Research question(s)**	**Outcome measures**
Tumours				
De Blok et al 2019 [75] The Netherlands	**Range** 31–57 years **Median** 47 years **At start of hormone treatment** Range: 21–38 years Median: 28 years	Retrospective, nationwide cohort study n=3 489 n=2 260 male at birth n=1 229 female at birth **Duration of treatment** **Transwomen** Median 18 years Range 7–37 years **Transmen** Median 15 years Range 2–17 years	Incidence and characteristics of breast cancer in transgender people. **Intervention** Gender affirming hormone treatment.	Breast cancer: Incidence and characteristics (histology, hormone receptor status)
Joint et al 2018 [73] United Kingdom	Not reported	Systematic Review 43 articles included (33 case reports, 5 cohort, 3 case-control, 2 cross-sectional)	Assess breast and reproductive cancer prevalence. Elucidate any associations between gender-affirming hormones and risk of these cancers.	Breast/reproductive cancer: : In transgender women: breast cancer, neovaginal cancer, testicular cancer, prostate cancer. In transgender men: breast cancer, ovarian cancer, uterine/cervical cancer, vaginal cancer.
McFarlane et al 2018 [74] Australia	**At commencement of hormone treatment** 23–49 years	Systematic Review 43 studies included (7 cohort studies, 2 cross-sectional 34 case reports) **Follow-up** 2 months – 41 years	Determine whether tumour risk in transgender individuals differs from the general population. **Duration of hormone treatment** Range 2 months – 41 years	Sex hormone-dependent tumours, all organs : Breast, Prostate, Other (lung, gastric, leukaemia, glioblastoma, meningioma, colon, haematological, GI tract, brain, melanoma, lymphoma)

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Nota et al 2018 [76] The Netherlands	**At start of cross-sex hormone treatment** **Median** Transwomen 31 years Transmen 23 years	Retrospective chart study 1972–2015 n=3 928 n=2 555 transwomen n=1 373 transmen **Follow-up** **Transwomen** Median 6.22 years Range 0.01–54.77 **Transmen** Median 4.16 years Range 0.02–41.66	Compare the incidence of common benign brain tumours in transgender individuals receiving cross-sex hormone treatment, with those reported in general Dutch or European populations. Previous interventions: In transgirls (<18 years): cyproterone acetate or triptorelin. In transboys (<18 years): lynestrenol or triptorelin, From age 16: cross-sex hormonal treatment combined with oestrogens (mostly oestradiol valerate, ethinylestradiol, or oestradiol hemihydrate) in transgirls and testosterone (mostly testosterone esters) in transboys. Adults: In transwomen: oestrogens (ethinylestradiol, conjugated oestrogens, oestradiol patches, oestradiol implants, oestradiol injections, oestradiol valerate, oestradiol gel) anti-androgens (cyproterone acetate , spironolactone) or orchiectomy. In transmen: testosterone gel, intramuscular testosterone esters, oral or intramuscular testosterone undecanoate, lynesterol	Benign brain tumours: meningiomas, pituitary adenomas (non-secretive and secretive), and vestibular schwannomas

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Cardiovascular				
Maraka et al 2017 [77] USA	**MtF:** Range of means: 19.3–43.7 years **FtM** Range of means: 21.7–37.5 years	Systematic Review up to 2015 29 included studies whereof 28 cohort studies and one randomized trial n=4 731 transgender patients n=3 231 MtF n=1 500 FtM **Follow-up** 3 months – 41 years	To evaluating the effect of sex steroid use on lipids, myocardial infarction, stroke, venous thromboembolism, and mortality in transgender individuals. Intervention: MtF: oestrogens, cyproterone acetate, GnRHa agonists (goserelin, triptorelin), spironolactone, anastrozole. FtM: testosterone	Serum lipids (TG, LDL-C, HDL-C, total cholesterol) Death Stroke Myocardial infarction Venous thromboembolism
van Velzen et al 2019 [78] The Netherlands	**Mean** 32.3 years (SD ±12.6) transwomen **Mean** 26.4 years (SD ±9.1) transmen	Prospective observational sub study 2010–2017 n=558 participants n=242 transwomen n=188 transmen from **Follow-up** up to 12 months	The effects of 1 year of treatment with oral or transdermal administration of oestrogen (plus cyproterone) and transdermal or IM application of testosterone on serum lipid levels and blood pressure were assessed in transgender persons. **Intervention** oestrogen, testosterone	Blood pressure, Serum lipids Total cholesterol High density lipoprotein Low density lipoprotein Triglycerides Haematocrit Creatinine
Dutra et al 2019 [80]		Review		Cardiovascular disease

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Getahun et al 2018 [79] USA	Age at index date: 18 to >55 years	Electronic medical record-based cohort study, enrolled 2006–2014 n=2 842 transwomen n=2 118 transmen **Matched to** n=48 686 cisgender men n=48 775 cisgender women **Follow-up** **Transwomen** mean 4.0 years **Transmen** mean 3.6 years	To examine the incidence of acute cardiovascular events in a cohort of transgender persons.	Acute cardiovascular events: Venous thromboembolism Ischemic stroke Myocardial infarction events
Goldstein et al 2019 [81] USA	Not reported	Systematic review 1989 and 2018 13 studies	To examine the degree to which routes of administration, patient comorbidities, and type of hormone utilized affect the safety of oestrogen therapy. **Previous intervention** ethinyl oestradiol, cyproterone acetate (CPA), conjugated oestrogens, 17β-oestradiol gel, oestradiol valerate, premarin, finasteride, spironolactone, progesterone	Venous thromboembolism

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Khan et al 2019 [82] USA	**Range** 21–44 years	Systematic review 12 articles included n=2 518 patients **Follow-up** Duration of monitoring for thrombotic events: range: 1–10 years	To conduct a systematic review and meta-analysis to provide an estimate of the risk of venous thrombotic events associated with oestrogen therapy in transgender women based on all available evidence.	Venous thromboembolism, incidence rate Medications Risk of thrombotic events
Wierckx et al 2013 [51] Belgium	**At the time of study** **Mean** Transwomen: 43.7 ± 12.6 years Transmen: 37.5 ± 11.0 years	Cross-sectional study, questionnaires 1986–2012 n=214 transwomen n=138 transmen age- and gender-matched control population. **Follow-up/treatment duration** **Transwomen** mean 7.7 years (3 months–35 years) **Transmen** mean 9.4 years (3 months–49 years)	Short- and long-term cardiovascular- and cancer-related morbidities during cross-sex hormone therapy. Previous intervention: Cross-sex hormone therapy: Transwomen: transdermal oestradiol, 17b-estradiol gel, oestradiol patch, oral oestrogens, oestradiol valerate, estriol, ethinyl oestradiol, ethinyl oestradiol oral contraceptive, orchiectomy. Transmen: intramuscular testosterone, testosterone esters (testosterone decanoate, testosterone isocaproate, testosterone phenylpropionate, testosterone propionate, testosterone undecanoate, transdermal testosterone, oral testosterone undecanoate, hysterectomy, ovariectomy	Cardiovascular disease: Physical health Adverse events

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Bone health				
Fighera et al 2019 [86] Brazil	**Range** 21–47 years	**Systematic Review** 19 included studies whereof 6 cross-sectional and 14 before and after studies n=1 299 n=487 transmen n=812 transwomen **Duration of cross-sex hormone treatment / exposure** Transmen: 12 months – 18 years Transwomen: 12 months – 16 years	Effects of cross-sex hormone treatment on bone mineral density (BMD) in transgender men and women. Intervention: cross-sex hormone treatment Transmen: Testosterone esters, testosterone undecanoate, transdermal testosterone, Testosterone isobutyrate, testosterone propionate Transwomen: Oestradiol valerate, mestranol, norethisterone, ethinyloestradiol, levonorgestrel, cyproterone, conjugated equine oestrogen, ethinyloestradiol, cyproterone acetate, levonorgestrel, depot oestrogens (oestradiol valerate or mestranol 1 norethisterone), transdermal oestradiol, oral oestradiol valerate, transdermal 17b-estradiol, spironolactone	Bone health: Bone mineral density assessed by DXA)Clinical factors affecting bone mass Physical activity, serum vitamin D levels, calcium intake, use of calcium and vitamin D supplements, duration of cross-sex hormone treatment, previous gender-affirming surgery, duration of follow-up, bone mineral density, T- score and Z-score for bone mineral density at various sites cross-sex hormone treatment duration
Joseph et al 2019 [83] United Kingdom	**Range** 12–14 years	Retrospective review of national cohort 2011–2016 n=70 in cohort over the first treatment year n=31 transgirls n=39 transboys n=31 longitudinal analysis where patients had scans over a 2-year treatment period n=10 transgirls n=21 transboys	Examine changes in BMD and bone mineral apparent density (BMAD) whilst on GnRHa therapy. **Intervention** Yearly dual energy X-ray absorptiometry (DXA) scans.	Bone health: bone mineral density bone mineral apparent density hip and lumbar spine

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Klink et al 2015 [84] The Netherlands	Mean age at start of GnRHa:15 years **At follow-up** 22 years	Longitudinal observational study n=34 subjects n=15 transwomen n=19 transmen **Follow-up** Gonadectomy between 1998–2012	Assess bone mineral density development during GnRHa therapy and at age 22 years in young adults with GD who started sex reassignment during adolescence. **Intervention** GnRHa monotherapy followed by CSH with discontinuation of GnRHa after gonadectomy. Treatment duration: GnRHa: 1.3–1.5 years CSH: 5.8–5.4 years	Bone mineral density
Singh-Ospina et al. 2017 [85] USA	**Range** 15–43 years	Systematic Review 1996–2015 13 articles included n=639 individuals n=392 MtF n=247 FtM **Follow-up** 12–63 months	Evaluate bone health in transgender individuals receiving sex steroids. **Previous intervention** MTF individuals: oral, transdermal, or intramuscular oestrogens, some regimens included cyproterone acetate, GnRH agonists (goserelin, triptorelin), spironolactone, or anastrozole. FTM individuals: intramuscular transdermal or oral testosterone	Bone health: lumbar spine, femoral neck, or total hip bone mineral density fractures
van Kesteren et al 1998 [90] The Netherlands www.sbu.se/307	**MtF:** Range: 16–38 years Mean: 25.4 years **FtM:** Range: 16–39 years Mean: 25.0 years	Observational n=39 n=20 MtF n=19 FtM **Follow-up** after 1 year and after 28–63 months	Whether long term cross-sex hormone treatment affects the human skeleton. **Intervention** Cross-sex hormones: anti-androgens, oestrogen, androgens, gonadectomy	Bone health: Bone mineral density Bone turnover markers (osteocalcin, alkaline phosphatase, fasting urinary calcium/creatinine, hydroxyproline/creatinine)

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Wiepjes et al 2019 [87] The Netherlands	**Transwomen** <50 years (mean 38 ± 9 years) ≥50 years (mean 60 ± 8 years) **Transmen** (mean 40 ± 14 years)	Nationwide cohort study, review of medical records. 2013 and 2015 n=1089 transwomen <50 years n=934 transwomen ≥50 years n=1 036 transmen Linked to a random population-based sample of 5 age-matched reference men and 5 age-matched reference women per person. **Follow-up** **Transwomen** using HT: median 8 years (<50 years) median 19 years (>50 years) **Transmen** using HT: median 9 years	To compare fracture incidence in transgender people using long-term hormone treatment with an age-matched reference population. Previous Intervention: HT treatment: Transwomen: anti-androgens (cyproterone acetate), orchiectomy, oestrogens (17-beta oestradiol, oral valerate, and oestradiol gel, ethinyl oestradiol, conjugated oestrogens) Transmen: testosterone gel, testosterone undecanoate, intramuscular testosterone esters Surgery: after >1 year of HT treatment and age > 18 years: vaginoplasty, orchiectomy, hysterectomy, oophorectomy.	Bone health: Bone mineral density measurements with DXA Fracture incidence Hormone blood levels (oestradiol, testosterone, LH)
Wiepjes et al 2019 [88] The Netherlands www.sbu.se/307	**Transwomen** Median: 35 years **Transmen** Median: 25 years	Retrospective chart review,1998 and 2016. n=711 transwomen n=543 transmen **Follow-up** DXA scans after 2, 5, and/or 10 years of HT	Investigate the change in BMD during the first 10 years of HT, to determine whether HT is safe and if assessing BMD during HT is necessary. Previous intervention: HT treatment: Transwomen: oestrogens, gonadectomy, anti-androgens. Transmen: testosterone. Surgery: after at least 1 to 1.5 years of HT	Bone health: BMD measurements with (DXA) Hormone blood levels (oestradiol, testosterone, LH)

Author Year Ref Country	Age	Study design n Follow-up	Aims/ Research question(s)	Outcome measures
Wiepjes et al 2019 [89] The Netherlands	**Age time of DEXA** 20–29 years 30–39 years 40–59 years	Retrospective chart review 2011–2016 n=535 transwomen n=473 transmen **Follow-up** After 5, 15, or 25 years of HT	And TBS in adult transgender people at different time points, up to 25 years, of HT **Previous intervention** HT treatment: Transwomen: oestrogens, gonadectomy, anti-androgens. Transmen: testosterone. DXA scans: at start of hormone treatment and every 5 years	Bone health: Hip structure analysis: measured by subperiosteal width, endocortical diameter, average cortical thickness, section modulus. Trabecular bone score: calculated based on lumbar spine DXA images.

Table 6 Articles on management of children and adolescents with gender dysphoria published from 2013 and onwards.

Psychosocial support

Author **Year** **Ref** **Country**	**Age** **(years)**	**Study design** **n**	**Aims/ Research question(s)**	**Outcome measures**
Alanko et al 2019 [91] Finland	**Range** 15–25 years **Mean** 20.0 (SD=2.5)	Survey, web questionnaire April–June 2013 n=1 613 n=370 transgender n=1 243 cisgender (=no gender conflict)	How the quality of relationships to parents, friends and partners affects the mental well-being. **Intervention** Web questionnaire investigating health and living conditions of sexual and gender minority youth.	Demographics Relationship quality Mental well-being: measured by Short Warwick–Edinburgh Mental Well-being Scale
Bebes et al 2015 [92] Israel	**Range** 14–21 years **Mean** 16.71 (SD 1.84)	Survey Recruited via Israeli adolescent LGBT internet sites n=234 lesbian, gay, bisexual and transgendered Israeli adolescents. N=8 identified themselves as female to male transgendered or ‘‘other’’	Associations between perceived parental acceptance, perceived parental psychological control and self-reported psychological symptoms.	Perceived parental acceptance and psychological control: measured with the Child Report of Parenting Behaviour Inventory (CRPBI) Psychological Symptoms: measured with the Brief Symptoms Inventory (BSI) Socio-Demographics
Costa et al 2015 [93] United Kingdom	**Mean** 15.5 years ± 1.4 years **At start of GnRHa** Range: 13–17 Mean: 16.5 years	Longitudinal 2010–2014 n=201 Natal male/natal female ratio: 1: 1.4 **Follow-up** 18 months	Global functioning after psychological support and puberty suppression GnRHa psychotherapeutic interventions	Gender Dysphoria: measured by Utrecht Gender Dysphoria Scale (UGDS) Psychosocial functioning: measured by Children’s Global Assessment Scale (CCAS)
de Vries et al 2016 [94] Holland and Canada	13–18 years	Retrospective, Amsterdam: 1996–2008 Toronto: 1980–2010 n=316 n=139 Amsterdam clinic n=177 Toronto clinic	To examine behavioural and emotional problems in children and adolescents with gender dysphoria in a comparative analysis between two clinics in Toronto, Ontario, Canada and Amsterdam, the Netherlands.	Child Behaviour Checklist (CBCL) Youth Self-Report (YSR) Demographic characteristics

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Johns et al 2018 [95]	11–26 years	Systematic Review 1999–2014 21 studies	To supplement the growing evidence on health risks encountered by transgender/ GV youth, we identified factors theorized to be protective for these youth across all four levels of Bronfenbrenner's socioecological model (individual, relationship, community, societal)	Protective factors to a health or behavioural outcome.
Levitan et al 2019 [96] Germany	11–18 years **Mean** 15.5 years (SD 1.33)	Cross-sectional, Questionnaire-based, single-subject study design. Sept 2013–June 2017 n=180 n=146 birth-assigned females n=34 birth-assigned males	Impact of poor peer relations and general family functioning on the development of psychological problems	Poor Peer Relations (PPR) General Family Functioning (GFF) Psychological functioning: The Youth Self-Report (YSR) Sociodemographics Clinical features
Simons et al 2013 [97] USA	12–24 years **Mean** 19.06 years (SD 2.88)	Survey February 2011 and April 2012 n=66 transgender youth n=32 birth-assigned male (asserted female) n=34 birth-assigned female (asserted male)	Relationships among parental support, quality of life, and depression	Parental support: assessed using the family subscale of the Multidimensional Scale of Perceived Social Support (help, advice, and confidante support), Quality of life: Satisfaction, Burden Depression: Beck Depression Inventory II

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Thorne et al 2019 [98] United Kingdom	16–25 years **Mean** 20.16 years (SD 2.69)	Questionnaire, part of a longitudinal study investigating the outcome of gender affirming medical treatment. June 2015–June 2017 N=388 young people n=331 (85.3 %) binary n=57 (14.7 %) non-binary **Follow-up** 2-years	This study aimed to compare levels of mental health symptomatology (anxiety, depression, and non-suicidal self-injury behaviour) and social support of treatment seeking non-binary transgender young individuals with those self-identified as binary transgender young individuals.	Anxiety and depression (Hospital Anxiety and Depression Scale, HADS) Self-esteem (The Rosenberg Self-Esteem Scale, RSE) Non-suicidal self-injury (Non-Suicidal Self-Injury (NSSI): Treatment Related (SIQ-TR) Social support (Multidimensional Scale of Perceived Social Support, MSPSS)
Weinhardt et al 2019 [99] USA	13–21 years **Mean** 17.35 years (SD 2.04)	Mixed-methods study (quantitative and qualitative data) survey at a Pride event in a Midwest US city n=154 transgender and gender nonbinary youth 92 % female at birth; 27 % identified as transmasculine, 38 % genderqueer, 24 % more than one gender.	To describe the relationship between social support, resilience, and well-being among transgender youth. Quantitative procedures were conducted with the Gender Identity and Health Youth Survey (GIHYS)	Living as one's affirmed gender, Social support: measured by the Multidimensional Scale of Perceived Social Support (MSPSS), Affirmed gender: a single item from the GMSR measure, Mental health: two questions about experiences of depression and anxiety, Meaning in life: Meaning in Life Questionnaire (MLQ), Quality of life: assessed by the Youth Quality of Life scale (YQoL 2.0), Resilience: two subscales of the Gender Minority Stress and Resilience Measure: community connectedness and pride; Demographic characteristics

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Wilson et al 2016 [100] USA	16–24 years	Cross-sectional, August 2012–Dec 2013 n=216 transgender females	We assessed differences in mental health outcomes based on exposure to discrimination among transgender female youth in the San Francisco Bay Area	Mental health outcomes: Psychological distress: measured with Brief Symptom Inventory (BSI-18), Trauma symptoms: assessed by the primary care posttraumatic stress disorder screen items from the brief New York Posttraumatic Stress Disorder Risk Score Resiliency Promoting Protective Factors: Connor Davidson Resilience Scale (CD-RS) Social support: adapted measure developed based on the 12-item Multidimensional Scale of Perceived Social Support (MSPSS) Support from transgender peers: we used our transgender community connectedness measure Socio-demographic Factors
Yadegarfard et al 2014 [101] Thailand	**Range** 15–25 years **Mean** 20 years	Survey questionnaire n=260 male respondents n=129 transgender n=131 non-transgender	This study examined the influence of family rejection, social isolation, and loneliness on negative health outcomes among Thai male-to-female transgender adolescents.	Family rejection Social support Loneliness Depression Protective factors Suicidal thoughts and attempts Sexual risk behaviour

Psychotherapy and other psychological treatments

Author Year Ref Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Costa et al 2015 [93] United Kingdom	**Mean** 15.5 years ±1.4 years **At start of GnRHa** Range: 13–17 Mean: 16.5 years	Longitudinal 2010–2014 n=201 Natal male/ natal female ratio: 1: 1.4 **Follow-up** 18 months	Global functioning after psychological support and puberty suppression GnRHa psychotherapeutic interventions	Gender Dysphoria: measured by Utrecht Gender Dysphoria Scale (UGDS) Psychosocial functioning: measured by Children's Global Assessment Scale (CCAS)
Grossman et al 2016 [102] USA	**Mean** 18 years (SD 1.74)	Survey Longitudinal study of a community sample n=129 transgender and gender nonconforming (TGNC) youth: Female-to-male (FTM) Male-to-female (MTF) Female-to-different-gender (FTDG) Male-to-different gender (MTDG)	**Intervention** Interpersonal psychological theory of suicide (IPTS) was used to examine suicidal thoughts and behaviours	Suicide attempts Suicidal ideation: assessed with INQ, Interpersonal Needs Questionnaire (INQ) Painful and Provocative Events (PPES) Acquired Capability Suicide Scale (ACSS) Self-Harm Behaviour Questionnaire (SHBQ) Demographic Characteristics
Turban et al 2019 [103] USA	Not reported	Survey Cross-sectional non-probability sample n=27 716 **Follow-up** lifetime exposure	To examine exposure to Psychological Attempts to Change a person's Gender Identity from transgender to cisgender (PACGI)	Lifetime exposure to PACGI Exposure to PACGI 2010-2015 Total number of transgender people in the United States exposed to PACGI

Puberty suppression

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Chew et al 2018 [104]	**At start of treatment** Range of means: 13–16 years	Systematic Review up to 2017 13 included studies	To review evidence for the physical, psychosocial, and cognitive effects of GnRHa, gender-affirming hormones, antiandrogens, and progestins on transgender adolescents. Intervention: GnRHa, Anti-androgens (progesterones, spironolactone), Testosterones, Oestrogens	Physical effects (blocking of puberty progression, anthropometric measurements, development of sexual characteristics, bone health, blood pressure, cholesterol) Cognitive effects (visuospatial ability, memory, executive functioning) Psychosocial effects (gender dysphoria, self-perception, body image, mood, anxiety, depression, bullying) Side effects
Costa et al 2015 [93] United Kingdom	**Mean** 15.5 years ±1.4 years **At start of GnRHa** Range: 13–17 Mean: 16.5 years	Longitudinal 2010–2014 n=201 Natal male/natal female Ratio: 1:1.4 **Follow-up** 18 months	Global functioning after psychological support and puberty suppression GnRHa psychotherapeutic interventions	Gender Dysphoria: measured by Utrecht Gender Dysphoria Scale (UGDS) Psychosocial functioning: measured by Children's Global Assessment Scale (CCAS)
de Vries et al. 2014 [52] The Netherlands	**Range** 13.6–20.7 years **Before the start of puberty suppression** Mean: 13.6 years; When cross-sex hormones were introduced: Mean: 16.7 years **>1 year after gender reassignment surgery** Mean: 20.7 years	Follow-up study. Individuals receiving puberty suppression during adolescence 2004–2011. N=55 n=22 natal males, n=33 natal females **Follow-up** >1 year after gender reassignment surgery	Longer-term longitudinal evaluation of puberty suppression by means of GnRHa	Psychological functioning: Gender dysphoria, body image, global functioning, depression, anxiety, emotional and behavioural problems; Objective wellbeing: social and educational/professional functioning; Subjective wellbeing: quality of life, satisfaction with life and happiness

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Joseph et al 2019 (83] United Kingdom	12–14 years	Retrospective review of national cohort (2011–2016) N=70 (n=70) cohort over the first treatment year (31 transgirls, 39 transboys). (n=31) longitudinal analysis where patients had scans over a 2-year treatment period (10 transgirls, 21 transboys).	Examine changes in bone mineral density and bone mineral apparent density whilst on GnRHa therapy. Intervention: Yearly DXA scans.	Bone health: bone mineral density (BMD) bone mineral apparent density (BMAD) hip and lumbar spine
Klaver et al 2018 [105] The Netherlands	**Age at start of GnRHa** Transwomen: 14.5 ± 1.8 years Transmen: 15.3 ± 2.0 years **Age at start of CHT** Transwomen: 16.4 ± 1.1 years Transmen: 16.9 ± 0.9 years	Retrospective study of medical records 1998–2014 n=71 transwomen (birth-assigned boys) n=121 transmen (birth-assigned girls) **Follow-up** Until age 22	To examine the change in body shape and composition from the start of treatment with GnRHa. Intervention: GnRHa: at a min age of 12 years Cross-sex hormonal treatment: from 16 years (oral 17b-estradiol or mixed testosterone esters) Duration of GnRHa monotherapy: Transwomen: 2.1 years (1.0–2.8) Transmen: 1.0 years (0.5–2.9) Duration of GnRHa + CHT: Transwomen:3.1 years (2.5–3.6) Transmen: 2.4 years (2.0–3.1) Duration of CHT monotherapy: Transwomen: 2.8 years (1.6–3.4) Transmen: 3.0 years (1.9–3.4)	Anthropometric and whole-body dual-energy x-ray absorptiometry data waist-hip ratio (WHR) total body fat (TBF) total lean body mass (LBM)
Kreukels et al 2011 [106]		Review		

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Klink et al 2015 [84] The Netherlands	**At start of GnRHa** 15 years **At follow-up** 22 years	Longitudinal observational study N=34 subjects n=15 transwomen n=19 transmen **Follow-up** Gonadectomy between 1998–2012	Assess bone mineral density development during GnRHa therapy and at age 22 years in young adults with gender dysphoria who started sex reassignment during adolescence. **Intervention** GnRHa monotherapy followed by cross-sex hormonal with discontinuation of GnRHa after gonadectomy. Duration: GnRHa: 1.3–1.5 years CSH: 5.8–5.4 years	Bone mineral density
Lynch et al 2015 [107] USA	Under 19 years	Retrospective chart review October 1995–March 2013. N=16 n=7 MtF n=6 FtM	Determine the efficacy and safety of medroxyprogesterone) for puberty sex hormone suppression	Age of onset of gender identity disorder symptoms comorbid diagnoses
Mahfouda et al 2017 [108]		Review		
Martinerie et al 2018 [109]		Review		

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Neyman et al 2019 [110] USA	**Range** 12–18.4 years **Mean** 16 years ± 1.77 **Median age when starting bicalutamide** 16.63 years	Retrospective review between 2013 and 2018 n=23 transwomen adolescents	Bicalutamide 50 mg daily as a second-line puberty blocker Monotherapy or with concurrent oestrogen treatment	Change in breast Tanner stage during treatment Age Timing of oestrogen initiation laboratory studies: liver function, sex steroids
Schagen et al 2016 [111] The Netherlands	**MtF (male-to-female)** Range 11.6–17.9 years Median: 13.6 years **FtM (female-to-male)** Range: 11.1–18.6 years Median: 14.2 years	Prospective observational 1998–2009 n=49 transwomen n=67 transmen **Follow-up** 12 months	To evaluate the efficacy and safety of GnRHa treatment to suppress puberty in gender dysphoric adolescents. Gonadotropin-releasing hormone agonists (GnRHa): triptorelin intramuscular injections 3.75 mg triptorelin . Duration of treatment with GnRHa alone depended on when the individual reached the age at which cross-sex hormone therapy could be added.	Physical examination: Tanner stage: breast development, testicular volume, genital development; height, weight, body mass index Blood samples: luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, oestradiol; Liver enzymes and renal function: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, g-glutamyl transferase, creatinine Body composition: evaluated using dual energy x-ray absorptiometry: lean body mass, fat percentage

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Schagen et al 2018 [112] The Netherlands	**Age at GnRHa start** Transgirls: Range: 11.6–17.9 years Mean: 14.0 years ± 1.6 Transboys: Range: 11.5–18.6 Mean: 14.3 ± 2.0 **Age at GAH start** Transgirls: Range: 13.9–18.9 Mean: 16.3 ± 1.2 Transboys: Range: 13.6–19.5 Mean: 16.8 ± 1.1	Prospective study. 1998–2009 n=127 n=73 transgirls n=54 transboys **Follow-up** 4 years	Effects of gonadotropin-releasing hormone analogues (GnRHa) treatment and gender-affirming hormone (GAH) treatment on adrenal androgen levels 2 years of GnRHa treatment only, 2 years of GnRHa combined with gender-affirming hormone treatment (oestradiol or testosterone) Treatment: intramuscular injections of the GnRHa triptorelin. Duration of treatment with GnRHa alone depended on when the individual reached the age at which gender-affirming hormone therapy could be added (approximately 16 years). Gender-affirming hormone treatment: daily oral doses of 17-beta oestradiol, intramuscular injections testosterone esters	Adrenal androgen levels: dehydroepiandrosterone-sulfate (DHEAS) Androstenedione
Staphorsius et al 2015 [70] The Netherlands	**MtF (male-to-female)** Mean: 15.1 ± 2.4 **FtM (female-to-male)** Mean: 15.8 ± 1.9	Unreported design, preclinical. N=41 n=22 FtM [n=12 of which were using GnRHa (suppressed FtM) and n=10 who were not (untreated FtM)) n=18 MtF [n=8 were using GnRHa (suppressed MtF) and 10 were not (untreated MtF))	To examine the effects of puberty suppression on executive functioning **Intervention** Tower-of-London test Magnetic resonance imaging of the brain	Executive functioning: performance on the Tower of London task, a commonly used EF task Region-of-interest analyses

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Stoffers et al 2019 [113] The Netherlands	**At start of GnRHa** Range: 11.8–18.0 years Median: 16.5 years **At start of testosterone** Range: 14.9–18.4 years Median: 17.2 years	Retrospective study, 2010–2018 N=62 FtM **Follow-up** median 12 months after testosterone treatment	This study aimed to investigate the efficacy and safety of testosterone treatment in transgender adolescents. **Intervention** GnRHa treatment and subsequent testosterone Duration of GnRHa: median 8 months (range 3-39 moths) Duration of testosterone: median 12 months (range 5–33 months)	Virilization (voice deepening, hair growth) Anthropometry (height, weight) Laboratory parameters (high density lipoprotein, cholesterol, sex hormone binding globulin, haematocrit, haemoglobin, prolactin, androstenedione, dehydroepiandrosterone sulphate, lipids, HbA1c, vitamin D) Bone mineral density
Tack et al 2018 [114] Belgium	**At the start of progestin** Mean: 16.2 ± 1.05 years in transboys Mean 16.3 ± 1.21 years in transgirls	Cohort study, who used progestins 2011–2017 n=44 transboys n=21 transgirls **Follow-up** Lynestrenol: 11.6 months (range 4–40) Cyproterone acetate: 10.6 months (range 5–31)	To study prospectively the evolution of body composition and bone mass in late-pubertal trans adolescents using the proandrogenic or antiandrogenic progestins lynestrenol (L) and cyproterone acetate (CA), respectively. **Intervention** lynestrenol (L) or cyproterone acetate (CA) Assessment before the start of progestin and before addition of cross-sex hormones.	Anthropometry (body weight, waist circumference) Grip strength, Body composition (bone mass, size, and density): using dual-energy X-ray absorptiometry Bone mineral density and bone geometry: using peripheral quantitative computed tomography Serum analyses (sex hormone–binding globulin (SHBG), total testosterone, free testosterone, total oestradiol, total testosterone/oestradiol ratio, follicle-stimulating hormone, luteinizing hormone, serum 25-OH vitamin D, parathyroid hormone (PTH), serum C-terminal telopeptide (s-CTX), and procollagen type I Nterminal propeptide (PINP))

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Turban et al 2018 [35]		Review		
Vlot et al 2017 [115] The Netherlands	**Transmen** Range: 11.7–21.9 years **Transwomen** Range: 11.5–20.9 years	Preclinical n=34 FtM (transmen) n=22 MtF (transwomen) **Follow-up** 24 months	Effect of pubertal suppression and cross-sex hormone therapy on bone turnover markers and bone mineral apparent density (BMAD) **Intervention** Treatment with GnRHa triptorelin and CSHT added in incremental doses from the age of 16 years. Transmen received testosterone esters and transwomen received 17-β estradiol.	Bone turnover markers (BTM): measured with: P1NP, osteocalcin, ICTP Bone mineral density: densitometry with DXA-scan of the lumbar spine and femoral neck of the non-dominant hip Body weight and height Stages of pubertal development: assessed according to Tanner

Gender affirming hormone treatment

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
de Vries et al 2014 [52] The Netherlands	Range 13.6–20.7 years **Before the start of puberty suppression** Mean: 13.6 years; **When cross-sex hormones were introduced** Mean: 16.7 years; >1 year after gender reassignment surgery: Mean: 20.7 years	Follow-up study. Individuals receiving puberty suppression during adolescence 2004–2011. n=55 n=22 natal males, n=33 natal females **Follow-up** >1 year after gender reassignment surgery	Longer-term longitudinal evaluation of puberty suppression by means of gonadotropin-releasing hormone analogues	Psychological functioning: gender dysphoria, body image, global functioning, depression, anxiety, emotional and behavioural problems; Objective wellbeing: social and educational/professional functioning; Subjective wellbeing: quality of life, satisfaction with life and happiness
Hahn et al 2016 [116] Austria	**Mean** 27.3 years (SD 6.4) (mean age controls 24.6 SD 5.2 years)	Brain imaging study, imaging before and after n=32 n=18 MtF n=16 healthy controls **Follow-up** at least 4 weeks	Assess the influence of continuous high-dose testosterone application on language processing in adult female-to-male transsexuals **Intervention** Testosterone (lynestrenol, desogestrel)	Morphometry analysis (grey matter volume) in Broca's and Wernicke's areas Structural connectivity Functional connectivity
Sequeira et al 2019 [117] USA	13–19 years	A retrospective chart review before and during testosterone use n=46 patients **Follow-up** 6 and 12 months after initiation.	The effect of testosterone on body mass index, z-score in transmasculine adolescents at 6 and 12 months after initiation.	Body mass index (BMI) z-score

Gender affirming surgery

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
de Vries et al. 2014 [52] The Netherlands	**Range** 13.6–20.7 years **Before the start of puberty suppression** Mean: 13.6 years; **When cross-sex hormones were introduced** Mean: 16.7 years; >1 year after gender reassignment surgery: Mean: 20.7 years	Follow-up study. Individuals receiving puberty suppression during adolescence 2004–2011. n=55 n=22 natal males, n=33 natal females **Follow-up** >1 year after gender reassignment surgery	Longer-term longitudinal evaluation of puberty suppression by means of gonadotropin-releasing hormone analogues	Psychological functioning: gender dysphoria, body image, global functioning, depression, anxiety, emotional and behavioural problems; Objective wellbeing: social and educational/professional functioning; Subjective wellbeing: quality of life, satisfaction with life and happiness
Marinkovic and Newfield 2017 [118] USA	**Age at initial visit** Range 4.7–20.9 years Mean: 15.2 years **Age at chest reconstruction** Range: 13.4–19.7 years (3 subjects <16 years) Mean: 17.2 years	Retrospective observational study Jan 2011–Dec 2017 n=167 chest reconstruction n= 55 transfemales n= 108 transmales n= 4 nonbinary	Chest reconstructive surgeries (female to male) in transgender youth, experience from one paediatric centre. **Type of procedure** Double incision, keyhole, Locations of surgery: San Diego, CA; San Francisco CA; Thousand Oaks, CA, Tijuana Mexico, Philadelphia PA, Annapolis MD.	Surgical complications: keloid, fluid collection, hematoma Satisfactions rate Initial visit age Onset of GD Testosterone start age Surgery age Medications at time of surgery: GnRHa, testosterone Other medical conditions: anxiety, Asperger's, ADHD, depression, bipolar, Hashimoto's thyroiditis, obesity, acne Additional medications: antidepressants, mood stabilizers, vitamins/minerals, acne creams

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Olson-Kennedy et al 2018 [119] USA	**Range** 13–25 years **Mean** 19 years (SD 2.5) postsurgical participants **Mean** 17 years (SD 2.5) nonsurgical participants	Survey data June 2016–Dec 2016 N=136 female at birth n=68 postsurgical participants n=68 nonsurgical participants **Follow-up** 1–5 years post-surgery	To examine the amount of chest dysphoria in transmasculine youth who had had chest reconstruction surgery compared with those who had not undergone this surgery.	Testosterone use Chest dysphoria composite score Desire for chest surgery Complications after surgery: hematoma, loss of nipple sensation, loss of sensation of other areas of the chest, keloid (excessive) scarring Regret
Cohen-Kettenis et al 1997 [120] The Netherlands	**At pre-test** Mean: 17.5 years Range: 15–20 years **At follow-up** Range: 19–27 years Mean: 22.0 years	Follow-up study. Interviews by independent psychologist. n=22 after sex reassignment surgery (SRS) n=15 FtM n=7 MtF **Follow-up** >1 year post surgery	To investigate postoperative functioning of the first 22 consecutive adolescent transsexual patients who underwent sex reassignment surgery.	Psychological, social, and sexual functioning: Gender Dysphoria: Utrecht Gender Dysphoria Scale Body Image Scale Personality Inventory: Dutch version of Minnesota Multiphasic Personality Inventory; Dutch Personality Questionnaire, Treatment Evaluation/satisfaction Social Reactions Questionnaire

Author Year Country	Age (years)	Study design n	Aims/ Research question(s)	Outcome measures
Smith et al 2001 [121] The Netherlands	**Treated* group** At pre-test: Range: 15–19 years Mean: 16.6 years **At Follow-up** Range: 19–23 years Mean: 21 years **Non-treated group** At pre-test: Range: 13.7–20.2 years Mean: 17.3 years **At Follow-up** Range: 15.7–26.2 years Mean: 21.6 years	Prospective follow-up study. March 1995–July 1999. n=20 treated adolescent transsexuals n=21 nontreated n=6 delayed-treatment adolescents *treated: indicates hormone treatment and sex reassignment surgery (SRS) **Follow-up** 1–4 years after surgery for treated patients 1–7 years after application for sex reassignment for nontreated patients	Prospective follow-up study with treated adolescent transsexuals to evaluate early sex reassignment, and with nontreated and 6 delayed-treatment adolescents to evaluate the decisions not to allow them to start sex reassignment at all or at an early age	Psychological, social, and sexual functioning. Intelligence: measured by Wechler scales (WISC-R) and WAIS Gender Dysphoria: measured by Utrecht Gender Dysphoria Scale Body Dissatisfaction: measured by Body Image Scale (BIS) Physical Appearance: measured by Appraisal of Appearance Inventory Psychological functioning: measured by Dutch Short MMPI (NVM) and the Dutch version of the Symptom Checklist 90 (SCL-90) Quality of Life: measured by the Affect Balance Scale Treatment Satisfaction Social and Sexual Functioning Satisfaction With Surgery Public Confrontation Questionnaire
Smith et al 2002 [122] The Netherlands	**Age at follow-up** Range: 18–27 years Mean: 22.5 years (SD 2.09)	Follow-up study N=19 adolescents n=6 MtF n=13 FtM **Follow-up** Mean: 58.5 months (SD 14.5) Range: 40.5–87.2 months	Assess postoperative psychological functioning in transsexuals who applied for sex reassignment in adolescence. **Intervention** Rorschach protocols before and after sex reassignment.	Postoperative psychological functioning: assessed by the Rorschach Comprehensive System

Table 7 Planned or ongoing systematic reviews registered in the PROSPERO data-base.

Author Year	Title	Organization	Age	Research question(s)	Intervention/ Exposure	Outcome
Aimee Morrison 2017	The Effects of Gender-Affirming Hormone Therapy on Fertility and Pregnancy: A Systematic Review.	Yale School of Medicine, USA	Any age	What is the effect of gender-affirming hormone therapy on fertility and pregnancy in the transgender population?	Receipt of long-term gender-affirming hormone therapy, including cross-hormones, puberty blockers, hormone antagonists.	Rates of fertility preservation and pregnancy, including both clinical pregnancy and live births.
Annie Wang 2018	Reporting outcomes and outcome measures in female-to-male microsurgical phalloplasty surgery: a systematic review.	University of British Columbia, Canada	Not indicated	What are the outcomes and outcome measures used to evaluate postoperative results for microsurgical phalloplasty surgery of female-to-male transgender patients?	Microsurgical phalloplasty	All published outcomes
Annie Wang 2018	Reporting outcomes and outcome measures in male-to-female transgender chest surgery: a systematic review.	University of British Columbia, Canada	Not indicated	What are the outcomes and outcome measures used to evaluate postoperative results for gender-reaffirming chest construction surgical procedures of male-to-female transgender patients?	Breast and chest construction surgeries	All published outcomes
Charlotte Wong 2017	Systematic review and meta-analysis of psychiatric comorbidities in gender identity disorder.	None, Hong Kong	>18 years	Does male to female transsexual group have a higher prevalence of Axis-1 psychiatric disorders than female to male transsexual group?	Not applicable.	Prevalence of Axis 1 psychiatric disorders and Personality disorder.
Christina Elise Holm-Larsen 2018	A systematic review of cardiovascular disease in oestrogen treated transgender women.	University of Southern Denmark, Faculty of Health Sciences; Denmark	Not indicated	The aim of this study is to assess the incidence of cardiovascular disease and death in transgender women treated with oestrogen.	Oestrogen that is administered intramuscular (i.m.), orally (p.o.), or t.d.	Cardiovascular disease All types (including hypertension and VTE) Excluded hypertension Excluded VTE All-cause mortality
Dina Greene 2018	Risk of thrombosis in transgender women receiving oestrogen therapy.	University of Washington, USA	>18 years	Is there an increase in thrombotic risk when transgender people are prescribed oestrogen therapy?	Exogenous oestrogen administration with or without progesterone	To identify risk, risk factors, and incidence of thrombosis

Author Year	Title	Organization	Age	Research question(s)	Intervention/ Exposure	Outcome
Felipe Ferreira 2018	Adverse effects of hormonal therapy in trans-woman undergoing transsexualization process: a systematic review.	University of Brasilia, Brazil	>18 years	What are the adverse drug reactions caused by hormonal and non-hormonal adjuvants used in the treatment of gender dysphoria in adult trans-woman?	Hormonal drug therapy and non-hormonal adjuvant used in the transsexualization process.	Adverse event to the hormonal drugs and non-hormonal adjuvants during the transsexualization process of trans-woman.
Haupt C et al. 2018	Antiandrogens or oestradiol treatments or both during hormone replacement therapy in transitioning transgender women. Cochrane Database of Systematic Reviews. 2018(10).	Cochrane Protocol	> 16 years	Efficacy and safety of hormone replacement therapy with antiandrogens or oestradiol or both in transitioning transgender women.	• Antiandrogens (cyproterone acetate or spironolactone) and oestradiol • Antiandrogens (cyproterone acetate or spironolactone) alone • Oestradiol alone	• Quality of life • Satisfaction • Adverse event
Helen Morgan 2018	A systematic review of parental influences on transgender and gender diverse children's and young people's health and wellbeing.	Murdoch University, Australia https://www.murdoch.edu.au/	0-25 years	How do parental influences impact on the health and wellbeing of trans and gender diverse children and young people?	Impact of parental influences; influence of the primary caregivers of the child/young person.	Aim: To comprehensively review relevant qualitative and quantitative empirical studies and grey literature regarding parental influences on trans and gender diverse (TGD) children's and young people's health and wellbeing.
Karine Schwarz 2016	Vocal treatment in gender dysphoria: a systematic review.	UFRGS, Brazil http://www.ufrgs.br/ufrgs/inicial	Not indicated	To identify and evaluate the effectiveness of the treatments used in the vocal treatment of individuals diagnosed with Gender Dysphoria, and the effect of treatment on pitch	Vocal and / or surgical treatment for voice.	Election of the best and most effective vocal treatment for gender dysphoria.

Author Year	Title	Organization	Age	Research question(s)	Intervention/ Exposure	Outcome
Karine Schwarz 2017	Effectiveness of speech therapy in male to female transgender people.	UFRGS, Brazil http://www.ufrgs.br/ufrgs/inicial	Not indicated	What is the best speech therapy for vocal feminization in male to female transsexuals?	Interventions for vocal feminization include speech therapy with vocal techniques to increase voice frequency as well as to adapt the vocal resonance system. Surgical techniques, such as type IV thyreoplasty or laser techniques, promote an increase in the fundamental frequency of voice.	Effects of speech therapy on the fundamental frequency of voice. Effects of phono surgery on the fundamental frequency of voice. The best technique of vocal feminization.
Kate Whitaker	What are the negative and positive factors associated with the mental health and wellbeing of transgender adults?	Royal Holloway, University of London, United Kingdom	>18 years	What are the negative and positive factors associated with the mental health and wellbeing of transgender adults?	None. Any factors that are investigated as relating to the mental health or wellbeing of transgender adults.	Outcomes of studies should include specific measurement of mental health or wellbeing, using a standardised tool or specifically designed measure.
Kathryn Bell 2017	Genital reconstructive surgery in male to female transgender patients: a systematic review of primary surgical techniques, adverse events and functional outcomes from 1950 to present day. www.sbu.se/307	Imperial College Healthcare NHS Trust, United Kingdom	Not indicated	What are the surgical techniques used to perform primary genital reconstructive surgery in trans-women?	Male to female primary genital reconstructive surgery	Adverse events for each surgical technique (including rectal injury, rectovaginal fistula, urethral meatal stenosis, vaginal stenosis, vaginal prolapse, clitoral necrosis, wound haematoma/ dehiscence/ infection and need for secondary surgery); functional outcomes for each surgical technique (including clitoral sensation, ability to orgasm, ability to have penetrative intercourse and satisfaction with aesthetics)

Author Year	Title	Organization	Age	Research question(s)	Intervention/ Exposure	Outcome
Lou Pryer CB.	Is Cognitive Behavioural Therapy (CBT) culturally adapted for transgender and gender nonconforming (TGNC) individuals accessing therapy?	University of Bath, United Kingdom	Not indicated	To review the evidence for affirmative CBT in TGNC populations.	Cognitive Behaviour Therapy. All formats of intervention delivery (group, individual and telephone).	Evidence for affirmative CBT in TGNC populations.
Michelle Tollit 2019	Measuring gender identity and gender dysphoria in transgender and gender diverse children and adolescents: a systematic review.	Murdoch Children's Research Institute, Royal Children's Hospital, University of Melbourne, Australia	up to 18 years	Which tools have been used to measure gender identity, gender incongruence or gender related distress (dysphoria)?	None; review of instruments/tools	Measurements of gender identity (or gender incongruence) or gender dysphoria in transgender and gender diverse children and adolescents. Measurement tools could be qualitative or quantitative. No Single item measures. What are the strengths, limitations and psychometric properties of these tools?
Pau Crego 2016	Regret and its consequences for transgender health: a systematic review.	University of California, Berkeley - School of Public Health, USA	Not indicated	How is regret understood in the literature regarding trans patients accessing gender-affirming hormonal and/or surgical treatments?	attempts to identify which patients truly need hormones and/or surgeries	Regret
Ritu Sharma 2019 www.sbu.se/307	Effects of gender-affirming surgeries for treatment of gender dysphoria in transgender people.	JHU.edu, USA (John Hopkins University)	Not indicated	Breast/Chest Surgery; Genital surgery	Gender-affirming surgeries for transgender people	Anger Anxiety, Depression Gender dysphoria Mental health Overall satisfaction Patient satisfaction Physical functioning Quality of life Regret, Satisfaction - request for revision Harms – oncological risks [breast reconstruction for transmen –KQ1a)

Author Year	Title	Organization	Age	Research question(s)	Intervention/ Exposure	Outcome
Ritu Sharma 2018	Effects of hormone therapy in transgender people.	John Hopkins University USA)	Not indicated		Hormone therapy drugs	Effects of hormone therapy treatment (before/after or one intervention compared to another intervention) in transgender people: Physical health outcomes (BMI, Weight, Height, metabolic outcomes, all of measure of bone mineal density and fractures) transition-related outcomes: (changes during testosterone and oestrogen administration, delay of puberty, impact on fertility, change in voice, masculinization caused by testosterone, feminization caused by oestrogen) adverse events
Ritu Sharma 2019	Interventions for speech, voice, and communication in transgender people.	John Hopkins University, USA	Not indicated		Behavioural, surgical, or endocrine interventions to change the voice as a part of sex reassignment:	Acoustic outcome, Perceptual outcomes, satisfaction and harms
Shan Siddiqui 2016	Suggested interventions for suicidal LGBT adolescents: a systematic review.	University of Texas Medical Branch, USA	10 - 19 years	What interventions can be used to address suicidality in lesbian, gay, bisexual, and transgender adolescents?	Interventions that address suicidality, sexuality, and/or mental health issues for sexual minority adolescents.	Reduced suicidal behaviours, attempted suicides, and/or suicides.

Author Year	Title	Organization	Age	Research question(s)	Intervention/ Exposure	Outcome
Stuart Macdonald 2019	Differences in the prevalence rates of depression, non-suicidal self-injury and suicidality between trans men and trans women: a systematic review.	University of Aberdeen, United Kingdom	18 - 65 years	Is depression, non-suicidal self-injury and suicidality more prevalent in trans men or trans women before psychological intervention?	Prevalence rates of depression, non-suicidal self-injury and suicidality in trans men and women.	It is anticipated that gender differences will be found on each of the three variables. Depression is hypothesised to be higher in Trans women, with NSSI and suicidality being higher in trans men.
Teresa Surace 2019	Prevalence of suicidality and non-suicidal self-injury in transgenders and people with gender dysphoria: a systematic review.	University of Catania, Italy	Not indicated	What is the prevalence of suicidality and non-suicidal self-injury in people with gender dysphoria or transgender people?	Prevalence only; No interventions or exposures	Prevalence of: (1) suicide rates (2) suicide attempts (3) suicidal ideation/thoughts (4) non suicidal self-injury If data will be available, we will divide outcome according to gender (male-to-female or female-to-male) and age.
Wai Chung Yong SUAS.	Association between transgender and osteoporosis: a systematic review and meta-analysis.	Baystate Franklin Medical Centre www.baystatehealth.org	18 years or older	Are patients after transgender associated with increased risk of osteoporosis	Transgender participants who had osteoporosis or osteopenia measured by bone mineral density as a predictor of fragility fracture.	Bone mineral density

Abbreviations
ASD = Autism spectrum disorder; DXA = Dual-energy X-ray absorptiometry; FtM = Female to male; GAS = Gender affirming surgery; GD = Gender dysphoria; GnRHa = Gonadotropin releasing hormone analogue; MtF = Male to female; PTSD = Posttraumatic stress syndrome, SD = Standard deviation, SRS = sex reassignment surgery