Region Västra Götaland, HTA-centrum
Regional activity based HTA [Verksamhetsbaserad HTA]
Health Technology Assessment
HTA report 2018:102

Gender affirmation surgery for gender dysphoria
- effects and risks

Georgas K[1], Beckman U[2], Bryman I[3], Elander A[4], Jivegård L[5], Mattelin E[3], Olsen Ekerhult T[6,7], Persson J[5], Sandman L[8], Selvaggi G[4], Stadig I[5], Vikberg Adania U[9], Strandell A[5]

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Gender affirmation surgery for gender dysphoria
- effects and risks

[Könskonfirmerande kirurgi vid könsdysfori
- effekter och risker]

Georgas K[1], Beckman U[2], Bryman I[3], Elander A[4], Jivegård L[5], Mattelin E[3], Olsen Ekerhult T[6,7], Persson J[5], Sandman L[8], Selvaggi G[4], Stadig I[5], Vikberg Adania U[9], Strandell A[5]

[1] Plastic Surgery Department, Sahlgrenska University Hospital, Gothenburg, Sweden
[2] Lundström Gender Identity Clinic, Södra Älvsborgs Hospital, Alingsås, Sweden
[3] Department of Obstetrics and Gynecology, Sahlgrenska University Hospital, Gothenburg, Sweden
[4] Plastic Surgery Department, Sahlgrenska University Hospital, Gothenburg, Sweden
[5] HTA-centrum of Region Västra Götaland, Sweden
[6] Institute of Clinical Sciences at Sahlgrenska University,
[7] Department of Urology, Reconstructive Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden
[8] Department of Work Life and Social Welfare, University of Borås, Borås, Sweden
[9] Medical Library, Sahlgrenska University Hospital, Göteborg, Sweden

[*]Corresponding author

Published September 2018
2018:102
Suggested citation: Georgas K, Beckman U, Bryman I, Elander A, Jivegård L, Mattelin E, Olsen Ekerhult T, Persson J, Sandman L, Selvaggi G, Stadig I, Vikberg Adania U, Strandell A.
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

Table of contents

1. Abstract

Background Gender dysphoria (or transsexualism) denotes individuals with a persistent cross-gender identification and discomfort with their anatomical sex manifested by a preoccupation with removing one's sex characteristics, or the perception of being born in the wrong sex. Gender affirmation surgery (GAS), affirming the patient's self-perceived gender, refers to genital, facial and body procedures. The prevalence of gender dysphoria in Sweden is estimated to 0.2-0.5 percent and referrals for evaluation increased threefold between 2013 and 2017 in Region Västra Götaland. In trans women (Male-to-Female, MtF), genital surgery aims at creating feminine genitalia. In trans men (Female-to-Male, FtM), genital surgical techniques include metoidioplasty using the clitoris to produce a small sensate phallus or phalloplasty using, e.g., a radial forearm flap to create a cosmetically satisfactory penis.

Objective To study if GAS compared with no surgery or less extensive reconstruction in adults affects quality of life (QoL), improves patient satisfaction, is associated with regret and cause complications.

Methods During January 2018 two authors performed systematic searches in PubMed, Embase, the Cochrane Library, PsychInfo and HTA-databases, selected studies, independently assessed the obtained abstracts, and made a first selection of full-text articles for inclusion. The selected articles were read by all authors and final inclusion was decided in a consensus meeting. The quality of comparative studies was assessed. Data were extracted by at least two authors.

Results The literature search resulted in 70 observational studies. Outcomes were grouped by transition direction. Most comparative studies were hampered by selection bias since different techniques had different indications. In general, study quality was poor and there were few comparative studies. For almost all outcomes (except for those shown below in Results) the certainty of evidence was very low (GRADE ⊕◯◯◯). No procedure related mortality was reported in any of the studies.

Trans men:
Quality of life Two studies comparing QoL after phalloplasty or metoidioplasty with a period on the waiting list, showed no significant improvement.
Satisfaction Patients generally reported high satisfaction after GAS. Conclusion: Satisfaction after mastectomy may be higher than satisfaction in patients on the waiting list (GRADE ⊕⊕◯◯). Satisfaction with the genital appearance after phalloplasty was significantly higher after, than before surgery in one study. Seven case series reported that 80-100% of patients responding to questionnaires were satisfied after phalloplasty or metoidioplasty.
Regret was not reported by any of 129 patients after hysterectomy/oophorectomy or of 25 patients after phalloplasty.
Complications Three studies showed less complications after mastectomy with the free nipple graft technique compared with peri-/circumareolar incision. Four studies compared different techniques for phalloplasty and additional procedures and the frequency of urethral fistulas and strictures ranged from 21 to 67%. For metoidioplasty, the frequency of urethral fistulas was high (median 36%, range 6.2- 64% in four studies). Conclusion: Major complications are probably common after genital GAS procedures (GRADE ⊕⊕⊕◯)
Reoperation: Three studies showed more reoperations (mainly revisional) after peri-/circumareolar incision than after free nipple graft mastectomy. Three studies of radial fore-arm flap phalloplasty showed frequent reoperations due to, e.g., partial or complete neophallus necrosis (4-25%) and urethral fistulas (up to 70%). One series of metoidioplasties reported 10% reoperations.

Trans women:
Quality of life One study showed that patients who had undergone facial feminisation surgery improved their health related QoL significantly more compared than those who had not. One study reported significantly higher QoL scores after genital reconstructive surgery than after no surgery.
Satisfaction In one study, patients who had undergone facial feminisation surgery scored significantly higher satisfaction than those who had not. In two case series, 75-96% of patients reported that they were satisfied after breast augmentation. For genital surgery, two studies compared different techniques of vaginoplasty, with no differences in satisfaction with aesthetic outcome and sexual function. Nine case series reported that the vast majority of patients were satisfied with aesthetic outcome and sexual function after genital surgery, but satisfaction was significantly lower in patients with complications after surgery.

Regret In a comparative study of two types of vaginoplasty, none of 25 patients reported any regret. Fifteen (6%) of 232 patients with penile-inversion vaginoplasty and sensate clitoroplasty reported that they sometimes felt regret.
Complications ranged from zero to 6% after facial feminisation surgery. After vaginoplasty, there were 5.7-9.4% major complications. Rectal complications ranged from 0.5 to 3.0% and urethral injuries from 0.8 to 18%. Conclusion: Major complications are common after genital GAS procedures (GRADE ⊕⊕⊕◯).
Reoperations, mainly for urological or cosmetic reasons, were common after vaginoplasty with, e.g., vulva corrections in 22-34%.

Concluding remarks The number of patients diagnosed with gender dysphoria increases rapidly as does gender affirmation surgery. The available literature includes only observational studies of mostly poor quality, comparative studies are few and data from long-term follow up are lacking. The certainty of evidence for the benefits of genital, facial and body gender affirmation surgery is generally very low (GRADE ⊕◯◯◯) while major surgical complications probably are frequent after *genital* gender affirmation surgery (GRADE ⊕⊕⊕◯). Nevertheless, the patients usually value the effects of the interventions highly. Gender affirmation surgery needs to be performed within research projects in order to improve the knowledge about benefits and risks.

2. Svensk sammanfattning – Swedish summary

Bakgrund Termen könsdysfori (eller “transsexualism”) används vid varaktig och stark identifiering till det motsatta könet samt upplevt obehag med sitt anatomiska kön manifesterat genom en upptagenhet av att göra sig av med sina könskarakteristika eller genom känslan av att vara född med fel kön. Könsbekräftande kirurgi (gender affirmation surgery, GAS), bekräftande patientens självupplevda kön, avser genitala, faciala och övriga kroppsliga ingrepp. Prevalensen av könsdysfori uppskattas i Sverige till 0,2-0,5% och remisser för utredning av sådana störningar ökade trefaldigt mellan 2013 och 2017 i Västra Götalandsregionen (VGR). Hos trans kvinnor (Male-to-Female, MtF) är målsättningen med genital kirurgi att skapa feminint perineo-genitalt utseende och funktion. Hos trans män (Female-to-Male, FtM) används vid så kallad metoidioplastik klitoris för att skapa en liten penis med bevarad känsel medan man vid falloplastik ofta använder en fri underarmslambå för att skapa en kosmetiskt tillfredsställande penis.

Syfte Att studera om GAS jämfört med ingen eller mindre omfattande kirurgi hos vuxna med könsdysfori förbättrar patienternas livskvalitet (QoL), tillfredsställelse, leder till ånger eller orsakar komplikationer.

Metod Två författare gjorde en systematisk litteratursökning (januari 2018) i PubMed, Embase, Cochrane Library, PsychInfo och HTA-databaser, selekterade studier, bedömde oberoende av varandra abstrakts samt gjorde ett första urval av artiklar i fulltext för inklusion. Dessa artiklar lästes av alla författare och inklusion beslutades slutligen vid ett konsensusmöte. Kvaliteten på jämförande studier utvärderades. Data extraherades av minst två författare.

Resultat Litteratursökningen resulterade i 70 observationsstudier. Utfallen grupperades efter transitionsriktning. Nästan alla jämförande studier belastades av selektionsbias eftersom olika tekniker hade olika indikationer. Studiekvaliteten var generellt låg och det fanns få jämförande studier. För nästan alla utfall (med undantag för slutsatser särskilt beskrivna nedan) var evidensläget otillräckligt (GRADE ⊕◯◯◯). Ingen operationsrelaterad dödlighet rapporterades i studierna.

Trans män: Patienterna rapporterade generellt hög tillfredsställelse efter GAS.
Livskvalitet I två studier förelåg ingen signifikant skillnad i QoL efter falloplastik eller metoidioplastik jämfört med när patienten var på väntelistan.
Nöjdhet var generellt hög efter GAS. Slutsats: Nöjdheten kan vara högre efter mastektomi än under tiden på väntelistan (GRADE ⊕⊕◯◯) Nöjdheten med genitalt utseende efter falloplastik var signifikant högre efter än före kirurgi i en studie. I sju fallserier var 80-100% av de patienter som svarat på enkäter nöjda efter falloplastik eller metoidioplastik.
Ånger Ingen av 129 patienter som genomgått borttagande av livmoder/äggstockar respektive av 25 patienter som genomgått falloplastik ångrade sig.
Komplikationer var färre efter mastektomi med fritt bröstvårtetransplantat än med peri/circumareolärt snitt. I fyra studier jämfördes olika tekniker för falloplastik, med vissa tilläggsingrepp, och uretrafistlar eller –strikturer uppkom efter 21-67% av ingreppen. Efter metoidioplastik var frekvensen uretrafistlar hög (median 36%, range 6,2-64%, fyra studier). Slutsats: Allvarliga komplikationer är troligen vanliga efter genitala ingrepp för könsdysfori (GRADE ⊕⊕⊕◯)
Reoperation Tre studier visade fler reoperationer (främst revision) efter mastektomi med peri/cirkumareolärt snitt jämfört med fritt bröstvårtetransplantat. Många reoperationer exempelvis på grund av partiell eller total penisnekros (4-25%) och uretrafistlar (upp till 70%) redovisades efter falloplastik med underarmstransplantat i tre studier. I en fallserie redovisades 10% reoperationer efter metoidioplastik.

Trans kvinnor: *Livskvalitet* Patienter som genomgått feminiserande ansiktskirurgi i en studie redovisade signifikant högre QoL än de som inte gjort det. I en annan studie redovisades signifikant bättre QoL efter genital kirurgi än hos patienter utan sådan kirurgi.
I nio fallserier rapporterades att det stora flertalet patienter var tillfredsställda med estetiskt resultat och sexualfunktion, men nöjdheten var signifikant lägre hos patienter med komplikationer efter kirurgi.
Nöjdhet I en studie var patienter som genomgått feminiserande ansiktskirurgi signifikant mer nöjda än de som inte gjort det. I två fallserier rapporterade 75-96% att de var nöjda efter bröstförstoring. Vad gäller genital kirurgi jämfördes i två studier olika tekniker för vaginalplastik utan påvisbara skillnader avseende estetiskt resultat och sexualfunktion.
Ånger I en studie jämförande två tekniker för vaginoplastik rapporterade ingen av 25 patienter ånger. Femton (6%) av 232 patienter med penisinverterande vaginoplastik och klitorisplastik med bevarad sensibilitet rapporterade att de ibland kände ånger.
Komplikationer efter feminiserande ansiktskirurgi rapporterades i 0-6%. Efter vaginoplastik rapporterades 5,7-9,4% allvarliga komplikationer. Ändtarmskomplikationer förelåg i 0,5-3,0% och uretraskador i 0,8-18%. Slutsats: Allvarliga komplikationer är troligen vanliga efter *genitala* ingrepp för könsdysfori (GRADE ⊕⊕⊕◯)

Reoperation, vanligen för urologiska eller kosmetiska komplikationer, var vanliga efter vaginoplastik med exempelvis 22-34% vulvakorrektioner.

Sammanfattande kommentar Antalet patienter diagnosticerade med könsdysfori ökar snabbt liksom antalet könsbekräftande kirurgiska ingrepp. Denna översikt 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.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 2018-06-27

Kvalitetssäkringsgruppen	
Bergenheim, Anna	PT, PhD
Bergh, Christina	MD, Professor
Bernhardsson, Susanne	PT, PhD
Hakeberg, Magnus	OD, Professor
Hansson-Olofsson, Elisabeth	PhD, Senior lecturer
Jivegård, Lennart	MD, Senior university lecturer
Larsson, Anders	MD, PhD
Nelzén, Olle	MD, Associate professor
Persson, Josefine	Health economist, PhD
Petzold, Max	Statistician, Professor
Rylander, Christian	MD, Associate professor
Samuelsson, Ola	MD, Associate professor
Sjögren, Petteri	DDS, PhD
Sjövall, Henrik	MD, Professor
Skogby, Maria	RN, PhD
Strandell, Annika	MD, Associate professor
Svanberg, Therese	HTA librarian
Wallerstedt, Susanna	MD, Professor

DDS Doctor of dental surgery
MD Medical doctor
PhD Doctor of Philosophy
PT Physiotherapist
RN Registered Nurse

3. Summary of Findings

Outcomes and procedures	Number of studies/ Study design	Specific procedures	Effect range	Certainty of evidence GRADE[1]
Trans men (Female to Male)				
Quality of life				
Genital surgery	1 before/after 1 cross-sectional	Phalloplasty Metiodioplasty	No difference	⊕◯◯◯
Patient satisfaction				
Mastectomy	1 cohort 3 case series	Mastectomy vs no	Δ 5.9 (scale 1-100) 79-94%	⊕⊕◯◯
Hysterectomy	1 case series		97%	-
Genital surgery	4 cohort 7 case series	Phalloplasty Metiodioplasty	80-100%	⊕◯◯◯
Regret				
Hysterectomy	1 case series		0/129	
Genital surgery	1 case series	Phalloplasty	0/25	-
Complications[2]				
Mastectomy	5 cohort, 2 case series	Areolar incision vs free nipple graft	1.5-21%	⊕◯◯◯
Hysterectomy	2 case series		4-89%	-
Genital surgery	7 cohort, 11 case series	Phalloplasty Metiodioplasty	Total complications 21-67%	⊕⊕⊕◯[3]
Re-operation				
Mastectomy	2+1 cohort 2 case series	Areolar incision vs free nipple graft	up to 30%	⊕◯◯◯
Hysterectomy	1 case series		1%	-
Genital surgery	1 cohort 5 case series	Phalloplasty Metiodioplasty	 up to 79%	-
Trans women (Male to Female)				
Quality of life				
Facial feminisation surgery	1 cross-sectional	Surgery vs no	Higher scores	⊕◯◯◯
Genital surgery	1 cross-sectional 2 case series	Vaginoplasty vs no	Higher scores High scores	⊕◯◯◯
Patient satisfaction				
Facial feminisation surgery	1 cross-sectional 2 case series	Surgery vs no	Higher satisfaction 70-81%	⊕◯◯◯
Breast augmentation	3 case series		65-96%	-
Genital surgery	2 cohort 10 case series	Vaginoplasty	No difference 62-90%	⊕◯◯◯
Regret				
Genital surgery	1 cohort 1 case series		0 6%	-
Complications[2]				
Facial feminisation surgery	2 case series		0-6%	-
Genital surgery	2 cohort 17 case series	Vaginoplasty	13-18% long term Total complications up to 58%	⊕⊕⊕◯[3]
Re-operation				
Genital surgery	10 case series	Vaginoplasty	1-34%	-

Footnotes:
[1] Selection bias was present in all studies, resulting in downgrading one level for almost all outcomes.
[2] Major complications are reported here, unless stated otherwise
[3]Uppgraded two levels compared with no surgery, based on very high relative risk.

Certainty of evidence

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

4. Abbreviations/Acronyms

FtM= Female to Male
GAS= Gender Affirmation Surgery
HRQoL= Health related quality of life
HSA= Hälso- och Sjukvårdsavdelningen
HTA= Health Technology Assessment
IVF=In Vitro Fertilisation
LGBT= Lesbian Gay Bisexual Transgender
MtF= Male to Female
QoL= Quality of life
SU= Sahlgrenska University Hospital
VGR= Region Västra Götaland, Sweden
WPATH= World Professional Association for Transgender Health

5. Background

Disease/disorder of interest and its degree of severity

Gender dysphoria ("transsexualism" according to the World Health Organization and ICD-10 classification) is the term used for individuals who show a strong and persistent cross-gender identification and a persistent discomfort with their anatomical sex, as manifested by a preoccupation with getting rid of one's sex characteristics, or the belief of being born in the wrong sex. According to the DSM classification gender dysphoria is the main symptom and result of transsexualism, which is included under the psychiatric diagnoses using the codes F64.X. The WHO and the ICD classification on the other hand include the transsexualism situation under the same code F64.0. Under the code F64.8 (other gender identity disorders) or F64.9 (unspecified gender identity disorders) the non-binary or genderqueer persons are included. They are not identifying themselves exclusively masculine or feminine and may express a combination of masculinity and femininity, or neither.

Since 1978, the Harry Benjamin International Gender Dysphoria Association (in honour of Dr. Harry Benjamin, one of the first physicians who made many clinicians aware of the potential benefits of gender affirmation surgery, at the time called gender reassignment surgery) has played a major role in the research and treatment of gender identity disorder, publishing the Standards of Care for Gender Dysphoric Persons (WPATH. *Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People*, 7th Version. WPATH 2011. http://www.wpath.org
Accessed 5 April 2018).
Transgender persons living in the United States report lower quality of life and in a lot of cases, face health professionals' insensitivity and discriminatory acts when seeking help.

Transgender individuals also have higher rates of depression and suicidality (attempts and ideation) compared with the general population (James et al. 2016, Adams et al. 2017). These higher rates of depression and suicidality may be due to social and structural discrimination experienced by trans and non-binary people as well as to the experienced continued distress that is caused by the lack of the requested surgery and hormonal therapy (Di Ceglie, 1998, Haas et al. 2014).

Studies of Swedish people have also shown that transgender patients have impaired quality of life and higher rates of depression and suicidality (attempts and ideation) compared with the general population. Gender affirmation treatment (which includes psychotherapy, hormonal therapy and surgery) has been reported to improve quality of life in patients affected by gender dysphoria (or gender identity disorder) (Lindqvist et al., 2017). In a Swedish study transgender people had a lower frequency, 12.5%, of suicide attempts after gender affirmation therapy compared with 35.9% before treatment (Dhejne, 2017).

Prevalence and incidence

The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, regrouped results from different investigations and reported an average prevalence of gender dysphoria of 1 in 12,000 biological men and 1 in 100,000 biological women (Michel et al. 2001; Bakker et al. 1993). These prevalences are based on old data. According to the Swedish National Board of Health and Welfare, the prevalence of gender dysphoria in the Swedish population is higher and estimated to 0.2-0.5%. There has been an increase in the number of patients who are diagnosed with gender dysphoria in recent years.
In Region Västra Götaland in Sweden, the diagnosis of gender dysphoria is established by the Lundström outpatient clinic in Alingsås. The patients are diagnosed before referral for hormonal treatment. During the years 2014 until 2017, a total of 744 individuals were assessed at the Lundström clinic and 267 (35.9%) of these were diagnosed with transsexualism or other unspecified sexual disorders which includes the non-binary patients. In Region Västra Götaland the referrals increased from 102 patients in 2013 to 343 in 2017 and the largest increase was in the age group between 12 and 26 years. There is no documentation supporting an increase in the number of diagnosed patients.

6. Health Technology at issue: Gender affirmation surgery (GAS)

In the middle of 20th century, the common term used was 'Gender Reassigment Surgery'. For a short period of time, the term 'Gender Confirmation Surgery' has been used (Monstrey 2013). Monstrey introduced the idea that transgender patients are not getting the gender ‘reassigned’ by surgery, but ‘confirmed’, as the ‘gender’ is already self-perceived. More recently, gender experts and advocates for this group of patients introduced and preferred the term 'Gender Affirmation Surgery', rather than 'confirmation'. To align with the contemporary terminology, we also use 'Gender Affirmation Surgery', or GAS, throughout the manuscript. The contemporary terms 'trans men' and 'trans women' are explained in the text by adding FtM (Female-to-Male) and MtF (Male-to-Female). The term GAS refers to all genital, facial and body procedures required to create a feminine or masculine appearance (Selvaggi & Bellringer 2011). Genital procedures, such as vaginoplasty, clitorolabioplasty, penectomy and orchidectomy in trans women and penile and scrotal reconstruction after hysterectomy, salpingoophorectomy and mostly vaginectomy in trans men, are the main procedures in gender affirmation surgery. Non-genital procedures, such as breast enlargement, mastectomy, facial feminisation surgery, voice surgery, and other procedures, complete the surgical treatment available.

Gender affirmation surgery in trans men (FtM)
Masculinising chest surgery (bilateral mastectomy with chest wall reconstruction) is often the first and sometimes the only form of GAS performed in trans men. Constructing a male chest contour facilitates trans men and non-binary patients to live more comfortably in their bodies. Mastectomy can be performed using a peri- or circumareolar skin incision, or by mastectomy with free nipple graft.

There are two main methods, metoidioplasty and phalloplasty, for genital affirmation surgery in trans men, with important differences in cosmetic result and function.
Metoidioplasty is usually a single-stage procedure in which the clitoris (hypertrophied by testosterone intake during hormone therapy) is used to produce a small sensate phallus, but not allowing for penetrative sexual intercourse. The clitoris is mobilised, so that it points ventrally. A flap of vaginal epithelium may then be used to tube the existing urethra forward to the tip of the clitoris. This procedure provides a phallus resembling a micropenis, especially when the labia minora are made into a scrotum with testicular implants.
Phalloplasty aims at creating a cosmetically satisfactory penis, possibly with a neourethra opening on the tip of the penis that is sensate and allows for penetrative sexual intercourse. Early attempts of phalloplasty used abdominal flaps, or variously shaped (e.g. tube-in-tube). With the advent of microsurgery, free flaps from forearm, fibula, thigh and latissimus dorsi muscle have been described (Selvaggi & Bellringer, 2011; Selvaggi & Elander, 2008). By these techniques a sensate penis with a neourethra can be achieved, though donor site morbidity and complications could be a disadvantage.

Gender affirmation surgery in trans women (MtF)
The shape of the thorax, nipple areola complex position, size of the pectoral muscles and, usually, absence (or very minimal) amount of breast tissue have a substantial influence on the technique and results (for example, implant size and pocket, and final cosmetic outcome) of breast augmentation in trans women (Kanhai et al., 1999).

Vocal cord and throat surgery has two purposes: to raise the pitch of the voice, and to remove the protruding part of the thyroid cartilage (Adam's apple), respectively. The most common form of pitch surgery is approximation of the cricoid and thyroid cartilages, which causes stretching of the vocal cords and elevation of pitch, although some surgeons use more complex techniques (Kanagalingam et al., 2005). A postoperative course of speech therapy is required to achieve a satisfactory result.

In facial feminisation, shaving of the frontal bossae (the prominent part of the forehead above the brow ridges), the brow ridges, the mandible angles and the chin, is sometimes accompanied by rhinoplasty. Other cosmetic surgical (e.g., liposuction or hair graft) and nonsurgical (e.g., use of botulinum toxin A or dermal filler injections) procedures might also be used.

Karim, Hage and Mulder (1996) defined the aim of GAS in trans women (MtF) as creating a perineo-genital complex as feminine in appearance and function as possible, with a short urethra with the direction of the urinary stream directed downward in the sitting position The neovagina should be free of stenosis or fistula and ideally lined with moist, elastic and hairless epithelium, with a depth of at least 10 cm and a diameter of 30 mm, with the sensation sufficient to provide satisfactory erogenous stimulus during sexual intercourse and, finally, without donor-site morbidity. Methods to line the neovagina in trans women may be classified into five categories: 1. application of nongenital skin grafts, 2. penile skin grafts, 3. penile-scrotal skin flaps, 4. nongenital skin flaps and 5. pedicled intestinal transplants (Selvaggi et al., 2005).

The normal pathway through the health care system and current wait time for medical assessment/treatment

Actually the transgender patients in Sweden start their way through the gender affirmation treatment chain by a psychological and psychiatrical evaluation by the specialised teams present in every health care region. Before diagnosis and start of hormonal treatment, referral for information and informed decision regarding fertility preservation is recommended, especially in younger patients. When the diagnosis of gender dysphoria (transsexualism) is established, patients who are candidates for surgery are referred to a specialised plastic surgery team. There are three university hospitals in Sweden that perform genital affirmation surgery, the Sahlgrenska, Karolinska and Linköping University Hospitals.

University hospitals like Uppsala Akademiska and Umeå Hospitals perform breast surgery in patients within their respective regions.
In Region Västra Götaland, the patients are seen by the Transgender Plastic Surgery Team at the Sahlgrenska University Hospital. For gynaecological consultation and surgery, patients are referred to the gynaecological department. During the first visit all the checkpoints established by the World Professional Association for Transgender Health (WPATH) are considered. The national guidelines from the National Board of Health and Welfare follow the recommendations of WPATH (WPATH. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th Version. WPATH 2011).

Breast or thyroid cartilage surgery can be booked after the first visit to the surgeon, but for genital affirmation surgery, the patient first needs approval from the National Board of Health and Welfare (Socialstyrelsen) in Stockholm and then a second consultation before proceeding to surgery. This is because this kind of surgery is more invasive, in most cases irreversible and with a high risk of complications.

The waiting times for consultation and surgery vary and depend on the resources of the health care system. In Region Västra Götaland, current waiting times are approximately one year for the majority of the procedures and up to two or three years for more complex procedures like phalloplasty requiring multidisciplinary surgical teams, more time and resources.

Number of patients per year who undergo gender affirmation surgery

According to the Sahlgrenska University Hospital registry, 83 patients underwent GAS in 2015, 78 in 2016 and 96 in 2017, to be compared with more than 70 patients already during the first half of 2018. Nine patients underwent hysterectomy/salpingoophorectomy 2015, four in 2016 and 11 in 2017. During the first half of 2018 only two surgeries have been performed and 18 patients are on waiting list.

Present recommendations from medical societies or health authorities

In 2015, The Swedish National Board of Health and Welfare published the “Good Care of Adults with Gender Dysphoria” (“God vård av vuxna med könsdysfori, Nationellt kunskapsstöd”), with guidelines for health care professionals in order to improve the care of transgender patients in Sweden. According to this text the Swedish health care regions are advised to offer GAS for people with gender dysphoria (Socialstyrelsen, 2015). The WPATH has recently published guidelines and standards of care for patients affected by gender dysphoria, including eligibility criteria for gender affirmation surgery (WPATH. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming *People*, 7th Version. WPATH 2011).

With this background and following the WPATH and the Swedish National Board of Health and Welfare recommendations, which are mainly based on the WPATH updated “Standards of Care”, the Sahlgrenska multidisciplinary GAS team was created.

7. Question at issue

In adults with gender dysphoria, does gender affirmation surgery affect quality of life (QoL) and cause complications compared with no surgery or less extensive reconstruction?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome
PICO 1 Trans men (female-to-male)
PICO 2 Trans women (male-to-female)

P: Adults with gender dysphoria (transvestism and intersexual conditions are not included in the diagnosis)

I: Gender affirmation surgery, specified procedure (not including secondary/correction surgery):
I1: In trans men (external genital reconstruction (including penile prosthesis), hysterectomy + salpingo-oophorectomy, mastectomy, hip liposuction)
I2: In trans women (genital surgery, breast surgery, facial feminisation surgery)

C1: No surgery
C2: Less extensive gender affirmation surgical techniques

O: Critical for decision-making:
Mortality
Quality of life (QoL), including health related QoL (measured by validated technique)
Patient satisfaction, including voiding measures and sexual function (measured by validated techniques)
Regret/retransition
Surgical complications, other complications
Reoperation

8. Methods

Systematic literature search (Appendix 1)

During January 2018 two authors (IS, UWA) performed systematic searches in PubMed, Embase, the Cochrane Library, PsychInfo and a number of HTA databases. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria, and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The selected articles were sent to all participants of the project group. All authors read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment.

Critical appraisal and certainty of evidence

The included articles and their design and patient characteristics are presented in Appendix 2. The excluded studies and the reasons for exclusion are presented in Appendix 3.
The included comparative studies have been critically appraised using a checklist for assessment of cohort studies. The results, and the assessed quality of each comparative article, have been summarised per outcome in Appendix 4. Data were extracted per outcome by one author and checked by at least one more author. When feasible, data were presented graphically in forest plots. Meta-analyses were not conducted due to high heterogeneity among studies.

Summary results per outcome and the associated certainty of evidence are presented in a Summary of findings table (SoF-table, page 8). The certainty of evidence was defined according to the GRADE system (Atkins et al, 2004; GRADE Working group).

Ongoing research

Searches in Clinicaltrials.gov (2018-04-16) using the search terms (Gender dysphoria OR transgender OR transsexualism OR transsexual OR male-to-female OR mtf OR female-to-male OR ftm OR lgtb OR reassignment) identified 123 trials. None of these were relevant for the question at issue.

9. Results

Systematic literature search (Appendix 1)

The literature search identified 2027 articles after removal of duplicates. After reading the abstracts 1840 articles were excluded. Another 58 articles were excluded after having been read in full text by the two authors. The remaining 128 articles were sent to all participants of the project group, and 70 observational studies were finally included in the assessment (Appendix 2). All outcome tables (Appendix 4) are primarily grouped by transition direction; trans men (FtM) and trans women (MtF), and secondarily by type of surgical procedure. All outcomes were considered as critical for decision making. All comparative studies were hampered by selection bias. Due to obvious baseline difference between groups, data were not pooled in meta-analyses but only presented in forest plots.

Results per outcome

PICO 1. Trans men (FtM) (Appendix 4.1)

Mortality

No study reported any procedure related mortality.

Quality of life (QoL) (Appendix 4.1.1)

Mastectomy

No study evaluated QoL after mastectomy.

Hysterectomy/oophorectomy

No study evaluated QoL after hysterectomy/oophorectomy.

Genital surgery

Two observational studies (n=84) compared QoL after phalloplasty and metoidioplasty with the period on the waiting list. None of these showed any significant improvement. In a cross-sectional study trans men after GAS reported lower health related QoL compared with men and women in the general population.
Conclusion: It is uncertain whether phalloplasty or metoidioplasty affects quality of life or health related quality of life. Very low certainty of evidence (GRADE ⊕◯◯◯).

Patient satisfaction (Appendix 4.1.2)

Mastectomy

In a prospective cohort study (n=185), dissatisfaction was significantly higher when no mastectomy (with or without testosterone treatment) was performed compared with mastectomy and testosterone treatment.
Two observational studies (n=271) compared periareolar incision with free nipple graft. Similar scores for satisfaction were reported, ranging from 79% to 89%. In one case series self-reported satisfaction was 94%.
Conclusion: Patients are generally very satisfied after surgery. There may be an improved satisfaction with the body appearance after mastectomy compared with no mastectomy.
Low certainty of evidence (GRADE ⊕⊕◯◯).

Hysterectomy/oophorectomy

In one case series (n=48), 97% of patient reported satisfaction after the procedure.

Genital surgery
One cohort study (n=54) reported satisfaction after phalloplasty compared with the period on the waiting list. Satisfaction with the genital appearance was significantly higher after surgery, while changes in sexual and urinary functions were not significant. Different techniques for phalloplasty and metoidioplasty have been compared in small series.
To be able to void standing is one important technical aim of the surgery, and such ability postoperatively was reported to range from 42% to 100% after different techniques for metoidioplasties in three studies (n=282). In one small cohort study (n=21) sexual function was significantly better after metoidioplasty than after phalloplasty, while there was no significant difference in voiding outcomes.

Seven case series (n=909) reported patient satisfaction without any comparison. Satisfaction overall, cosmetic result, cutaneous sensitivity, and sexual function was generally high, ranging from 80% to 100%. In one case series (n=55), only 9% of patients reported erogenous sensitivity after phalloplasty. Fifty-one per cent of patients with erectile prosthesis reported sexual satisfaction. Two case series (n=304) reported 100% satisfaction with erogenous sensation and sexual function after metoidioplasty.

Conclusion: It is uncertain whether phalloplasty compared with metoidioplasty improves satisfaction with voiding and sexual functions. Patients scored higher when evaluating masculinity and genital appearance after phalloplasty compared with being on the waiting list. It is uncertain whether there is any difference in sexual and urinary function after phalloplasty compared with being on the waiting list. Very low certainty of evidence (GRADE ⊕◯◯◯).

Regret (Appendix 4.1.3)
There were no comparative studies reporting regret.

Mastectomy
No study reported the outcome regret or retransition after mastectomy.

Hysterectomy/oophorectomy
In one case series, none of 129 patients reported regret after hysterectomy/oophorectomy.

Genital surgery
In one observational study of three different phalloplasty techniques, none of 25 patients reported regret.

Conclusion: There were no reported cases of regret in two case series of hysterectomy/oophorectomy and phalloplasty respectively, among 154 patients.

Complications (Appendix 4.1.4)

Mastectomy
Five cohort studies (n=1104) compared the peri- or circumareolar incision with the free nipple graft technique. Data were extractable per individual in three of those. Results were not pooled due to severe selection bias, but illustrated in forest plots (Figures 1-2).

Fig.1. Major complications in mastectomy comparing peri- or circumareolar incision with free nipple graft.

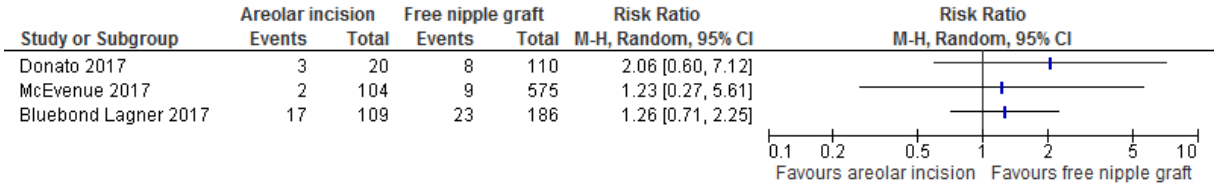
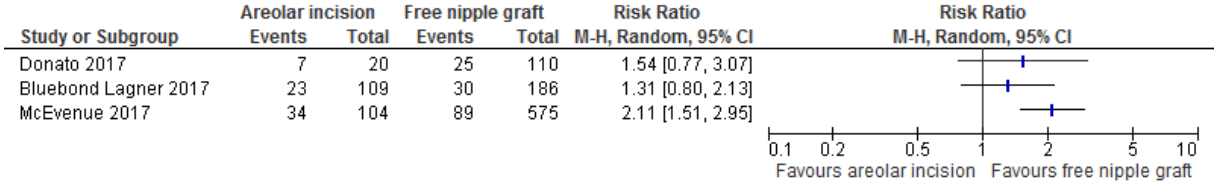


Fig.2. Total complications in mastectomy comparing peri-or circumareolar incision with free nipple graft.



Major complications were reported in the range of 1.5 to 21%.
One small cohort study reported complications from the transplantation site.

Conclusion: It is uncertain whether peri- or circumareolar incision compared with free nipple graft at mastectomy is associated with any difference in the rate of complications.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Hysterectomy/oophorectomy
One case series (n=134) reported any complication in 89% of patients. Another series (n=83) reported 3.6% major and 3.6% minor complications.

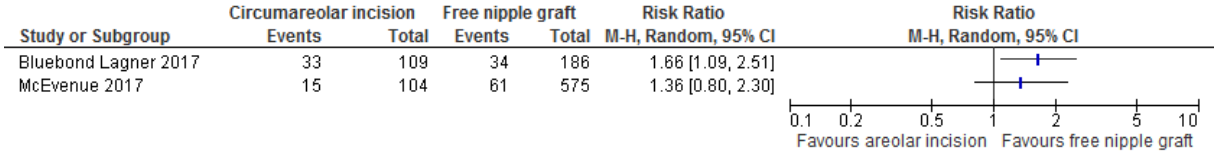
Genital surgery
Four observational studies (n=563) reported comparisons between phalloplasties of different techniques and the inclusion of additional procedures like urethroplasty and vaginectomy. Urethral complication rates, mainly fistulas and strictures, ranged from 21 to 67%. Six case series (n= 914) gave additional detailed information on the types of complications.
Four observational studies (n=453) reported on complications after metoidioplasties. One small cohort study (n=21) compared all types of phalloplasties with metoidioplasty and reported urethral complications to be more common after phalloplasty. Voiding standing, a desirable outcome after metoidioplasty, was reported to range from 88 to 93% in one cohort study using two different surgical techniques.

Conclusion: Surgical complications, particularly urethral, are probably common after phalloplasty, ranging from 21 to 67% (GRADE ⊕⊕⊕◯) No conclusions can be drawn regarding differences between techniques, based on comparative studies.

Reoperation (Appendix 4.1.5)

Mastectomy
Three cohort studies (n=1076) comparing the peri- or circumareolar incision with the free nipple graft technique reported the incidence of reoperation and revision. Reoperations were mainly of revisional character and occurred in up to 30%. Data were extractable per individual in two of those. Results were not pooled due to severe selection bias, but illustrated in a forest plot (Fig. 3).

Fig. 3. Reoperations including revisions after mastectomy comparing circumareolar incision with free nipple graft.



Conclusion: It is uncertain whether circumareolar incision compared with free nipple graft at mastectomy is associated with any difference in the rate of reoperations.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Hysterectomy/oophorectomy
One case series (n=83) reported a 1.2 % reoperation rate after hysterectomy.

Genital surgery
Three observational studies reported reoperations after radial fore-arm flap phalloplasty. The rate of reoperation was generally high. Reoperations were due to partial or complete necrosis of the neophallus in 4-25%, urethral fistulas in up to 70%, and urethral stenosis in up to 12%.
One case series of metoidioplasties reported a 10% rate of reoperation, mainly urethral.

Conclusion: Reoperations due to severe complications are common. No conclusions can be drawn regarding differences between techniques, based on comparative studies.

PICO 2. Trans women (MtF) (Appendix 4.2)

Mortality
No study reported any procedure related mortality.

Quality of life (Appendix 4.2.1)

Facial feminisation surgery
One cross-sectional study compared patients who had undergone facial feminisation surgery with those who had not. There was a significant difference in scoring mental health related QoL (SF-36, mental component summary).
Conclusion: It is uncertain whether facial feminisation surgery improves quality of life compared with no surgery.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Breast augmentation
No study evaluated quality of life after breast augmentation.

Genital surgery
One cross-sectional study reported significantly higher scores of QoL, comparing genital surgery with no surgery. Two case series were also available. Both reported high scoring of QoL after genital surgery. Additional surgery did not affect QoL, while lower QoL was reported after complications with pain in vagina.
Conclusion: It is uncertain whether genital surgery increases QoL compared with no surgery.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Satisfaction (Appendix 4.2.2)

Facial feminisation surgery
In one cross-sectional study (n=247), patients who had undergone facial feminisation surgery reported significantly higher satisfaction than those who had not. Two additional case series were available. For rhinoplasty and forehead reconstruction, postoperative satisfaction ranged from 70 to 81%.
Conclusion: It is uncertain whether facial feminisation surgery in comparison to no surgery improves satisfaction.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Breast augmentation
In three case series, 65, 75 and 96% of patients, respectively, reported that they were satisfied.

Genital surgery
Two cohort studies (n=127) compared different techniques of vaginoplasty, without any significant differences between groups in satisfaction with aesthetic outcome and sexual function. Ten case series (n=1225) reported different aspects of satisfaction, using different scales. The vast majority of patients (range 62-90%), were satisfied with the result after surgery, aesthetic outcome, and sexual function. Happiness with sexual function as well as happiness with GAS result was significantly lower in patients with complications after surgery.
Conclusion: It is uncertain whether genital surgery improves satisfaction.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Regret (Appendix 4.2.3)

Facial feminisation surgery
No study reported regret or retransition after facial feminising surgery.

Breast augmentation
No study reported regret or retransition after breast augmentation.

Genital surgery
In a cohort study of two types of vaginoplasty, none of 25 patients reported any regret. One case series of patients undergoing penile-inversion vaginoplasty and sensate clitoroplasty (two publications) reported that 15/232 (6%) sometimes felt regret.
Conclusion:
There were 15 reported cases of regret in one case series with 232 patients.

Complications (Appendix 4.2.4)

Facial feminisation surgery
Two case series (n=233) reported complications after facial feminisation surgery ranging from zero to 6%.

Breast augmentation
None of the two studies on breast augmentation reported complications.

Genital surgery
Two cohort studies (n=757) and 17 case series (n=3046) reported complications after genital surgery. In a large cohort study (n=475) comparing penile inversion vaginoplasty with, versus without full thickness skin

graft, major complications were reported in 5.7% versus 9.4%, respectively. In a cohort study (n=282) vaginal prolapse was reported in 4.1% and 12.3%, depending on the suture technique.
In the 17 case series severe complications included mainly rectal injuries (range 0.5-3.0%) with or without recto-vaginal fistulas and urethral injuries (range 0.8-18%).

Conclusion: Major complications are probably common (GRADE ⊕⊕⊕◯) In the comparative studies, no conclusions can be drawn regarding differences between techniques.

Reoperation (Appendix 4.2.5)

Facial feminisation surgery
No study reported reoperation after facial feminisation surgery.

Breast augmentation
No study reported reoperation after breast augmentation.

Genital surgery
Ten case series (n=2379) reported reoperations after genital surgery. Reoperations were conducted in 1-34%, including revisional surgery.

10. Ethical issues

Gender dysphoria is a complex condition that affects many areas of life and may lead to much suffering. The suffering may motivate higher risk taking by the patient as well more extensive resources. On the other hand, the patient group is also very heterogeneous and the degree of severity is extremely variable – hence individual assessment is essential. At the same time there is a lack of research and well-established instruments to assess patient need and evaluating the outcomes of GAS.

Gender dysphoria patients choosing to undergo GAS generally value the effects as positive, even when taking complications into account. There is a clear and positive impact of having one's gender identity affirmed by the proper body representation.

Demands of equality require that the assessment of need, effect of treatment and reasonable resource use is not biased by discriminatory attitudes towards people with a non-heteronormative gender or sexual orientation. This situation means that the caregiver has a large responsibility and requires extensive experience and knowledge of transgender care in order to make good decisions. Lack of knowledge about the transgender group among healthcare professionals may cause faulty clinical judgement and lead to discrimination within the health care system and educational interventions in Lesbian-Gay-Bisexual-Transgender (LGBT)-issues are essential.

More research would likely result in better matching between patient need and interventions and thereby a more fair and effective resource use. Lack of cost-effectiveness data makes the assessment of a proper priority for this patient group difficult. Since many of the GAS procedures are resource demanding, there is a risk of displacement effects.

Moreover, it is recommended that interventions generally are provided within ongoing research or evaluation projects. However, when it comes to particularly vulnerable groups such as children and adolescents, the benefits and risk are even more unclear, for example when suppressing puberty. Given the lack of data and the extensive intervention GAS normally implies, a careful patient assessment and information is essential to provide patient with a reasonable chance to exercise autonomy based on realistic evidence and not resort to wishful thinking.

11. Organisational aspects

One way of organising the GAS care is by creation of multidisciplinary teams performing GAS. Such teams can include psychiatrists, psychologists, plastic surgeons, urologists, general surgeons, gynaecologists, endocrinologists, oto-rhino-laryngologists and speech therapists but also other specialists when required. A multidisciplinary surgical team has been organised since GAS was started at the Sahlgrenska University Hospital. The surgical procedures include various primary as well as corrective procedures, and treatment of complications performed by different specialists. Fertility aspects must be considered and preservation of gametes must be performed before genital surgical interventions.

Time frame for the putative introduction of the new health technology

The Sahlgrenska University Hospital already provides a specialised multidisciplinary GAS team of health care professionals performing the following tasks: 1. Evaluation of the patients, 2. Performing GAS, 3. Evolving the surgical techniques, 4. Monitoring the results and taking care of the complications, 5. Conducting research and developing new techniques in the field, 6. Taking in consideration and actively elaborating the bioethical aspects and 7. Establishing national and international multidisciplinary collaborations in surgery and research.

The Plastic Surgery Clinic of the Sahlgrenska University Hospital in Gothenburg has performed GAS since 2011. New methods are continuously under consideration for this surgery. Many of the methods have already been used in clinical practice for other patient groups, but the indication, i.e. to be used for gender affirmation, is new. The introduction of these new methods also depends on the requests and needs of the patients, as advised from the Swedish National Board of Health and Welfare 2015, and adequate financing of medical material, competence and education of the medical staff.

The GAS procedures are mainly allocated to the Department of Plastic Surgery in close cooperation with the Departments of Gynecology and Urology and recently also from the colorectal unit. For non-GAS procedures, e.g., gynaecological and fertility procedures as well as secondary urethra revisions the procedures are located at the Departments of Gynecology and Reproductive Medicine and Urology.

Present use of the technology in other hospitals in Region Västra Götaland

Gender affirmation surgery in Region Västra Götaland is performed only at the Sahlgrenska University Hospital.

Consequences of the new health technology for personnel

Contact with this specific category of patients requires special training seminars of the physicians and the other medical staff regarding treatment of the LGBT group in the hospital environment. Moreover, physicians and medical staff need training regarding GAS and management of its complications and consequences.

Consequences for other clinics or supporting functions at the hospital or in the Region Västra Götaland

Adequate transgender patient flow necessitates the participation of specialists and medical staff from all these disciplines described above. Resources need to be generated and redirected also for supporting functions, multidisciplinary conferences, and patient education in order to provide health care according to the WPATH and the Swedish National Board of Health and Welfare standards of care. The GAS-team also needs an established assignment to give priority to the work.

The multidisciplinary surgical team needs more trained surgeons within all the mentioned specialities. To ascertain continuity each speciality need two to three trained specialists as well as assigned trained nurses,

psychologists, social workers and administrative support. Network meetings and multidisciplinary conferences regarding patient cases with difficult treatment decisions are established, but need more priority structure. Patient education was started a few years ago. This education has been given by a sociologist, a contact nurse and a patient, and has been appreciated by the patients. However, further development is needed.

Gender affirmation surgery is considered highly specialised care and assigned as national health care. Three units have been established for the national care. To qualify as a national centre for GAS in the future organisation, the above mentioned development of a multidisciplinary treatment team is necessary.

12. Economic aspects

Present costs of gender affirmation surgery

During 2017, the total cost for 107 surgeries completed at the Plastic Surgery Department and the Department of Gynecology at the Sahlgrenska University Hospital due to gender affirmation was 6.6 million SEK. The corresponding total cost during 2016 for 82 surgeries was 5.8 million SEK (Table 1).

There is a gap between the number of transgender persons referred to the Plastic Surgery Department of the Sahlgrenska University hospital and the number of operations performed. This can partly be explained by the waiting time for the operations being longer than the waiting time for consultation. Furthermore, there is a number of patients who choose not to proceed with surgery, mostly genital surgery in trans men, due to the known high frequency of complications.

Table 1. Cost of gender affirmation surgery at the Sahlgrenska University Hospital.

Year	**2016**		**2017**	
	Number of surgeries	Costs (SEK)	Number of surgeries	Costs (SEK)
Breast surgery				
Mastectomy	31	1,150,000	43	1,600,000
Breast augmentation	7	240,000	15	510,000
Other breast surgery	2	130,000	10	640,000
Genital surgery				
Vaginoplasty	15	1,860,000	8	990,000
Other corrections	22	1,360,000	19	1,300,000
External genital reconstruction (trans men)	1	800,000	1	800,000
Gynaecological surgery				
Hysterectomies	4	288,000	11	792,000
Total cost		**5,828,000**		**6,632,000**

Data source: Departments of Plastic Surgery and Gynaecological and Reproductive Medicine at the Sahlgrenska University Hospital. Cost per patient: Mastectomy: 37,000 SEK; Breast augmentation: 34,000 SEK; Vaginoplasty: 124,000 SEK; Penile reconstruction: 800,000 SEK; Hysterectomy: 72,000 SEK. This table includes all patients referred to Sahlgrenska Transgender Unit at Department of Plastic Surgery, ie both patients from Region Västra Götaland and from other parts of Sweden.

Other costs of gender affirmation
In this economic analysis, only surgery costs of gender affirmation are considered. However, gender affirmation is a long process during several years with the need of lifelong follow up of the hormonal treatment. The Swedish Institute for Health Economics (Hjalte, Norrlind & Ragnarsson Tennvall, 2015) has estimated the cost per individual going through the process of gender affirmation, both for trans women and trans men.

The cost per trans woman (MtF), during the first four years was estimated to 245,000 SEK, and consists of:

- Examination for diagnosis of gender dysphoria and psychological treatment was estimated to 70,000 SEK, with highest costs during the first two year (year 1: 38,000 SEK and year 2: 25,000 SEK).
- Endocrine treatment was estimated to 50,000 SEK (year 2: 22,000 SEK, year 3: 16,000 SEK, year 4, 11,000 SEK).
- Skin treatment was estimated from 20,000 SEK to 68,000 SEK.
- Vocal treatment was estimated to 72,000 SEK during year 2 to 4.
- Fertility treatment was estimated to 13,000 SEK during year 2.

The cost per trans man (FtM), during the first four years was estimated to 176,000 SEK, and consists of:

- Examination for diagnosis of gender dysphoria and psychological treatment was estimated to 70,000 SEK, with highest costs during the first two year (year 1: 38,000 SEK and year 2: 25,000 SEK).
- Endocrine treatment was estimated to 40,000 SEK (year 2: 16,000 SEK, year 3: 12,000 SEK, year 4, 12,000 SEK).
- Vocal treatment was estimated to 36,000 SEK during year 2 and 3.
- Fertility treatment was estimated to 30,000 SEK during year 2.

At present all non-surgical procedures performed at the Sahlgrenska University Hospital have been performed within the budgets.

This means that the increased number of treatments such as endocrine, vocal, hair removal and fertility treatments have long waiting times and are also leaving other diagnosis waiting or put on wait due to lack of resources.

Expected costs of gender affirmation surgery according to referrals

The number of referrals to the Department of Plastic Surgery during 2016 and 2017 were 167 and 138 respectively. The corresponding number of referrals to the Department of Gynecology and Reproductive Medicine were 16 and 23. The present economic analysis is based on a scenario to estimate the total costs if all individuals who were referred to the departments also had surgery. An assumption has been made that the current proportion of the different surgeries would remain. Table 2 thus presents the number of referrals and total cost per surgery if all referred patients had surgery.

However, we know that the present numbers of gender affirmation surgeries are too low. During 2017 the Department of Plastic Surgery had less operating theatres and surgeon capacity than needed. The production of surgeries has increased during 2018. During January to June 2018, 77 plastic GAS procedures have been performed. Still the waiting list is long and the waiting time to surgery is one to two years depending on the type of procedures that are planned.
The more complicated procedures, the more complex multidisciplinary team and coordination are needed and more resources need to be allocated. For the Department of Gynecology and Reproductive Medicine the number of referrals for hysterectomies has increased and has, in combination with reduced access to operation theatre, contributed to an increase in waiting time for surgery to 12 months. In addition the waiting time for preoperative assessment has increased to 6-8 months.

Table 2. Cost of gender affirmation surgery if all referred individuals had surgery.

Year	2016		2017	
	Number of referrals	Costs (SEK)	Number of referrals	Costs (SEK)
Breast surgery				
Mastectomy	67	2,480,000	62	2,300,000
Breast augmentation	15	510,000	22	740,000
Other breast surgery	4	280,000	14	920,000
Genital surgery				
Vaginoplasty	32	4,000,000	12	1,420,000
Other corrections	47	3,000,000	27	1,820,000
Penile reconstruction	2	1,700,000	1	1,140,000
Gynaecological surgery				
Hysterectomies	16	1,152,000	23	1,656,000
Total cost		**13,122,000**		**9,996,000**

Data source: Plastic Surgery Department and Gynaecological Department at the Sahlgrenska University hospital.
Cost per patient: Mastectomy: 37,000 SEK; Breast augmentation: 34,000 SEK; Vaginoplasty: 124,000 SEK; External genital reconstruction: 800,000 SEK; Hysterectomy: 72,000 SEK.

Total change of cost

During 2017, the total referrals (to all involved departments) were 161 and 107 (66%) surgeries were completed, which includes patients from Region Västra Götaland as well as from other parts of Sweden. During 2016, the total referrals were 183 and 82 (45%) surgeries were completed. If all individuals with referrals had surgery, the excess cost would be approximately 3.4 million SEK during the year 2017 and 7.3 million SEK during the year 2016.

There are some issues regarding future costs and need for resources to finance further development of the transgender unit. The project group recognises the following needs:
1. Need for more endocrinological resources. After diagnosis and referral for hormonal treatment the waiting time has increased to more than 12 months.
2. Fertility treatment, i.e. oocyte and sperm freezing, as well as IVF-treatment is steadily increasing due to the change in the Swedish legislation 2013 (sterilisation not mandatory) resulting in increasing number of patients and lower ages. This part of the treatment is presently performed within the budget, with very long waiting times.
3. Need for a more established team to cope with a higher capacity and competence for all surgical procedures. The demand for surgical procedures is estimated to approximately 140 per year to keep an acceptable waiting time for the coming two to three years. New demands from the patients and new legislations may change over time and necessitates close surveillance.
4. A larger team with sustainable competence and capacity for surgery and multidisciplinary conferences: three plastic surgeons, two gynaecologists, two urologists, two contact nurses, and one secretary for administration.
5. Resources for psychological support during the surgical processes are lacking and a psychologist included in the surgical team is strongly needed.
6. Further development of present and new surgical procedures are needed
7. Development of penile epithesis (combination of prosthesis and implant).
8. Research and development is needed. Due to the low level of evidence for these surgical treatments more research regarding quality, most appropriate surgery and patient reported outcomes.

Other costs of gender affirmation
When considering also other costs of gender affirmation during the first four years presented by Hjalte, Norrlind and Ragnarsson Tennvall (2015), a scenario could be estimated. During 2016, 82 individuals had surgeries and 183 individuals had referrals, meaning that 101 individuals had referrals but did not complete the surgery. Assuming that the proportion of gender affirmation were 30% trans men and 70% trans women, this corresponds to 29 trans men and 70 trans women. The total change of costs if all individuals with referrals also had surgery was estimated to an excess cost of 22.3 million SEK.

Possibility to adopt and use the new technology within the present budget

As mentioned above the need of resources for endocrine as well as fertility treatment are not possible to cover in the present budgets for the Departments of Endocrinology and Gynecology and Reproductive Medicine respectively.

The development of the present Transgender Unit at the Department of Plastic Surgery has been possible due to an agreement between the Sahlgrenska University hospital and the County Health Care Department (Hälso och sjukvårdsavdelningen, HSA) to pay for each procedure as if the surgeries were bought from a unit outside Region Västra Götaland. With this agreement this highly specialised care could be developed and the present team was established. The technologies, i.e. the present surgical procedures, vary in complexity and some procedures are not yet performed on this type of indication. Due to this and the fact that more research is needed to consolidate these treatments to patient volumes and surgical quality, as well as developing patient reported outcome measures for specific procedures as well as for the whole process, adoption within the present fixed budget is not possible.

The Transgender Unit at the Sahlgrenska University hospital estimates the need for transgender surgery to about 140 surgeries per year, including 10 microsurgical procedures, 25-30 vaginoplasties, 50 mastectomies, 40 hysterectomies, 20 breast augmentations and 10 facial feminisation surgeries for Region Västra Götaland and Region Skåne. To ensure this production it is estimated that four operating theatres per week are needed.

The hysterectomy is a prerequisite for genital surgery for trans men and has been performed in the Department of Gynecology to utilise the resources of laparoscopic and robot assisted surgery. So far the surgery has not been included in the agreement between the Sahlgrenska University hospital and the County Health Care Department (Hälso och sjukvårdsavdelningen HSA) which must be considered in the future.

Available health economic evaluations

There are no available health economic evaluations.

13. Discussion

The present systematic review has demonstrated that although there is a number of studies reporting results of GAS, there is a lack of controlled studies. The vast majority of studies are case series. All comparative studies were hampered by selection bias. Conclusions regarding benefits were generally based on very low quality of evidence (GRADE ⊕◯◯◯), while complication rates are probably high after *genital* gender affirmation surgery (GRADE ⊕⊕⊕◯). Despite this, patients responding to questionnaires scored high on quality of life and satisfaction after GAS, and regret was uncommon.

There is a recent systematic review from the Swedish National Board of Health and Welfare (Socialstyrelsen. God vård av vuxna med könsdysfori: Nationellt kunskapsstöd [Internet]. Stockholm: Socialstyrelsen; 2015) with similar conclusions as those in the present HTA.

We decided to do the present HTA since the literature search in the mentioned systematic review was made in 2013 and since there has been a rapid increase in the number of GAS procedures during the last five years. We did not include studies published before 1990 since the earlier surgical techniques are not relevant today.

Apart from studies being small, the study quality is often poor. Heterogeneous patient groups and a significant number of patients lost to follow-up make the results unreliable. Selection bias is a common feature of the studies and blinding is usually not possible. There are few validated questionnaires that are suited for the transgender population. Measuring satisfaction is complex, as the impact is diverse and multifaceted. There are many published techniques for assessment of outcomes on sexuality, satisfaction in general, satisfaction with appearance, function, etc. This heterogeneity makes comparison across studies difficult.

Some studies that reported more extensive QoL or satisfaction outcomes were excluded because the results after a specific surgical procedure were not reported separately. For the patient as well out of a clinical perspective, the study of the results of a specific surgical procedure may be regarded as less relevant compared to the results of the entire gender affirming treatment. When analysing single surgical components of the gender affirming treatment, there is a risk that one might lose track of the combined impact for the patient of the entire treatment process.

The external validity of the data is generally good and has been taken into consideration in the review. Generalisability of the results could however be questioned due to different legislative circumstances.

The clinical experience of the GAS team of the Sahlgrenska University Hospital is in congruence with the literature which reports high satisfaction of the operated transgender persons even if there is a high rate of complications in all categories of the GAS procedures.

There is an obvious need for a methodological registration of the outcomes of GAS in order to assess the effectiveness and safety of all different methods. For this purpose, a Swedish national registry for GAS has been initiated and is expected to come in use during 2018.

In parallel with the registration of outcomes, there is need for more systematic research using scientific methodology of higher quality. Gender affirmation surgery needs to be performed within research projects in order to improve the knowledge about benefits and risks.

14. Future perspective

Scientific knowledge gaps

There is limited evidence for the benefit of the various GAS procedures. In particular, there is a lack of long term data. Complications as well as postoperative functions are often rated differently by surgeons and patients, so patient reported outcome measures are needed. Such outcome measures might be difficult to use, but are important since the general impact of these procedures is the subjective sense of the body. The main outcome of gender affirmative treatment is less gender dysphoria, but this outcome is rarely measured – and not conceptualised in the same way across studies. Regret could be regarded as a deeply undesirable effect and a failure. The currently reported incidence of regret is low, but the outcome is seldom reported.

Ongoing research

Searches in Clinicaltrials.gov did not identify any study that was relevant for the question at issue.

Interest at the clinic to start studies within the research field at issue

Several studies are planned.

15. Participants in the project

The question was nominated by

Anna Elander, Professor, Head of the department, Plastic Surgery Department, Sahlgrenska University Hospital, Gothenburg, Sweden

Participating health care professionals

Ulrika Beckman, psychologist, Lundström Gender Identity Clinic, Södra Älvsborgs Hospital, Alingsås, Sweden
Inger Bryman, MD, PhD, Department of Obstetrics and Gynaecology, Sahlgrenska University Hospital, Gothenburg, Sweden
Konstantinos Georgas, MD, Specialist in General Surgery, Resident in Plastic Surgery, Plastic Surgery Department, Sahlgrenska University Hospital, Gothenburg, Sweden
Ellenor Mattelin, MD, Resident at the Department of Obstetrics and Gynaecology, Sahlgrenska University Hospital, Gothenburg, Sweden
Teresa Olsen Ekerhult, MD, Senior consultant, PhD, Director of Studies for the resident program in Urology, Institute of Clinical Sciences at Sahlgrenska University, Department of Urology, Reconstructive Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden
Anna Elander, Professor, Head of the department, Plastic Surgery Department, Sahlgrenska University Hospital, Gothenburg, Sweden
Gennaro Selvaggi, MD, PhD, MSc (Health Management), MA (Bioethics), Associate Professor Department of Plastic Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, at Sahlgrenska University Hospital, Gothenburg, Sweden

Participants from the HTA-centrum

Annika Strandell, MD, Associate professor
Lennart Jivegård, MD, PhD, Senior University Lecturer
Josefine Persson, health economist, PhD
All three at HTA-centrum Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden
Lars Sandman, professor, Department of Work Life and Social Welfare, University of Borås, Borås, Sweden
Ida Stadig, Librarian, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden
Ulla Vikberg Adania, Librarian, MA and Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden

External reviewers

Åsa Tivesten, Professor/Chief physician, Dept of Endocrinology, Wallenberg Laboratory for Cardiovascular and Metabolic Research, Sahlgrenska University Hospital, Gothenburg, Sweden
Ulla Karilampi, Researcher PhD/Psychologist MSc, Sahlgrenska University Hospital, Gothenburg, Sweden

Declaration of interest

I declare that I have published several papers in the field of Gender Affirmation Surgery, previously called Gender Reassignment Surgery and / or Sex Reassignment Surgery. Some of these papers have been assessed within this systematic review.
Gennaro Selvaggi, MD, PhD, MSc (Health Management), MA (Bioethics), Associate Professor, Department of Plastic Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, at Sahlgrenska University Hospital, Sweden

Project time

HTA was accomplished during the period of 2017-12-14– 2018-06-27.
Literature searches were made in January 2018.

Appendix 1: Search strategy, study selection and references

Question(s) at issue:
In adults with gender dysphoria, does gender affirmation surgery affect quality of life (QoL) and cause complications compared with no surgery or less extensive reconstruction?

PICO: (*P=Patient I=Intervention C=Comparison O=Outcome*)

	PICO 1 Trans men (female-to-male) **PICO 2 Trans women (male-to-female)**
P	Adults with gender dysphoria (transvestism and intersexual conditions are not included in the diagnosis)
I	Gender affirmation surgery, specified procedure (not including secondary/correction surgery): **I1** = In trans men (external genital reconstruction (including penile prosthesis), hysterectomy + salpingo-oophorectomy, mastectomy, hip liposuction) **I2** = In trans women (genital surgery, breast surgery, facial feminisation surgery)
C	**C1**: No surgery **C2**: Less extensive gender affirmation surgical techniques
O	Critical for decision-making: Mortality Quality of life (QoL), including health related QoL (measured by validated technique) Patient satisfaction, including voiding measures and sexual function (measured by validated techniques) Regret/retransition Surgical complications, other complications Reoperation

<u>Eligibility criteria</u>

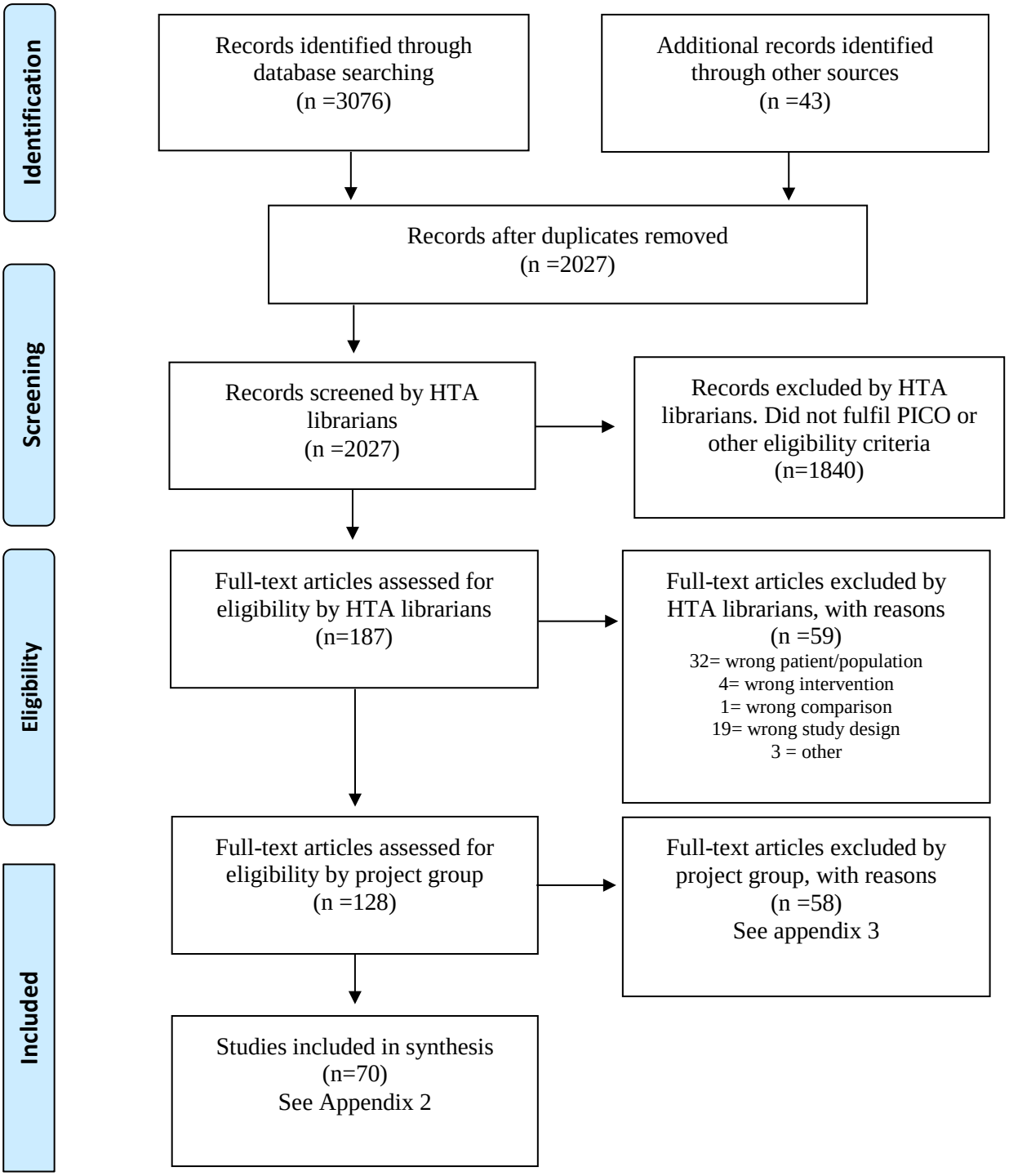
Study design:
Case series (≥ 50 patients per surgical procedure, ≥ 1 year follow up for non-surgical outcomes)
Cohort studies
Randomised controlled trials (RCT)
Systematic reviews (SR)

Reporting:
Only studies reporting outcomes per specified procedure are included.

Language:
English, Swedish, Norwegian, Danish

Publication date:
1990-
(SR) 2010-

Selection process – flow diagram



Search strategies
Database: PubMed
Date: 2018-01-05
No of results: 1098

Search	Query	Items found
#23	**Search #17 NOT #18** Filters: **Publication date from 1990/01/01 to 2018/12/31; Danish; English; Norwegian; Swedish**	**1098**
#22	Search #17 NOT #18 Filters: Publication date from 1990/01/01 to 2018/12/31; Danish; English; Norwegian	1097
#21	Search #17 NOT #18 Filters: Publication date from 1990/01/01 to 2018/12/31; Danish; English	1095
#20	Search #17 NOT #18 Filters: Publication date from 1990/01/01 to 2018/12/31	1235
#19	Search #17 NOT #18	1417
#18	Search (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp])	1595497
#17	Search #15 NOT #16	1488
#16	Search ((animals[mh]) NOT (animals[mh] AND humans[mh]))	4410723
#15	Search #13 NOT #14	1509
#14	Search ((child[mh]) NOT (child[mh] AND adult[mh]))	1103381
#13	Search #11 OR #12	1566
#12	Search Sex Reassignment Surgery[mh] OR ((reassignment[tiab] OR re-assignment[tiab] OR sex change[tiab] OR sex reversal[tiab] OR sex-affirm*[tiab] OR gender change[tiab] OR gender correction[tiab] OR gender confirmation[tiab] OR gender-affirm*[tiab] OR gender transition*[tiab]) AND surg*[tiab]) OR “male-to-female surgery”[tiab] OR “male-to-female surgeries”[tiab] OR “female-to-male surgery”[tiab] OR “female-to-male surgeries”[tiab] OR “MTF surgery”[tiab] OR “MTF surgeries”[tiab] OR “FTM surgery”[tiab] OR “FTM surgeries”[tiab]	969
#11	Search #1 AND #10	892
#10	Search #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	184182
#9	Search ((face[tiab] OR facial[tiab] OR cranofacial[tiab] OR forehead[tiab] OR jaw[tiab] OR mandible[tiab] OR chin[tiab] OR cheeks[tiab] OR nose[tiab] OR eyes[tiab] OR orbits[tiab] OR ears[tiab] OR lips[tiab] OR brows[tiab]) AND (feminization[mh] OR femin*[tiab] OR recountour*[tiab] OR contour*[tiab] OR confirmation[tiab]) AND (surg*[tiab] OR reconstruction* OR construction*)) OR ((feminization[mh] OR femin*[tiab] OR recountour*[tiab] OR contour*[tiab] OR confirmation[tiab]) AND (rhinoplasty[mh] OR rhinoplast*[tiab] OR genioplasty[mh] OR genioplast*[tiab] OR cranioplast*[tiab]))	2851
#8	Search breast reconstruction*[tiab] OR breast augmentation*[tiab] OR Breast Implants[mh] OR breast implant*[tiab] OR breast prosthes*[tiab]	1230
#7	Search vaginoplast*[tiab] OR neovagin*[tiab] OR neo-vagin*[tiab] OR vulvoplast*[tiab] OR vaginal reconstruction*[tiab] OR vaginal construction*[tiab] OR clitoroplast*[tiab] OR neoclitor*[tiab] OR neo-clitor*[tiab] OR labiaplast*[tiab] OR labioplast*[tiab] OR penis amputation*[tiab] OR penectom*[tiab] OR Orchiectomy[mh] OR orchiectom*[tiab] OR orchidectom*[tiab]	21175
#6	Search (hip[mh] OR hip[tiab] OR hips[tiab]) AND (lipectomy[mh] OR lipectom*[tiab] OR liposuction*[tiab] OR lipolysis[tiab] OR lipolyses[tiab] OR lipoplast*[tiab] OR fat suction*[tiab])	161
#5	Search Mastectomy[mh] OR breast reduct*[tiab] OR (chest[tiab] AND reconstruct*[tiab]) OR (chest[tiab] AND surg*[tiab]) OR mastectom*[tiab] OR mastopex*[tiab]	69404
#4	Search Hysterectomy[mh] OR Hysterectom*[tiab] OR salpingo-oophorectom*[tiab] OR Ovariectomy[mh] OR Ovariectom*[tiab] OR Oophorectom*[tiab] OR Salpingectomy[mh] OR Salpingectom*[tiab]	79972
#3	Search penile reconstruction*[tiab] OR penile construction*[tiab] OR penis reconstruction*[tiab] OR penis construction*[tiab] OR phalloplast*[tiab] OR neophalloplast*[tiab] OR neo-phalloplast*[tiab] OR phallic construction*[tiab] OR phallic reconstruction*[tiab] OR metoidioplast*[tiab] OR peno-scrotal reconstruction*[tiab] OR penoscrotal reconstruction*[tiab] OR peno-scrotal construction*[tiab] OR penoscrotal construction*[tiab] OR Scrotal construction* OR Scrotal reconstruction* OR scrotoplast*[tiab] OR oscheoplast*[tiab] OR testicular prosthes*[tiab] OR Penile Prosthesis[mh] OR penile prosthes*[tiab] OR penis prosthes*[tiab] OR Penile Implantation[mh] OR penile implant*[tiab] OR vaginectom*[tiab] OR clitoridectom*[tiab] OR “vaginal closure”[tiab] OR “vaginal closures”[tiab]	3452
#2	Search genital reconstruction*[tiab] OR genital construction*[tiab] OR genital surger*[tiab] OR genitoplast*[tiab] OR Mammaplasty[mh] OR mammaplast*[tiab] OR mammoplast*[tiab] OR mastoplast*[tiab]	13343
#1	Search Gender Dysphoria[mh] OR Gender Dysphor*[tiab] OR Transgender Persons[mh] OR Transgender*[tiab] OR Trans-gender*[tiab] OR Transsexualism[mh] OR transsexual*[tiab] OR trans-sexual*[tiab] OR transwoman[tiab] OR transwomen[tiab] OR trans-woman[tiab] OR trans-women[tiab] OR transman[tiab] OR transmen[tiab] OR trans-man[tiab] OR trans-men[tiab] OR transpeople[tiab] OR trans-people[tiab] OR transpopulation[tiab] OR trans-population[tiab] OR male-to-female[tiab] OR MTF[tiab] OR MTFTS[tiab] OR female-to-male[tiab] OR FTM[tiab] OR FTMTS[tiab] OR autogynephilia[tiab] OR autoandrophilia[tiab] OR cross-gender*[tiab] OR gender-varian*[tiab] OR gender varian*[tiab] OR Gender queer*[tiab] OR Genderqueer*[tiab] OR LGBT[tiab] OR LGBTTQ[tiab] OR LGBTQ[tiab] OR LGBTQIA[tiab] OR male-born[tiab] OR “assigned male”[tiab] OR “assigned males”[tiab] OR female-born[tiab] OR “assigned female”[tiab] OR “assigned females”[tiab] OR Gender incongru*[tiab] OR Sex incongru*[tiab] OR Bigender*[tiab] OR Bi-gender*[tiab] OR Intergender*[tiab] OR Inter-gender*[tiab] OR Gender identit*[tiab] OR Gender nonconform*[tiab] OR Gender non-conform*[tiab]	22818

Database: Embase 1974 to 2017 January 09 (OvidSP)
Date: 2018-01-04
No of results: 1264

#	Searches	Results
1	exp transsexualism/ or exp gender dysphoria/	4625
2	exp transgender/	2607
3	exp transgenderism/	364
4	(Gender Dysphor$ or Transgender$ or (Trans adj1 gender$) or transsexual$ or transwoman or transwomen or "trans woman" or "trans women" or transman or transmen or "trans man" or "trans men" or transpeople or "trans people" or transpopulation or "trans population" or (male adj1 female) or MTF or MTFTS or FTM or FTMTS or autogynephilia or autoandrophilia or (cross adj1 gender$) or (gender adj1 varian$) or (Gender adj1 queer$) or Genderqueer$ or LGBT or LGBTTQ or LGBTQ or LGBTQIA or (male adj 1 born) or (assigned adj1 male$) or (female adj1 born) or (assigned adj1 female$) or (Gender adj1 incongru$) or (Sex adj1 incongru$) or Bigender$ or (bi adj1 gender$) or Intergender$ or (Inter adj1 gender$) or (Gender adj1 identit$) or (Gender adj1 nonconform$) or (Gender adj1 non-conform$)).ab,ti.	34418
5	1 or 2 or 3 or 4	35668
6	exp breast reconstruction/	19220
7	((genital adj1 reconstruction$) or (genital adj1 construction$) or genital surger$ or genitoplast$ or mammaplast$ or mammoplasty$ or mastoplast$).ab,ti.	4625
8	6 or 7	20513
9	penis prosthesis/	3325
10	(((penile or penis) adj1 (reconstruction$ or construction$)) or phalloplast$ or neophalloplast$ or (neo adj1 phalloplast$) or (phallic adj1 (construction$ or reconstruction$)) or metoidioplast* or ((penoscrotal or scrotal) adj1 (reconstruction$ or construction$)) or scrotoplast$ or oscheoplast$ or ((testicular or penile or penis) adj1 (prosthes$ or implant$)) or (vaginal adj1 closure$) or vaginectom$ or clitoridectom$).ab,ti.	4823
11	9 or 10	5764
12	exp salpingooophorectomy/	12784
13	exp salpingectomy/	3816
14	exp ovariectomy/	34307
15	exp hysterectomy/	64850
16	(Hysterectom$ or salpingooophorectom$ or Ovariectom$ or Oophorectom$ or Salpingectom$).ab,ti.	88601
17	12 or 13 or 14 or 15 or 16	122082
18	exp mastectomy/	50166
19	((breast adj1 reduct$) or (chest adj3 (reconstruct$ or surg$)) or mastectom$ or mastopex$).ab,ti.	33999
20	18 or 19	60398
21	exp hip/	51479
22	(hip or hips).ab,ti.	160303
23	21 or 22	170960
24	exp lipectomy/ or exp liposuction/	5649
25	(lipectom$ or liposuction$ or lipolysis or lipolyses or lipoplast$ or (fat adj1 suction$)).ab,ti.	18370
26	24 or 25	20536
27	23 and 26	184
28	exp orchiectomy/	16498
29	exp vagina reconstruction/	3735
30	exp penis amputation/	1331
31	(Vaginoplast$ or neovagin$ or (neo adj1 (vagin$ or clitor$)) or vulvoplast$ or (vagina$ adj1 (reconstruction$ or construction$)) or clitoroplast$ or neoclitor$ or labiaplast$ or labioplast$ or (penis adj1 amputation$) or penectom$ or orchiectomy$ or orchidectom$).ab,ti.	13498
32	28 or 29 or 30 or 31	25693
33	exp breast implant/	2067
34	exp breast prosthesis/	4908
35	(breast$ adj1 (reconstruction$ or augmentation$ or implant$ or prosthes$)).ab,ti.	13435
36	33 or 34 or 35	15606
37	exp feminization/	1712

38	(femin$ or recountour$ or contour$ or confirmation$).ab,ti.	144083
39	37 or 38	144657
40	(face or facial or craniofacial or forehead or jaw or mandible or chin or cheeks or nose or eyes or orbits or ears or lips or brows).ab,ti.	619318
41	(surg$ or reconstruction$ or construction$).ab,ti.	2476308
42	39 and 40 and 41	3177
43	(rhinoplast$ or genioplast$ or cranioplast$).ab,ti.	7679
44	39 and 43	510
45	42 or 44	3460
46	8 or 11 or 17 or 20 or 27 or 32 or 36 or 45	226978
47	5 and 46	1414
48	exp sex reassignment/	761
49	(reassignment or ((sex or gender) adj1 (change or reversal or affirm$ or correction or confirmation or transition$))).ab,ti.	5000
50	48 or 49	5252
51	surg$.ab,ti.	2231697
52	50 and 51	1357
53	("male-to-female surgery" or "male-to-female surgeries" or "female-to-male surgery" or "female-to-male surgeries" or "MTF surgery" or "MTF surgeries" or "FTM surgery" or "FTM surgeries").ab,ti.	29
54	52 or 53	1370
55	47 or 54	2351
56	(child not (child and adult)).sh.	1088616
57	55 not 56	2272
58	(animal not (animal and human)).sh.	1391823
59	57 not 58	2252
60	**limit 59 to ((danish or english or norwegian or swedish) and yr="1990 -Current" and (article or conference paper or note or "review"))**	**1264**

Database: Psychinfo (EBSCOhost)
Date: 2018-01-04
No of results: 678

#	Undran	Resultat
S27	**S25 OR S26**	**678**
S26	TI (((reassignment OR re-assignment OR “sex change” OR “sex reversal” OR sex-affirm* OR “gender change” OR “gender correction” OR “gender confirmation” OR gender-affirm* OR gender-transition*) AND surg*) OR “male to female surgery” OR “male to female surgeries” OR “female to male surgery” OR “female to male surgeries” OR “MTF surgery” OR “MTF surgeries” OR “FTM surgery” OR “FTM surgeries”) OR AB (((reassignment OR re-assignment OR “sex change” OR “sex reversal” OR sex-affirm* OR “gender change” OR “gender correction” OR “gender confirmation” OR gender-affirm* OR gender-transition*) AND surg*) OR “male to female surgery” OR “male to female surgeries” OR “female to male surgery” OR “female to male surgeries” OR “MTF surgery” OR “MTF surgeries” OR “FTM surgery” OR “FTM surgeries”)	591
S25	S3 AND S24	805
S24	S4 OR S5 OR S8 OR S11 OR S16 OR S17 OR S18 OR S23	7,921
S23	S19 OR S22	165
S22	S20 AND S21	3
S21	TI (rhinoplast* OR genioplast* OR cranioplast*) OR AB (rhinoplast* OR genioplast* OR cranioplast*)	107
S20	TI (femin* OR recountour* OR contour* OR confirmation) OR AB (femin* OR recountour* OR contour* OR confirmation)	45,532
S19	TI ((face OR facial OR craniofacial OR forehead OR jaw OR mandible OR chin OR cheeks OR nose OR eyes OR orbits OR ears OR lips OR brows) AND (femin* OR recountour* OR contour* OR confirmation) AND (surg* OR reconstruction* OR construction*)) OR AB ((face OR facial OR craniofacial OR forehead OR jaw OR mandible OR chin OR cheeks OR nose OR eyes OR orbits OR ears OR lips OR brows) AND (femin* OR recountour* OR contour* OR confirmation) AND (surg* OR reconstruction* OR construction*))	164
S18	TI (breast reconstruction* OR breast augmentation* OR breast implant* OR breast prosthes*) OR AB (breast reconstruction* OR breast augmentation* OR breast implant* OR breast prosthes*)	350
S17	TI (vaginoplast* OR neovagin* OR neo-vagin* OR vulvoplast* OR vaginal reconstruction* OR vaginal construction* OR clitoroplast* OR neoclitor* OR neo-clitor* OR labiaplast* OR labioplast* OR penis amputation* OR penectom* OR orchiectom* OR orchidectom*) OR AB (vaginoplast* OR neovagin* OR neo-vagin* OR vulvoplast* OR vaginal	326

	reconstruction* OR vaginal construction* OR clitoroplast* OR neoclitor* OR neo-clitor* OR labiaplast* OR labioplast* OR penis amputation* OR penectom* OR orchiectom* OR orchidectom*)	
S16	S14 AND S15	3
S15	TI (lipectom* OR liposuction* OR lipolysis OR lipolyses OR lipoplast* OR fat suction*) OR AB (lipectom* OR liposuction* OR lipolysis OR lipolyses OR lipoplast* OR fat suction*)	171
S14	S12 OR S13	5,393
S13	TI (hip OR hips) OR AB (hip OR hips)	5,363
S12	DE "Hips"	1,127
S11	S9 OR S10	1,783
S10	TI (breast reduct* OR (chest AND reconstruct*) OR (chest AND surg*) OR mastectom* OR mastopex*) OR AB (breast reduct* OR (chest AND reconstruct*) OR (chest AND surg*) OR mastectom* OR mastopex*)	1,577
S9	DE "Mastectomy"	703
S8	S6 OR S7	4,830
S7	TI (Hysterectom* OR salpingo-oophorectom* OR Ovariectom* OR Oophorectom* OR Salpingectom*) OR AB (Hysterectom* OR salpingo-oophorectom* OR Ovariectom* OR Oophorectom* OR Salpingectom*)	4,253
S6	(DE "Hysterectomy") OR (DE "Ovariectomy")	3,004
S5	TI (penile reconstruction* OR penile construction* OR penis reconstruction* OR penis construction* OR phalloplast* OR neophalloplast* OR neo-phalloplast* OR phallic construction* OR phallic reconstruction* OR metoidioplast* OR peno-scrotal reconstruction* OR penoscrotal reconstruction* OR peno-scrotal construction* OR penoscrotal construction* OR Scrotal construction* OR Scrotal reconstruction* OR scrotoplast* OR oscheoplast* OR testicular prosthes* OR penile prosthes* OR penis prosthes* OR penile implant* OR vaginectom* OR clitoridectom* OR “vaginal closure” OR “vaginal closures”) OR AB (penile reconstruction* OR penile construction* OR penis reconstruction* OR penis construction* OR phalloplast* OR neophalloplast* OR neo-phalloplast* OR phallic construction* OR phallic reconstruction* OR metoidioplast* OR peno-scrotal reconstruction* OR penoscrotal reconstruction* OR peno-scrotal construction* OR penoscrotal construction* OR Scrotal construction* OR Scrotal reconstruction* OR scrotoplast* OR oscheoplast* OR testicular prosthes* OR penile prosthes* OR penis prosthes* OR penile implant* OR vaginectom* OR clitoridectom* OR “vaginal closure” OR “vaginal closures”)	447
S4	TI (genital reconstruction* OR genital construction* OR genital surger* OR genitoplast* OR mammaplast* OR mammoplast* OR mastoplast*) OR AB (genital reconstruction* OR genital construction* OR genital surger* OR genitoplast* OR mammaplast* OR mammoplast* OR mastoplast*)	463
S3	S1 OR S2	79,794
	TI (Gender Dysphor* OR Transgender* OR Trans-gender* OR transsexual* OR trans-sexual* OR transwoman OR transwomen OR trans-woman OR trans-women OR transman OR transmen OR trans-man OR trans-men OR transpeople OR trans-people OR transpopulation OR trans-population OR “male to female” OR MTF OR MTFTS OR “female to male” OR FTM OR FTMTS OR autogynephilia OR autoandrophilia OR cross-gender* OR gender-varian* OR Gender-queer* OR Genderqueer* OR LGBT OR LGBTTQ OR LGBTQ OR LGBTQIA OR male-born OR “assigned male” OR “assigned males” OR female-born OR “assigned female” OR “assigned females” OR Gender incongru* OR Sex incongru* OR Bigender* OR Bi-gender*OR Intergender*OR Inter-gender* OR "gender identity" OR "gender identities" OR Gender nonconform* OR Gender non-conform*) OR AB (Gender Dysphor* OR Transgender* OR Trans-gender* OR transsexual* OR trans-sexual* OR transwoman OR transwomen OR trans-woman OR trans-women OR transman OR transmen OR trans-man OR trans-men OR transpeople OR trans-people OR transpopulation OR trans-population OR “male to female” OR MTF OR MTFTS OR “female to male” OR FTM OR FTMTS OR autogynephilia OR autoandrophilia OR cross-gender* OR gender-varian* OR Gender-queer* OR Genderqueer* OR LGBT OR LGBTTQ OR LGBTQ OR LGBTQIA OR male-born OR “assigned male” OR “assigned males” OR female-born OR “assigned female” OR “assigned females” OR Gender incongru* OR Sex incongru* OR Bigender* OR Bi-gender*OR Intergender*OR Inter-gender* OR "gender identity" OR "gender identities" OR Gender nonconform* OR Gender non-conform*)	68,545
S1	DE "Gender Identity" OR DE "Transgender" OR DE "Transsexualism"	20,703

Database: The Cochrane Library
Date: 2018-01-05
No of results: 36
Cochrane reviews 0
Other reviews 1
Technology assessments 7
Trials 27
Economic evaluations 1

ID	Search	Hits
#1	MeSH descriptor: [Gender Dysphoria] explode all trees	0
#2	MeSH descriptor: [Transgender Persons] explode all trees	14
#3	MeSH descriptor: [Transsexualism] explode all trees	22
#4	Gender Dysphor* or Transgender* or Trans-gender* or transsexual* or trans-sexual* or transwoman or transwomen or trans-woman or trans-women or transman or transmen or trans-man or trans-men or transpeople or trans-people or transpopulation or trans-population or male-to-female or MTF or MTFTS or female-to-male or FTM or FTMTS or autogynephilia or autoandrophilia or cross-gender* or gender-varian* or gender varian* or Gender queer* or Genderqueer* or LGBT or LGBTTQ or LGBTQ or LGBTQIA or male-born or "assigned male" or "assigned males" or female-born or "assigned female" or "assigned females" or Gender incongru* or Sex incongru* or Bigender* or Bi-gender*OR Intergender*OR Inter-gender* or Gender identit* or Gender nonconform* or Gender non-conform*:ti,ab,kw (Word variations have been searched)	2300
#5	#1 or #2 or #3 or #4	2300
#6	MeSH descriptor: [Mammaplasty] explode all trees	356
#7	genital reconstruction* or genital construction* or genital surger* or genitoplast* or mammaplast* or mammoplast* or mastoplast*:ti,ab,kw (Word variations have been searched)	1191
#8	#6 or #7	1220
#9	MeSH descriptor: [Penile Prosthesis] explode all trees	17
#10	MeSH descriptor: [Penile Implantation] explode all trees	8
#11	penile reconstruction* or penile construction* or penis reconstruction* or penis construction* or phalloplast* or neophalloplast* or neo-phalloplast* or phallic construction* or phallic reconstruction* or metoidioplast* or peno-scrotal reconstruction* or penoscrotal reconstruction* or peno-scrotal construction* or penoscrotal construction* or Scrotal construction* or Scrotal reconstruction* or scrotoplast* or oscheoplast* or testicular prosthes* or penile prosthes* or penis prosthes* or penile implant* or vaginectom* or clitoridectom* or "vaginal closure" or "vaginal closures":ti,ab,kw (Word variations have been searched)	121
#12	#9 or #10 or #11	121
#13	MeSH descriptor: [Hysterectomy] explode all trees	1860
#14	MeSH descriptor: [Salpingectomy] explode all trees	32
#15	MeSH descriptor: [Ovariectomy] explode all trees	307
#16	Hysterectom* or salpingo-oophorectom* or Ovariectom* or Oophorectom* or Salpingectom*:ti,ab,kw (Word variations have been searched)	4813
#17	#13 or #14 or #15 or #16	4813
#18	MeSH descriptor: [Mastectomy] explode all trees	1578
#19	breast reduct* or (chest and reconstruct*) or (chest and surg*) or mastectom* or mastopex*:ti,ab,kw (Word variations have been searched)	8811
#20	#18 or #19	8811
#21	MeSH descriptor: [Hip] explode all trees	388
#22	hip or hips:ti,ab,kw (Word variations have been searched)	14406
#23	#21 or #22	14406
#24	MeSH descriptor: [Lipectomy] explode all trees	97
#25	lipectom* or liposuction* or lipolysis or lipolyses or lipoplast* or fat suction*:ti,ab,kw (Word variations have been searched)	981
#26	#24 or #25	981
#27	#23 and #26	25
#28	MeSH descriptor: [Orchiectomy] explode all trees	355

#29	vaginoplast* or neovagin* or neo-vagin* or vulvoplast* or vaginal reconstruction* or vaginal construction* or clitoroplast* or neoclitor* or neo-clitor* or labiaplast* or labioplast* or penis amputation* or penectom* or orchiectom* or orchidectom*:ti,ab,kw (Word variations have been searched)	698
#30	#28 or #29	698
#31	MeSH descriptor: [Breast Implants] explode all trees	90
#32	breast reconstruction* or breast augmentation* or breast implant* or breast prosthes*:ti,ab,kw (Word variations have been searched)	885
#33	#31 or #32	885
#34	MeSH descriptor: [Feminization] explode all trees	2
#35	femin* or recountour* or contour* or confirmation:ti,ab,kw (Word variations have been searched)	4354
#36	#34 or #35	4354
#37	face or facial or craniofacial or forehead or jaw or mandible or chin or cheeks or nose or eyes or orbits or ears or lips or brows:ti,ab,kw (Word variations have been searched)	55569
#38	surg* or reconstruction* or construction*:ti,ab,kw (Word variations have been searched)	147580
#39	#36 and #37 and #38	103
#40	MeSH descriptor: [Rhinoplasty] explode all trees	206
#41	MeSH descriptor: [Genioplasty] explode all trees	7
#42	rhinoplast* or genioplast* or cranioplast*:ti,ab,kw (Word variations have been searched)	359
#43	#40 or #41 or #42	359
#44	#36 and #43	1
#45	#39 or #44	103
#46	#8 or #12 or #17 or #20 or #27 or #30 or #33 or #45	15573
#47	#5 and #46	22
#48	MeSH descriptor: [Sex Reassignment Surgery] explode all trees	3
#49	((reassignment or re-assignment or "sex change" or "sex reversal" or sex-affirm* or "gender change" or "gender correction" or "gender confirmation" or gender-affirm* or gender-transition*) and surg*) or "male-to-female surgery" or "male-to-female surgeries" or "female-to-male surgery" or "female-to-male surgeries" or "MTF surgery" or "MTF surgeries" or "FTM surgery" or "FTM surgeries":ti,ab,kw (Word variations have been searched)	20
#50	#48 or #49	20
#51	**#47 or #50 Publication Year from 1990 to 2018**	**36**

The web-sites of **SBU** and **Folkehelseinstituttet** were visited 2018-01-20.
Nothing relevant to the question at issue was found

Reference lists
A comprehensive review of reference lists brought 43 new records

---

Reference lists

Included studies:

Ainsworth TA, Spiegel JH. Quality of life of individuals with and without facial feminization surgery or gender reassignment surgery. Qual Life Res. 2010;19(7):1019-24.

Antoszewski B, Bratos R, Sitek A, Fijalkowska M. Long-term results of breast reduction in female-to-male transsexuals. Pol Przegl Chir. 2012;84(3):144-51.

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. J Urol. 2018;199(1):206-14.

Barrett J. Psychological and social function before and after phalloplasty. Int J Transgend. 1998;2(1).

Bellinga RJ, Capitan L, Simon D, Tenorio T. Technical and clinical considerations for facial feminization surgery with rhinoplasty and related procedures. JAMA Facial Plast Surg. 2017;19(3):175-81.

Berry MG, Curtis R, Davies D. Female-to-male transgender chest reconstruction: a large consecutive, single-surgeon experience. J Plast Reconstr Aesthet Surg. 2012;65(6):711-9.

Bluebond-Langner R, Berli JU, Sabino J, Chopra K, Singh D, Fischer B. Top surgery in transgender men: how far can you push the envelope? Plast Reconstr Surg. 2017;139(4):873e-82e.

Bucci S, Mazzon G, Liguori G, Napoli R, Pavan N, Bormioli S, et al. Neovaginal prolapse in male-to-female transsexuals: an 18-year-long experience. Biomed Res Int. 2014:240761.

Buncamper ME, van der Sluis WB, de Vries M, Witte BI, Bouman MB, Mullender MG. Penile inversion vaginoplasty with or without additional full-thickness skin graft: to graft or not to graft? Plast Reconstr Surg. 2017;139(3):649e-56e.

Buncamper ME, van der Sluis WB, van der Pas RS, Ozer M, Smit JM, Witte BI, et al. Surgical outcome after penile inversion vaginoplasty: a retrospective study of 475 transgender women. Plast Reconstr Surg. 2016;138(5):999-1007.

Capitan L, Simon D, Kaye K, Tenorio T. Facial feminization surgery: the forehead. Surgical techniques and analysis of results. Plast Reconstr Surg. 2014;134(4):609-19.

Capitan L, Simon D, Meyer T, Alcaide A, Wells A, Bailon C, et al. Facial feminization surgery: simultaneous hair transplant during forehead reconstruction. Plast Reconstr Surg. 2017;139(3):573-84.

Cregten-Escobar P, Bouman MB, Buncamper ME, Mullender MG. Subcutaneous mastectomy in female-to-male transsexuals: a retrospective cohort-analysis of 202 patients. J Sex Med. 2012;9(12):3148-53.

Davis SA, Meier SC. Effects of testosterone treatment and chest reconstruction surgery on mental health and sexuality in female-to-male transgender people. Int J Sex Health. 2014;26(2):113-28.

Djordjevic ML, Bizic MR. Comparison of two different methods for urethral lengthening in female to male (metoidioplasty) surgery. J Sex Med. 2013;10(5):1431-8.

Donato DP, Walzer NK, Rivera A, Wright L, Agarwal CA. Female-to-male chest reconstruction: a review of technique and outcomes. Ann Plast Surg. 2017;79(3):259-63.

Doornaert M, Hoebeke P, Ceulemans P, T'Sjoen G, Heylens G, Monstrey S. Penile reconstruction with the radial forearm flap: an update. Handchir Mikrochir Plast Chir. 2011;43(4):208-14.

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 Int. 2018;121:139-44.

Falcone M, Timpano M, Ceruti C, Sedigh O, Oderda M, Gillo A, et al. A Single-center analysis on the learning curve of male-to-female penoscrotal vaginoplasty by multiple surgical measures. Urology. 2017;99:234-9.

Fang RH, Lin JT, Ma S. Phalloplasty for female transsexuals with sensate free forearm flap. Microsurg. 1994;15(5):349-52.

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. J Urol. 2017;17:77717-8.

Garaffa G, Christopher NA, Ralph DJ. Total phallic reconstruction in female-to-male transsexuals. Eur Urol. 2010;57(4):715-22.

Garcia MM, Christopher NA, De Luca F, Spilotros M, Ralph DJ. Overall satisfaction, sexual function, and the durability of neophallus dimensions following staged female to male genital gender confirming surgery: the Institute of Urology, London U.K. experience. Transl Androl Urol. 2014;3(2):156-62.

Goddard JC, Vickery RM, Qureshi A, Summerton DJ, Khoosal D, Terry TR. Feminizing genitoplasty in adult transsexuals: early and long-term surgical results. BJU Int. 2007;100(3):607-13.

Hage JJ, Goedkoop AY, Karim RB, Kanhai RC. Secondary corrections of the vulva in male-to-female transsexuals. Plast Reconstr Surg. 2000;106(2):350-9.

Hage JJ, van Turnhout AA. Long-term outcome of metaidoioplasty in 70 female-to-male transsexuals. Ann Plast Surg. 2006;57(3):312-6.

Hess J, Rossi Neto R, Panic L, Rubben H, Senf W. Satisfaction with male-to-female gender reassignment surgery. Dtsch Arztebl Int. 2014;111(47):795-801.

Hoebeke PB, Decaestecker K, Beysens M, Opdenakker Y, Lumen N, Monstrey SM. Erectile implants in female-to-male transsexuals: our experience in 129 patients. Eur Urol. 2010;57(2):334-40.

Huang TT. Twenty years of experience in managing gender dysphoric patients: I. Surgical management of male transsexuals. Plast Reconstr Surg. 1995;96(4):921-30; discussion 31-4.

Jarolim L, Sedy J, Schmidt M, Nanka O, Foltan R, Kawaciuk I. Gender reassignment surgery in male-to-female transsexualism: A retrospective 3-month follow-up study with anatomical remarks. J Sex Med. 2009;6(6):1635-44.

Kanhai RC. Sensate Vagina Pedicled-Spot for Male-to-Female Transsexuals: The Experience in the First 50 Patients. Aesthetic Plast Surg. 2016;40(2):284-7.

Kanhai RC, Hage JJ, Mulder JW. Long-term outcome of augmentation mammaplasty in male-to-female transsexuals: a questionnaire survey of 107 patients. Br J Plast Surg. 2000;53(3):209-11.

Karim RB, Hage JJ, Bouman FG, de Ruyter R, van Kesteren PJ. Refinements of pre-, intra-, and postoperative care to prevent complications of vaginoplasty in male transsexuals. Ann Plast Surg. 1995;35(3):279-84.

Kim SK, Moon JB, Heo J, Kwon YS, Lee KC. A new method of urethroplasty for prevention of fistula in female-to-male gender reassignment surgery. Ann Plast Surg. 2010;64(6):759-64.

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. Plast Reconstr Surg. 2017;139(6):1260e-72e.

Krege S, Bex A, Lummen G, Rubben H. Male-to-female transsexualism: a technique, results and long-term follow-up in 66 patients. BJU Int. 2001;88(4):396-402.

Lawrence AA. Factors associated with satisfaction or regret following male-to-female sex reassignment surgery. Arch Sex Behav. 2003;32(4):299-315.

Lawrence AA. Patient-reported complications and functional outcomes of male-to-female sex reassignment surgery. Arch Sex Behav. 2006;35(6):717-27.

Leriche A, Timsit MO, Morel-Journel N, Bouillot A, Dembele D, Ruffion A. Long-term outcome of forearm flee-flap phalloplasty in the treatment of transsexualism. BJU Int. 2008;101(10):1297-300.

Massie JP, Morrison SD, Wilson SC, Crane CN, Chen ML. Phalloplasty with urethral lengthening: addition of a vascularized bulbospongiosus flap from vaginectomy reduces postoperative Urethral Complications. Plast Reconstr Surg. 2017;140(4):551e-8e.

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. Aesthet Surg J. 2017;38(1):49-57.

Monstrey S, Hoebeke P, Dhont M, Selvaggi G, Hamdi M, Van Landuyt K, et al. Radial forearm phalloplasty: A review of 81 cases. Eur J Plast Surg. 2005;28(3):206-12.

Monstrey S, Selvaggi G, Ceulemans P, Van Landuyt K, Bowman C, Blondeel P, et al. Chest-wall contouring surgery in female-to-male transsexuals: a new algorithm. Plast Reconstr Surg. 2008;121(3):849-59.

Morrison SD, Satterwhite T, Grant DW, Kirby J, Laub DR, Sr., VanMaasdam J. Long-term outcomes of rectosigmoid neocolporrhaphy in male-to-female gender reassignment surgery. Plast Reconstr Surg. 2015;136(2):386-94.

Perovic SV, Stanojevic DS, Djordjevic ML. Vaginoplasty in male transsexuals using penile skin and a urethral flap. BJU Int. 2000;86(7):843-50.

Rachlin K, Hansbury G, Pardo ST. Hysterectomy and oophorectomy experiences of female-to-male transgender individuals. Int J Transgend. 2010;12(3):155-66.

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. J Sex Med. 2015;12(8):1837-45.

Reed HM. Aesthetic and functional male to female genital and perineal surgery: feminizing vaginoplasty. Semin Plast Surg. 2011;25(2):163-74.

Rieger UM, Majenka P, Wirthmann A, Sohn M, Bozkurt A, Djedovic G. Comparative study of the free microvascular groin flap: optimizing the donor site after free radial forearm flap phalloplasty. Urology. 2016;95:192-6.

Rossi Neto R, Hintz F, Krege S, Rubben H, Vom Dorp F. Gender reassignment surgery--a 13 year review of surgical outcomes. Int Braz J Urol. 2012;38(1):97-107.

Selvaggi G, Hoebeke P, Ceulemans P, Hamdi M, Van Landuyt K, Blondeel P, et al. Scrotal reconstruction in female-to-male transsexuals: a novel scrotoplasty. Plast Reconstr Surg. 2009;123(6):1710-8.

Sigurjonsson H, Rinder J, Mollermark 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.

Smith YL, Van Goozen SH, Kuiper AJ, Cohen-Kettenis PT. Sex reassignment: outcomes and predictors of treatment for adolescent and adult transsexuals. Psychol Med. 2005;35(1):89-99.

Spehr C. Male-to-female sex reassignment surgery in transsexuals. Int J Transgend. 2007;10(1):25-37.

Spiegel JH. Facial determinants of female gender and feminizing forehead cranioplasty. Laryngoscope. 2011;121(2):250-61.

Stojanovic B, Bizic M, Bencic M, Kojovic V, Majstorovic M, Jeftovic M, et al. One-stage gender-confirmation surgery as a viable surgical procedure for female-to-male transsexuals. J Sex Med. 2017;14(5):741-6.

Takamatsu A, Harashina T. Labial ring flap: a new flap for metaidoioplasty in female-to-male transsexuals. J Plast Reconstr Aesthet Surg. 2009;62(3):318-25.

Tavakkoli Tabassi K, Djavan B, Hosseini J, Ghoreifi A, Ershadi M, Hosseini E. Fold-back perineoscrotal flap plus penile inversion vaginoplasty for male-to-female gender reassignment surgery in circumcised subjects. Eur J Plast Surg. 2014;38(1):43-8.

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. 2017b:1-11.

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 after genital gender-confirming surgery in transmen. J Sex Med. 2017c;14(12):1621-8.

Van Noort DE, Nicolai JPA. Comparison of two methods of vagina construction in transsexuals. Plast Reconst Surg. 1993;91(7):1308-15.

Vukadinovic V, Stojanovic B, Majstorovic M, Milosevic A. The role of clitoral anatomy in female to male sex reassignment surgery. Sci World J. 2014:437378.

Wagner S, Greco F, Hoda MR, Inferrera A, Lupo A, Hamza A, et al. Male-to-female transsexualism: technique, results and 3-year follow-up in 50 patients. Urol Int. 2010;84(3):330-3.

Weyers S, Monstrey S, Hoebeke P, De Cuypere G, Gerris J. Laparoscopic hysterectomy as the method of choice for hysterectomy in female-to-male gender dysphoric individuals. Gynecol Surg. 2008;5(4):269-73.

Weyers S, Selvaggi G, Monstrey S, Dhont M, Van Den Broecke R, De Sutter P, et al. Two-stage versus one-stage sex reassignment surgery in female-to-male transsexual individuals. Gynecol Surg. 2006;3(3):190-4.

Wierckx K, Elaut E, Van Hoorde B, Heylens G, De Cuypere G, Monstrey S, et al. Sexual desire in trans persons: associations with sex reassignment treatment. J Sex Med. 2014;11(1):107-18.

Wierckx K, Van Caenegem E, Elaut E, Dedecker D, Van de Peer F, Toye K, et al. Quality of life and sexual health after sex reassignment surgery in transsexual men. J Sex Med. 2011;8(12):3379-88.

Wirthmann AE, Majenka P, Kaufmann MC, Wellenbrock SV, Kasper L, Huttinger 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):235-241.

Wolter A, Diedrichson J, Scholz T, Arens-Landwehr A, Liebau J. Sexual reassignment surgery in female-to-male transsexuals: an algorithm for subcutaneous mastectomy. J Plast Reconstr Aesthet Surg. 2015;68(2):184-91.

Zielinski T. Phalloplasty using a lateral groin flap in female-to-male transsexuals. Acta Chir Plast. 1999;41(1):15-9.

Excluded studies:

Bandini E, Fisher AD, Castellini G, Lo Sauro C, Lelli L, Meriggiola MC, et al. Gender identity disorder and eating disorders: similarities and differences in terms of body uneasiness. J Sex Med. 2013;10(4):1012-23.

Bertolotto M, Liguori G, Bucci S, Iannelli M, Vedovo F, Pavan N, et al. MR imaging in patients with male-to-female sex reassignment surgery: postoperative anatomy and complications. Br J Radiol. 2017;90(1072):20170062.

Bettocchi C, Ralph DJ, Pryor JP. Pedicled pubic phalloplasty in females with gender dysphoria. BJU Int. 2005;95(1):120-4.

Bjerrome Ahlin H, Kolby L, Elander A, Selvaggi G. Improved results after implementation of the Ghent algorithm for subcutaneous mastectomy in female-to-male transsexuals. J Plast Surg Hand Surg. 2014;48(6):362-7.

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. J Sex Med. 2014;11(7):1835-47.

Boza C, Perry KN. Gender-related victimization, perceived social support, and predictors of depression among transgender Australians. Int J Transgend. 2014;15(1):35-52.

Cardenas-Camarena L, Dorado C, Guerrero MT, Nava R. Surgical masculinization of the breast: clinical classification and surgical procedures. Aesthetic Plast Surg. 2017;41(3):507-16.

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.

De Cuypere G, T'Sjoen G, Beerten R, Selvaggi G, De Sutter P, Hoebeke P, et al. Sexual and physical health after sex reassignment surgery. Arch Sex Behav. 2005;34(6):679-90.

De Cuypere G, Elaut E, Heylens G, Van Maele G, Selvaggi G, T'Sjoen G, et al. Long-term follow-up: psychosocial outcome of Belgian transsexuals after sex reassignment surgery. Sexologies. 2006;15(2):126-33.

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(6):543-56.

Dhejne C, Lichtenstein P, Boman M, Johansson AL, Langstrom N, Landen M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. PLoS One. 2011;6(2):e16885.

Djordjevic ML, Stanojevic D, Bizic M, Kojovic V, Majstorovic M, Vujovic S, et al. Metoidioplasty as a single stage sex reassignment surgery in female transsexuals: Belgrade experience. J Sex Med. 2009;6(5):1306-13.

Eldh J, Berg A, Gustafsson M. Long-term follow up after sex reassignment surgery. Scand J Plast Reconstr Surg Hand Surg. 1997;31(1):39-45.

Frederick MJ, Berhanu AE, Bartlett R. Chest surgery in female to male transgender individuals. Ann Plast Surg. 2017;78(3):249-53.

Hage JJ, Bloem JJ. Chest wall contouring for female-to-male transsexuals: Amsterdam experience. Ann Plast Surg. 1995;34(1):59-66.

Hage JJ, Karim RB. Sensate pedicled neoclitoroplasty for male transsexuals: Amsterdam experience in the first 60 patients. Ann Plast Surg. 1996;36(6):621-4.

Hess J, Hess-Busch Y, Kronier J, Rubben H, Rossi Neto R. Modified preparation of the neurovascular bundle in male to female transgender patients. Urol Int. 2016;96(3):354-9.

Heylens G, Verroken C, De Cock S, T'Sjoen G, De Cuypere G. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. J Sex Med. 2014;11(1):119-26.

Hoebeke P, Selvaggi G, Ceulemans P, De Cuypere G, T'Sjoen G, Weyers S, et al. Impact of sex reassignment surgery on lower urinary tract function. Eur Urol. 2005;47(3):398-402.

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. J Sex Med. 2015;12(6):1499-512.

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(10):2736-45.

Jarolim L. Surgical conversion of genitalia in transsexual patients. BJU Int. 2000;85(7):851-6.

Kaariainen 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.

Kanhai RC, Hage JJ, Asscheman H, Mulder JW. Augmentation mammaplasty in male-to-female transsexuals. Plast Reconstr Surg. 1999;104(2):542-9; discussion 50-1.

Kanhai RC, Hage JJ, Karim RB. Augmentation mammaplasty in male-to-female trans-sexuals: facts and figures from Amsterdam. Scand J Plast Reconstr Surg Hand Surg. 2001;35(2):203-6.

Krueger M, Yekani SAH, von Hundt G, Daverio PJ. Use of erectile prostheses in patients with free forearm flap phalloplasty. Int J Transgend. 2007;10(1):19-22.

Kuhn A, Bodmer C, Stadlmayr W, Kuhn P, Mueller MD, Birkhauser M. Quality of life 15 years after sex reassignment surgery for transsexualism. Fertil Steril. 2009;92(5):1685-9.e3.

Kuhn A, Santi A, Birkhauser M. Vaginal prolapse, pelvic floor function, and related symptoms 16 years after sex reassignment surgery in transsexuals. Fertil Steril. 2011;95(7):2379-82.

Lawrence AA. Sexuality before and after male-to-female sex reassignment surgery. Arch Sex Behav. 2005;34(2):147-66.

Lindqvist EK, Sigurjonsson H, Mollermark 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(3):223-6.

Maycock LB, Kennedy HP. Breast care in the transgender individual. J Midwifery Womens Health. 2014;59(1):74-81.

Monstrey S, Hoebeke P, Dhont M, De Cuypere G, Rubens R, Moerman M, et al. Surgical therapy in transsexual patients: a multi-disciplinary approach. Acta Chir Belg. 2001;101(5):200-9.

Morrison SD, Shakir A, Vyas KS, Kirby J, Crane CN, Lee GK. Phalloplasty: A review of techniques and outcomes. Plast Reconstr Surg. 2016a;138(3):594-615.

Morrison SD, Vyas KS, Motakef S, Gast KM, Chung MT, Rashidi V, et al. Facial feminization: systematic review of the literature. Plast Reconstr Surg. 2016b;137(6):1759-70.

Motmans J, Meier P, Ponnet K, T'Sjoen G. Female and male transgender quality of life: socioeconomic and medical differences. J Sex Med. 2012;9(3):743-50.

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. J Sex Med. 2016;13(11):1758-64.

Perovic SV, Stanojevic DS, Djordjevic ML. Vaginoplasty in male to female transsexuals using penile skin and urethral flap. Int J Transgend. 2005;8(1):43-64.

Pfäfflin F. Regrets after sex reassignment surgery. J Psychol Hum Sex. 1992;5(4):69-85.

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? Plast Reconstr Surg. 2018;141(2):220e-229e.

Riggs DW, Coleman K, Due C. Healthcare experiences of gender diverse Australians: a mixed-methods, self-report survey. BMC Public Health. 2014;14:230.

Schaff J, Papadopulos NA. A new protocol for complete phalloplasty with free sensate and prelaminated osteofasciocutaneous flaps: experience in 37 patients. Microsurg. 2009;29(5):413-9.

Sehnal B, Sottner O, Zahumensky J, Maresova P, Holy P, Halaska M. Comparison of three hysterectomy methods in a set of female to male transsexuals. Geburtshilfe Frauenheilkd. 2008;68(6):625-8.

Sigurjonsson H, Rinder J, Lindqvist EK, Farnebo F, Lundgren TK. Solely penile skin for neovaginal construction in sex reassignment surgery. Plast Reconstr Surg Glob Open. 2016;4(6):e767.

Simbar M, Nazarpour S, Mirzababaie M, EmamHadi MA, Tehrani FR, Majd HA. Quality of life and body image of individuals with gender dysphoria. J Sex Marital Ther. 2018.

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(4):241-7.

Simonsen RK, Hald GM, Kristensen E, Giraldi A. Long-term follow-up of individuals undergoing sex-reassignment surgery: somatic morbidity and cause of death. Sex Med. 2016;4(1):e60-8.

Testa RJ, Rider GN, Haug NA, Balsam KF. Gender confirming medical interventions and eating disorder symptoms among transgender individuals. Health Psychol. 2017;36(10):927-36.

Top H, Balta S. Transsexual mastectomy: selection of appropriate technique according to breast characteristics. Balkan Med J. 2017;34(2):147-55.

Tsoi WF. Follow-up study of transsexuals after sex-reassignment surgery. Singapore Med J. 1993;34(6):515-7.

van de Grift TC, Elaut E, Cerwenka SC, Cohen-Kettenis PT, De Cuypere G, Richter-Appelt H, et al. Effects of medical interventions on gender dysphoria and body image: a follow-up study. Psychosom Med. 2017a;79(7):815-23.

van de Grift TC, Elfering L, Bouman MB, Buncamper ME, Mullender MG. Surgical indications and outcomes of mastectomy in transmen: a prospective study of technical and self-reported measures. Plast Reconstr Surg. 2017d;140(3):415e-24e.

van der Sluis WB, Bouman MB, Buncamper ME, Mullender MG, Meijerink WJ. Revision vaginoplasty: a comparison of surgical outcomes of laparoscopic intestinal versus perineal full-thickness skin graft vaginoplasty. Plast Reconstr Surg. 2016;138(4):793-800.

van der Sluis WB, Bouman MB, Buncamper ME, Pigot GL, Mullender MG, Meijerink WJ. Clinical characteristics and management of neovaginal fistulas after vaginoplasty in transgender women. Obstet Gynecol. 2016;127(6):1118-26.

van Kesteren PJ, Gooren LJ, Megens JA. An epidemiological and demographic study of transsexuals in the Netherlands. Arch Sex Behav. 1996;25(6):589-600.

Wedler V, Meuli-Simmen C, Guggenheim M, Schneller-Gustafsson M, Kunzi W. Laparoscopic technique for secondary vaginoplasty in male to female transsexuals using a modified vascularized pedicled sigmoid. Gynecol Obstet Invest. 2004;57(4):181-5.

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(3):752-60.

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. J Plast Reconstr Aesthet Surg. 2018;71(3):344-352.

Other references:

Adams N, Hitomi M, Moody C. Varied reports of adult transgender suicidality: synthesizing and describing the peer-reviewed and gray literature. Transgend Health. 2017;2(1):60-75.

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004;328(7454):1490-4.

Bakker A, van Kesteren PJ, Gooren LJ, Bezemer PD. The prevalence of transsexualism in The Netherlands. Acta Psychiatr Scand. 1993;87(4):237-8.

Caplan A, Purves D. A quiet revolution in organ transplant ethics. J Med Ethics. 2017;43(11):797-800.

[Checklist from SBU regarding cohort studies. (Modified) Version 2010:1]. [Internet]. [cited 2018 Mar 23] Available from: https://www2.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/Mall%20B03_Granskningsmall%20f%c3%b6r%20kohortstudier%20med%20kontrollgrupp.doc

Dhejne C. On gender dysphoria [dissertation]. Stockholm: Karolinska Institutet; 2017.

Di Ceglie D. Management and therapeutic aims in working with children and adolescents with gender identity disorders, and their families. In: Di Ceglie D, Freedman D, editors. A stranger in my own body: atypical gender identity development and mental health. London: Karnac Books; 1998. p. 185-97.

GRADE Working Group. [Internet]. [Place unknown]: GRADE Working Group, c200-2017 [cited 2017 Feb 13]. Available from: http://www.gradeworkinggroup.org

Haas AP, Rodgers PL, Herman JL. Suicide attempts among transgender and gender non-conforming adults: finding of the national transgender discrimination survey [Internet]. Los Angeles: Williams institute and American foundation for suicide prevention; 2014. [cited 2018 Apr 5]. Available from: https://williamsinstitute.law.ucla.edu/wp-content/uploads/AFSP-Williams-Suicide-Report-Final.pdf

Hjalte F, Norrlind H, Ragnarsson Tennvall G. Ekonomiska konsekvenser för sjukvården utifrån prioriteringsgruppens rekommendationer för vård och behandling av personer med könsdysfori. Lund: Institutet för Hälso- och sjukvårdsekonomi; 2015.

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. J Sex Med. 2015;12(6):1499-512.

James SE, Herman JL, Rankin S, Keisling M, Mottet L, Anafi M. The report of the 2015 U.S. transgender survey [Internet]. Washington DC: National center for transgender equality; 2016. [cited 2018 May 15]. Available from: https://www.transequality.org/sites/default/files/docs/USTS-Full-Report-FINAL.PDF

Kanagalingam J, Georgalas C, Wood GR, Ahluwalia S, Sandhu G, Cheesman AD. Cricothyroid approximation and subluxation in 21 male-to-female transsexuals. Laryngoscope. 2005;115(4):611-8.

Kanhai RC, Hage JJ, Karim RB, Mulder JW. Exceptional presenting conditions and outcome of augmentation mammaplasty in male-to-female transsexuals. Ann Plast Surg. 1999;43(5):476-83.

Karim RB, Hage JJ, Mulder JW. Neovaginoplasty in male transsexuals: review of surgical techniques and recommendations regarding eligibility. Ann Plast Surg. 1996;37(6):669-75.

Liao SM. Health (care) and human rights: a fundamental conditions approach. Theor Med Bioeth. 2016;37(4):259-74.

Lindqvist EK, Sigurjonsson H, Mollermark 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(3):223-6.

Michel A, Mormont C, Legros JJ. A psycho-endocrinological overview of transsexualism. Eur J Endocrinol. 2001;145(4):365-76.

Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.

Monstrey S. Recent developments in gender confirming surgery. Paper presented at: The Amsterdam gender identity meeting; 2013 Jun 6–7; Amsterdam.

Niveau G, Ummel M, Harding T. Human rights aspects of transsexualism. Hum Rights. 1999;4(1):134-64.

Selvaggi G, Bellringer J. Gender reassignment surgery: an overview. Nat Rev Urol. 2011;8(5):274-82.

Selvaggi G, Ceulemans P, De Cuypere G, VanLanduyt K, Blondeel P, Hamdi M, et al. Gender identity disorder: general overview and surgical treatment for vaginoplasty in male-to-female transsexuals. Plast Reconstr Surg. 2005;116(6):135e-145e.

Selvaggi G, Elander A. Penile reconstruction/formation. Curr Opin Urol. 2008;18(6):589-97.

Selvaggi G, Kolby L, Elander A. Prioritization for Plastic Surgery Procedures Aimed to Improve Quality of Life: Moral Considerations. Plast Reconstr Surg Glob Open. 2017;5(8):e1437.

Socialstyrelsen. God vård av vuxna med könsdysfori: Nationellt kunskapsstöd [Internet]. Stockholm: Socialstyrelsen; 2015. [cited 2018 May 15]. Available from: https://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/19798/2015-4-7.pdf

WPATH. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th Version. WPATH 2011 Available from:www.wpath.org [Accessed 5 April 2018].

Project: Gender dysphoria

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Follow-up (mean months)	Trans men (n)	Trans women (n)	Surgical intervention 1	Surgical intervention 2	Mean Age (years)	Outcome variables
Ainsworth 2010 USA	Cross sectional	NR		247	Facial feminisation surgery (FFS) Genital surgery (GRS)	No surgery	50	Quality of life (FFS, GRS) Satisfaction (FFS)
Antoszewski 2012 Poland	Case series	12-168	98		Mastectomy		36	Satisfaction
Ascha 2018 USA	Cohort	6	149 vs 64		RFF Phalloplasty	Phalloplasty anterolateral thigh pedicled flap	36	Complication
Barrett 1998 USA	Cross-sectional	46 (1-195)	31 vs 23		Phalloplasty		35	Quality of life Satisfaction
Bellinga 2017 Spain	Case series	32 (12-77)		200	Facial surgery		40 (18-70)	Satisfaction
Berry 2012 UK	Cohort	7(4-34)	90		Mastectomy Periareolar standard or extended	Mastectomy free nipple graft	28 (18-55)	Complication Reoperation
Bluebond-Langner 2017 USA	Cohort	>6	109 vs 186		Mastectomy circumareolar incision	Mastectomy free nipple graft	29	Complication Reoperation
Bucci 2014 Italy	Cohort	12		217 vs 65	Prolapse prevalence after GAS		NR	Complication (prolapse)
Buncamper 2017 The Netherlands	Cohort	12		68 vs 32	Penile Inversion Vaginoplasty with full thickness skin graft	Penile Inversion Vaginoplasty without full thickness skin graft	NR	Satisfaction
Buncamper 2016 The Netherlands	Cohort	Median 94 (12-155)		405 vs 70	Penile Inversion Vaginoplasty penile inversion with full thickness skin graft	Penile Inversion Vaginoplasty without full thickness skin graft	38 (18-70)	Complication Reoperation
Capitan 2014 Spain	Case series	6 - 65		172	Facial feminisation surgery		39 (18-61)	Satisfaction

Project: Gender dysphoria

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Follow-up (mean months)	Trans men (n)	Trans women (n)	Surgical intervention 1	Surgical intervention 2	Mean Age (years)	Outcome variables
Capitan 2017 Spain	Case series	26 (12-40)		65	Facial feminization surgery		38 (18-60)	Complication
Cregten-Escobar 2012 The Netherlands	Cohort	NR	202		Mastectomy without skin resection	Mastectomy with skin resection	NR	Reoperation
Davis 2014 USA	Cohort	NR	72 vs 46		Chest reconstruction suregry	C1: Testosterone C2: No hormones	Mean 27-36	Satisfaction
Djordjevic 2013 Serbia	Cohort	Median 39 (12-116)	49 vs 158		Metoidioplasty with clitorial skin flap	Metoidioplasty with labial skin flap	NR	Satisfaction Complication
Donato 2017 USA	Cohort	>6	130		Mastectomy circumareaolar incision	Mastectomy free nipple graft	28 (14-56)	Complication
Doornaert 2011 Belgium	Case series	NR	306		Penile reconstruction		NR	Complication Reoperation
Falcone 2017 Italy	Case series	Median 5 (2-8)		69	Penoscrotal vaginoplasty		NR	Complication
Falcone 2018 Italy	Case series	Median 20 (7-123)	247		Penile prosthesis insertion		38 (21-69)	Satisfaction Complication
Fang 1994 China	Cohort	NR	56		Phalloplasty with neourethra	Phalloplasty with other neourethra method	NR	Complication Reoperation
Gaither 2017 USA	Case series	3-73		330	Penile inversion vaginoplasty		35 (18-76)	Complication
Garaffa 2010 UK	Case series	Median 26 (1-270)	115		Radial forearrn flap (RFF) Phalloplasty		34 (20-55)	Satisfaction Complication Reoperation

Project: Gender dysphoria

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Follow-up (mean months)	Trans men (n)	Trans women (n)	Surgical intervention 1	Surgical intervention 2	Mean Age (years)	Outcome variables
Garcia 2014 USA	Cohort	I 82 II 27 III 27	15 vs 10		RFF phalloplasty with I (n=10) or without II (n=5) cutaneous-clitoral anastomosis	III Supra pubic pedicle flap phalloplasty	I 35 II 34 III 39	Satisfaction Regret
Goddard 2007 UK	Case series	36 (9-96)		222	Penectomy		Median 43 (19-76)	Complication
Hage 2000 The Netherlands	Case series 390	42 (2-204)		390	Vaginoplasty		35 (17-71)	Reoperation
Hage 2006 The Netherlands	Cohort	96 (54-140)	23 vs 47		Metoidioplasty	Metoidioplasty + scrotoplasty	30 (19-53)	Complication Reoperation
Hess 2014 Germany/Brasil	Case series	60 (12-42)		119	Vaginoplasty		36 (16-68)	Satisfaction
Hoebecke 2010 Belgium	Case series	30 (0-132)	129		Penile prosthesis insertion		34 (17-53)	Complication Reoperation
Huang 1995 USA	Case series	>12		121	Vaginoplasty		32 (18-71)	Complication
Jarolim 2009 Czech Republic	Case series	3		121 + 8	Penile Inversion Vaginoplasty	Sigmoidovaginoplasty	31 (18-54)	Complication
Kanhai 2016 The Netherlands	Case series	46 (17-73)		50	Vaginoplasty with clitoris		38 (19-65)	(Satisfaction) Sexual function
Kanhai 2000 The Netherlands	Case series	58 (7-156)		107	Augmentation Mammaplasty		35 (18-71)	Satisfaction
Karim 1995 The Netherlands	Case series	22 (6-102)		200	Vaginoplasty		35 (18-75)	Complication Reoperation

Project: Gender dysphoria

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Follow-up (mean months)	Trans men (n)	Trans women (n)	Surgical intervention 1	Surgical intervention 2	Mean Age (years)	Outcome variables
Kim 2010 Korea	Cohort	54	38 vs 34		Urethroplasty	Modified urethroplasty	34 (19-45)	Complication
Knox 2017 Canada/USA	Cohort	NR	101		I: Mastectomy concentric circular (n=46)	II: Mastectomy free nipple graft (n=55)	I:27 (15-48) II: 33 (18-65)	Complication Reoperation
Krege 2001 Germany	Case series	>6		66	Vaginoplasty		37 (20-57)	Complications
Lawrence 2003 USA	Case series	NR		232	Vaginoplasty		44 (18-70)	Quality of life Satisfaction Regret
Lawrence 2006 USA	Case series	3		232	Vaginoplasty, clitoroplasty		44 (18-70)	Quality of life Satisfaction, Regret Complication
Leriche 2008 France	Case series	110 (11-204)	56		Phalloplasty		30 (20-44)	Satisfaction Complication
Massie 2017 USA	Cohort	3	215 vs 9		Phalloplasty and vaginectomy (n=209)	Phalloplasty with vaginal preservation (n=9)	37	Complication
McEvenue 2017 Canada	Cohort	1	104 vs 575		Mastectomy circumareolar incision	Mastectomy free nipple graft	27	Complication Reoperation
Monstrey 2005 Begium	Case series	NR	81		Phalloplasty	-	NR	Complication
Monstrey 2008 Belgium	Case series	NR	184		Concentric circular mastectomy (n=70)	-	31 (20-60)	Complication Reoperation
Morrison 2015 USA	Case series	26		83	Neocolporhaphy	-	35 (19-61)	Satisfaction Complication Reoperation

Project: Gender dysphoria

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Follow-up (mean months)	Trans men (n)	Trans women (n)	Surgical intervention 1	Surgical intervention 2	Mean Age (years)	Outcome variables
Perovic 2000 Yogoslavia	Case series	55 (3-72)		85	Inverted penile skin flap vaginoplasty	-	28 (18-56)	Complication
Rachlin 2010 USA	Case series	NR	134		Hysterectomy and oophorectomy	-	37 (21-67)	Regret Complication
Raigosa 2015 Spain	Case series	12 (14-46)		60	Vaginoplasty	-	28 (19-50)	Complication Reoperation
Reed 2011 USA	Case series	NR		250	Vaginoplasty	-	NR	Complication
Rieger 2016 Austria	Cohort	>10	20 vs 7		Full thickness skingraft for reconstruction of the arm	Groin free flap for reconstruction of the arm	30/28	Complication
Rossi Neto 2012 Germany	Case series	>2		332	Vaginoplasty	-	36 (19-68)	Complication Reoperation
Selvaggi 2009 Belgium	Case series	>2	240		Scrotoplasty	-	24 (18-58)	Complication
Sigurjonsson 2015 Sweden	Case series	NR		205	Inversion penile vaginoplasty two stage	-	35 (18-76)	Complication
Smith 2005 The Netherlands	Case series	21(12-47)		67	Breast augmentation Vaginoplasty	-	31 (18-68)	Satisfaction
Spehr 2007 Germany	Case series	NR		500	Vaginoplasty	-	NR	Complication Reoperation
Spiegel 2011 USA	Case series	2-53		49	Forehead feminisation cranioplasty	-	31 (18-62)	Complication

Project: Gender dysphoria

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Follow-up (mean months)	Trans men (n)	Trans women (n)	Surgical intervention 1	Surgical intervention 2	Mean Age (years)	Outcome variables
Stojanovic 2017 Serbia	Case series	44	79		Metoidioplasty, hysterectomy + colpectomy	-	32	Complication Reoperation
Takamatsu 2009 Japan	Cohort	7 (3-96)	7 vs 36 +26		Metoidioplasty + Oophoro-hysterectomy + vaginal closure (n=7),	Metaidoplasty + Oophoro-hysterectomy (n=36)	(18-33)	Satisfaction
Tavakkoli Tabassi 2014 Iran	Case series	1		112	Vaginoplasty	-	26	Satisfaction Complication
Van de Grift 2017b ("Surgical satisfaction…")	Case series	NR	51	81	Mastectomy Hysterectomy Vaginoplasty		36 (17-63)	Satisfaction
Van de Grift 2017c ("A longitudinal…")	Cohort	31(13-99)	15 vs 6		Phalloplasty	Metoidioplasty	40	Quality of life Complication
Van Noort 1993 The Netherlands	Cohort	42 mo		16 vs 11	Penile + scrotal skin flap vaginoplasty (n=16)	Penile skin vaginoplasty (n=11)	24 (21-57)	Satisfaction Regret
Vukadinovic 2014 Serbia	Case series	30 (13-69)	97		Metoidioplasty	-	29 (18-41)	Satisfaction Complication
Wagner 2010 Germany	Case series	3		50	Vaginoplasty	-	39	Satisfaction Complication Reoperation
Weyers 2008 Belgium	Case series	NR	83		Hysterectomy + mastectomy (n=63)	Hysterectomy (n=20)	32 (18-50)	Complication Reoperation
Weyers 2006 Belgium	Cohort	NR	105		Vaginectomy + phalloplasty + total hysterectomy (n=69)	Vaginectomy + phalloplasty (n=36)	NR	Complication

Project: Gender dysphoria

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Follow-up (mean months)	Trans men (n)	Trans women (n)	Surgical intervention 1	Surgical intervention 2	Mean Age (years)	Outcome variables
Wierckx 2014 Belgium	Case series	Trans men (FtM) after hormonal therapy: 72 (3-588) Trans women (MtF) after hormonal therapy : 84 (3-420)	138	214	GAS (phalloplasty or vaginoplasty)	-	Trans men 37 Trans women 45	Satisfaction
Wierckx 2011 Belgium	Case series	96 (24-264)	49		Phalloplasty	-	30 (16-49)	Quality of life Satisfaction
Wirthmann 2017 Gemany	Case series	NR	229		Radial forearrn flap phalloplasty	-	33 (17-64)	Complication Reoperation
Wolter 2015 Germany	Case series	NR	173		Mastectomy		29 (18-54)	Satisfaction Complication Reoperation
Zielinski 1999 Poland	Case series	NR	127		Phalloplasty (lateral groin flap)	-	21-55	Complication

NR= not reported, GAS= Gender Affirmation Surgery, RFF= Radial Forearm Flap

Project: Gender dysphoria
Appendix 3 - Excluded articles

Author, year	Reason for exclusion
Bandini 2013	Wrong outcome (body uneasiness)
Bertolotto 2017	Not relevant focus
Bettocchi 2005	Compares one and two stages, but >30% were still waiting for second stage. Too few for case series.
Bjerrome Ahlin 2014	Too few cases
Bouman 2014	Gender dysphoria is one of several indications
Boza 2014	Not surgery in all patients
Cardenas-Camarena 2017	Too few cases (22 female – male)
Castellano 2015	Too few cases (46 vs 14)
De Cuypere 2005	Too few cases (32 vs 23)
De Cuypere 2006	Too few cases (35 vs 27)
Defreyne 2017	Review of non systematic character
Dhejne 2011	Type of surgery not specified
Djordjevic 2009	Double publication with Djordjevic 2013
Eldh 1997	Not specified by gender
Frederick 2017	Too few (40 and 48)
Hage 1995	Not specified per technique
Hage 1996	Not defined outcome
Hess 2016	Insufficient description of comparative method
Heylens 2014	No outcomes according to PICO
Hoebeke 2005	Too few (24FtM and 31 MtF)
Horbach 2015	Systematic review, not to be included
Imbimbo 2009	Outcome not presented in relation to technique
Jarolim 2000	Too few patients per technique
Kaariainen 2017	Too few patients per technique (29 vs 28)
Kanhai 1999	Double publication with Kanhai 2000
Kanhai 2001	Inadequate presentation of results
Krueger 2007	Inadequate presentation of results
Kuhn 2009	Surgery type not specified
Kuhn 2011	Surgery type not specified, Too few patients per technique
Lawrence 2005	Double publication,
Lindqvist 2017	Unclear intervention
Maycock 2014	Non-systematic review
Monstrey 2001	Different interventions not specified in results
Morrison 2016 “Facial Feminization”	Systematic review, not to be included
Morrison 2016 “Phalloplasty”	Systematic review, not to be included
Motmans 2012	Different interventions not specified in results
Neuville 2016	No data availible
Perovic 2005	Double publication

Project: Gender dysphoria

Appendix 3 - Excluded articles

Author, year	Reason for exclusion
Pfäfflin 1992	Interventions not presented separately
Remington 2018	Wrong patients (including also other diagnosis)
Riggs 2014	Different interventions, unclear follow-up, wrong outcomes
Schaff 2009	Patients <50 and complex surgical procedure?
Sehnal 2008	Three different techniques (n<50), unclear follow-up
Sigurjonsson 2016	Wrong follow-up (<1 year)
Simbar 2018	Unclear intervention
Simonsen 2016	Unclear intervention
Simonsen 2016	Unclear intervention
Testa 2017	Numbers per group not reported
Top 2017	Patients <50 per surgical procedure
Tsoi 1993	Wrong comparison
Van de Grift 2017a ("Effects…")	Outcomes not reported per procedure
Van de Grift 2017d (Surgical indications…)	Patients <50 per surgical procedure
van der Sluis 2016	Wrong intervention (secondary/correction surgery)
van der Sluis 2016	Wrong intervention (secondary/correction surgery)
Van Kesteren 1996	Outcomes not specified related to treatment
Wedler 2004	Wrong intervention (secondary/correction surgery)
Weyers 2009	Patients <50 per surgical procedure
Wolter 2017	Double publication

Project: Gender dysphoria
Appendix 4.1.1 Trans men (FtM)
Outcome variable: **Quality of life**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1	Intervention 2				
Mastectomy No studies								
Hysterectomy/oophorectomy No studies								
Genital surgery								
Barrett 1998 UK	Cohort	63	*Phalloplasty after surgery* n=31 SRPS Total 0.47 95% CI for difference -0.16; 0.25	*Phalloplasty accepted for surgery* n=23 SRPS Total 0.42	Social Role Performance Schedule (SRPS) Scale 0-3. 0 no problems coping 3could not cope at all	?	?-	-
Van de Grift 2017c The Netherlands	Case series (before/ after)	21	*Postoperative measurements* Phalloplasty with free radial forearm flap (FRFF) +/-anteriolateral thigh flap (n=15) and Metoidioplasty with/ without urethral lengthening (n=6) mean (SD) SWLS: 21.7 (7.1) ns SHS: 4.6 (1.5) ns CL: 6.6 (1.5) ns	*Preoperative measurements* mean (SD) SWLS: 22.0 (6.5) SHS: 4.8 (1.4) CL: 7.0 (1.5)	Satisfaction with life scale (SWLS), Score range 5-35 Subjective Happiness Scale (SHS) Score range 1-7 Cantril Ladder (CL) Visual scale, range 0-10 Highest value denotes highest QoL	+	-	-
Wierckx 2011 Belgium	Cross-sectional in original study design. Case series according to PICO	49	*Phalloplasty/ Metaidoioplasty* n= 46/1 Transmen n=47 / Men n=976 / Women n=976 Subscale: Transmen mean (SD) / Men mean (SD) / Women mean (SD) Physical functioning: 85.9 (15.0) / 85.4 (21.0) ns / 80.4 (24.2) p=0.015 Vitality: 62.1 (20.7) / 71.9 (18.3) p=0.002 / 64.3 (19.7) ns Mental Health: 72.6 (19.2) / 79.3 (16.4) p=0.02 / 73.7 (18.2) ns Patients with (n=43) or without prosthesis (n=14), did not score differently in one of the subscales.		SF 36 Subscales were compered to men and women of the general Dutch population. 3/8 scaled scores differed significantly. (Comparison not according to PICO)	+	?	-

Project: Gender dysphoria
Appendix 4.1.2 Trans men (FtM)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	**Intervention 2/ Control** n (%)				
Mastectomy								
Davis 2014 USA	Prospective cohort	208 genderqueer, genderfluid, FtM 5 Intersex patients were included	*Mastectomy and testosterone* n=70 24.7	*No mastectomy, only testosterone* n=45 30.6, p<0.001 *No mastectomy, no testosterone* (n=70 31.4, p<0.001	Body dissatisfaction 10 question Likert scale (0-100, 100 denotes maximal dissatisfaction)	+?	+?	+?
Antoszewski 2012 Poland	Cohort	98	*Peri-areolar mastectomy* n=74 Good 47 (63.5) Satisfactory 19 (25.6) Unsatisfactory 8 (10.8)	*Free nipple graft* n=24 Good 11 (45.8) Satisfactory 8 (33.3) Unsatisfactory 5 (20.9)	3 different peri-aerolar techniques questionnaire. Result postoperatively. No comparisons between groups.			
Wolter 2015 Germany	Cohort	173	*Peri-areolar mastectomy* n=132 Satisfaction Very good 65 (49.2) Good 51 (38.6) Less satisfied 15 (11.4) Not satisfied 1 (0.8) Nipple-areola sensitivity n=264 nipples Very good 110 (41.7) Good 102 (38.6) Moderate 48 (18.2) Not sensitive 4 (1.5)	*Free nipple graft* n=26 Satisfaction Very good 12 (46.1) Good 11 (42.3) Less satisfied 3 (11.5) Not satisfied -	Satisfaction Survey 3 different peri-aerolar techniques No comparisons between groups. Nipple-aerola sensitivity, subjectively rated per nipple. Free nipple graft implies per se no sensitivity in the nipple.			
Van de Grift 2017 b The Netherlands	Case series	51	*Mastectomy n=49* Selfreported satisfaction 34 (94%) Missing data 13 (27%)		Numbers do not add up to the same sum			

Project: Gender dysphoria
Appendix 4.1.2 Trans men (FtM)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2/ Control** n (%)				
Hysterectomy/oophorectomy								
Van der Grift 2017b The Netherlands	Case series	51	*Hysterectomy* *n= 48* Self-reported satisfaction 34 (97) Missing data 13 (27)		Numbers do not add up to the same sum			
Genital surgery								
Barrett 1998 UK	Cohort	63	*Phalloplasty* n=31 BSRI 51.0 Genital appearance: mean 3.84 Sexual function: mean 3.45 Urinary function: mean 2.29	*On waiting list for phalloplasty* n=23 BSRI 41.7 Δ 9.3 (95% CI 2.5; 16.0) mean 1.35 Δ 1.49 (1.87; 3.11) mean 3.00 Δ 0.45 (-0.38; 1.28) mean 1.5 Δ 0.79 (-0.12; 1.71)	Bem Sex Role Inventory (BSRI) Scale score 0-100 < 50 masculine >50 feminine Δ = difference Satisfaction Scale range 1-5	?	?-	-
Garcia 2014 USA (UK)	Cohort	25	*Phalloplasty* *Radial forearm flap (RFF)* n=15 Overall satisfaction (mean) *With* NA n=10: 8.7; *Without NA* n=5: 9.4 Ever achieved orgasm (n/n) *With* NA: Pre-op 7/10, Post-op 8/10; *Without NA*: Pre-op 4/5, Post-op 5/5	*Suprapubic pedicle flap phalloplasty* n=10 Overall satisfaction 9.6 Ever achieved orgasm (n/n) Pre-op 9/10 Post-op 10/10	Cutaneous nerve- clitoral nerve anastomosis (NA) Measured by Likert scale 1-10 (10 denotes highest satisfaction) No significance tests performed	?	?	-

Project: Gender dysphoria
Appendix 4.1.2 Trans men (FtM)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2/ Control n (%)				
Takamatsu 2009 Japan	Cohort	69	*Oophoro-hysterectomy+ metaidoioplasty with labial ring flap technique +/- vaginal closure (VC)* n=43 (7/36) Voiding standing VC + 5/7 (71%) p=0.34 VC- 24/36 (67%) p=0.10	*Oophoro-hysterectomy+ metaidoioplasty with Hages technique (no labial ring flap)* n=26 Voiding standing 11/26 (42%)	Observation of voiding No significance tests performed	-	-	-
Van de Grift 2017 c The Netherlands	Cohort	21	*Phalloplasty* *Radial forearm flap (RFF)* n=8 *RFF + Anteriolateral thigh flap* (ALTF) n= 5 ALTF n= 2 Total number = 15 mean (SD) IPSS 11.3 (8.3) Voiding Function 1.9 (1.4) Sexual function 1.3 (1.3)	*Metoidioplasty with urethral lengthening* n=2 *Metoidioplasty without urethral lengthening* n=4 Total number = 6 mean (SD) IPSS 13.0 (10.2) Voiding Function 2.0 (1.3) Sexual function 3.0 (0.9) p=0.009	International Prostate symptoms score (IPSS) assessing storage and voiding complaints, range 0-35 <7 mild symptoms >8 moderate symptoms >19 severe symptoms Specified questions on voiding and sexual function, scale 0-4, (0 dis-satisfied- 4 satisfied)	+	-	-
Djordevic 2013 Serbia	Case series	207 (Two case series 49+158)	*Metoidioplasty Utrethal lengthening with buccal mucosa* Completely satisfied - Somewhat satisfied Esthetic appearance 193 (93) 14 (7) Clitoral sensation 207 (100) No problems in sexual arousal, masturbation or orgasm		I: dorsal clitoral skin flap (n= 49) II: labia minora flap (n = 158) Postoperative questionnaire 1 = dissatisfied 2 = somewhat satisfied 3 = completely satisfied			
Falcone 2018 UK	Case series	247	*Penile Prosthesis implanted after Phalloplasty* n=104 Phallic sensation 86 (83) Able to operate the device 104 (100) Penetrative sex 80 (77) Achieved orgasm 86 (83) Satisfied with phallus 91 (88) Partner satisfaction 62.4 (60)		Specific non-validated questionnaire 7 items yes/no was answered by 104 pat. Radial fore arm flap (n=157) Suprapubic flap (n=90)			

Project: Gender dysphoria
Appendix 4.1.2 Trans men (FtM)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	**Intervention 2/ Control** n (%)				
Garaffa 2010 United Kingdom	Case series	115	*Phalloplasty, Radial forearm flap (RFF)* Satisfaction n (%) Cosmetic and size of phallus 112 (97.5) Sensation of phallus Complete 82 (71.5) Partial 17 (14.7) None 6 (5.2) Surgery stage 2 n= 84 Voiding standing n (%) 83 (99)		Retrospective review of patient records and telephone interview Phallus loss in 3 pat, Recent surgery/ no evaluation 6 pat Surgery in 3 stages			
Leriche 2007	Case series	56	*Phalloplasty, Radial forearm flap (RFF)* n=55 Overall body satisfaction 51 (93) Cosmetic aspects 50 (90) Cutaneous sensitivity 46 (83) Erogenous sensitivity 5 (9) Sexual satisfaction* n= 35 18 (51)		Specific questionnaire for follow up One patient died, 2 did not answer but were included in analysis 3 flaps were lost *Only patients with functional penile implant			
Vucadinovic 2014 Serbia	Case series	97	*Metoidioplasty* Satisfied with n (%) Completely Partially Dissatisfied Appearance of genitalia 81 (83.5) 12 (12.3) 4 (4.1) Quality of erection 91 (93.8) 6 (6.2) - Erogenous sensation 97 (100) - - Voiding while standing 97 (100) - - Satisfied - Neutral - Unsatisfied Overall sexual satisfaction 85 (87.6) 7 (7.2) 5 (5.15) Sexual arousal often n (%) 97 (100) Frequency masturbation (very) often 83 (85.6) sometimes 14 (14.4) Orgasm during masturbation (almost) always 68 (70.1) sometimes 29 (29,.)		Single stage metoidioplasty Structured postoperative interview Based on BVT Biographical Questionnaire for Transsexuals and Transvestites (Verschoor & Poortinga, 1988)			

Project: Gender dysphoria
Appendix 4.1.2 Trans men (FtM)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2/ Control** n (%)				
Wierckx 2011 Belgium	Case series	49	*Phalloplasty* n=46 Satisfaction with surgical results (%) / Phalloplasty n=46 / Erection Prosthesis n=32 Very unsatisfied 0.0 3.6 Unsatisfied 2.2 14.3 Neutral 8.9 14.3 Satisfied 31.1 46.4 Very satisfied 57.8 21.4 Complications after phalloplasty, or prosthesis or not, did not affect parameters of sexual outcome (frequency of sexual activity, masturbation, aroused easily or orgasm).					
Wierckx 2014 Belgium	Case series	138	*Phalloplasty (non specified)* Transmen who were less satisfied with their phalloplasty had higher HSDD (p=0.02) Otherwise experiences of complications, or prosthesis or not, did not affect frequency of sexual desire.		HSDD=hypo sexual desire disorder (distress based on low desire)			

Project: Gender dysphoria
Appendix 4.1.3 Trans men (FtM)
Outcome variable: **Regret, retransition**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1	Intervention 2				
Mastectomy No studies								
Hysterectomy/oophorectomy								
Rachlin 2010 USA	Case series	134 3 intersex patients included	*Hysterectomi (HE)/ Salpingo-Oophorectomi (SOE)* n= 129 HE+SOE (n=118), HE only (n= 7), SOE only (n= 2) Regrets 0/129 Comments 7/129		Survey via e-mail or website Website for transpeople Comments added; No option to have children, loss of sexual sensation, wish of a different procedure, another surgeon.			
Genital surgery								
Garcia 2014 USA UK	Cohort	25	*Phalloplasty Radial forearm-flap (RFF)* n=15 With NA Without NA 0/10 0/5	*Suprapubic pedicle flap phalloplasty (SP)* n=10 0/10	NA= cutaneous nerve-clitoral nerve anastomosis No significance test performed	?	?	-

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Mastectomy								
Berry 2012 UK	Cohort	92	<u>*Periareolar incision, standard or extended*</u>, n=11 Hematoma 1 (9)	<u>*Free nipple graft*</u>, *n=79* Hematoma 5 (6.3) Infection 3 (3.8) Nipple areola complex loss 2 (2.5)		+	-	-
McEvenue 2017 Canada	Cohort	679	<u>*Periareolar incision*</u> n=104 Total complications: 34 (32.7) p<0.001 Major(includes intervention) : Hematoma 2 (1.9) p=0.680 Nipple necrosis 0 (0) Minor: Seroma 19 (18.3) p<0.001 Hematoma 11 (10.6) p<0.01 Infection 5 (4.8) p=0.568 Hypertrophic scar 2 (1.9) p=0.753 Partial nipple necrosis 0 (0.0) p=1 Dehiscence 0 (0.0) p=1	<u>*Free nipple graft*</u> n=575 Total complications: 89 (15.5) Major (includes intervention) : Hematoma 9 (1.6) Nipple necrosis 0 (0) Minor: Seroma 25 (4.3) Hematoma 22 (3.8) Infection 20 (3.5) Hypertrophic scar 17 (3.0) Partial nipple necrosis 3 (0.5) Dehiscence 3 (0.5)	Surgical techniques based on patient characteristics	+	-	?
Bluebond Lagner 2017 USA	Cohort	295	<u>*Circumareolar incision*</u> n=109 Total complications 23 (21.1) p=0.35 Major: Infection 1 (0.9) p=0.43 Seroma 6 (5.5) p= 0.79 Hematoma 10 (9.2) p=0.24 Minor: Nipple necrosis 5 (4.6) p=0.24	<u>*Free nipple graft*</u> n=186 Total complications 30 (16.1) Major: Infection 4 (2.2) Seroma 9 (4.8) Hematoma 10 (5.4) Minor: Nipple necrosis 4 (2.2)	Surgical techniques based on patient characteristics	+	-	?

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Knox 2017 Korea	Cohort	101	<u>*Concentric circular mastectomy*</u> *n=46* **Minor complication** Infection 6 (6.5) Mastectomy flap necrosis 0 (0) NAC necrosis 3 (3.3) Hematoma 6 (6.5) Wound dehiscence 12 (13.0) **Major complication** Infection 1 (1.1) Mastectomy flap necrosis 0 (0) NAC necrosis 8 (8.7) Hematoma 2 (2.2) Wound dehiscence 6 (6.5)	<u>*Free nipple graft*</u> *n=55* **Minor complication** Infection 4 (3.6) Mastectomy flap necrosis 1 (0.9) NAC necrosis 0 (0) Hematoma 4 (3.6) Wound dehiscence 3 (2.7) **Major complication** Infection 0 (0) Mastectomy flap necrosis 0 (0) NAC necrosis 1 (0.9) Hematoma 0 (0) Wound dehiscence 0 (0)		+	-	-
Donato 2017 USA	Cohort	130	<u>*Periareolar incision*</u> n=20 Major: 3 (15) Minor: 4 (20)	<u>*Free nipple graft*</u> n=110 8 (7) 17 (15)	Surgical techniques based on patient characteristics	+	-	-
Rieger 2016 Austria	Cohort	20 vs 7	<u>*Full thickness skingraft for reconstruction of the arm*</u>, *n=20* Additional skin needed 0 Revised complications at the forearm 2 Revised complications at the groin 1	<u>*Groin free flap for reconstruction of the arm*</u>, *n=7* Additional skin needed 6 Revised complications at the forearm 1 Revised complications at the groin 0		+	-	-
Monstrey 2008 Belgium	Case series	70	<u>*Concentric circular mastectomy*</u> Major: 1 (1.4) (major hematoma) Minor: 2 (2.8) (hematoma: 1 and partial NAC loss: 2)		NAC=Nipple areolar complex			
Wolter 2015 Germany	Case series	81	<u>*Inferior pedicled mammoplasty*</u> Major: Full NAC necrosis 2 Hematoma with revision 17 Minor: Partial NAC necrosis 2					

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Hysterectomy/oophorectomy								
Rachlin 2010 USA	Case series	134	<u>*Hysterectomy and oophorectomy*</u> One complication post op in 118/134 (89) Post surgical bleeding 3% Bladder/Urinary problems 25% Increased urinary frequency 14% Chronic pain during urination 5% Keloid scarring 10 % Infection 8% Adhesion 6%					
Weyers 2008 Belgium	Case series	83	<u>*Laparoscopic hysterectomy*</u> Major : 3/83 (3.6) 2 bladder perforations, 1 hematoma requiring drainage and revision Minor: 3/83 (3.6)					
Genital surgery (phalloplasty, metoidioplasty, scrotoplasty, penile prosthesis)								
Ascha 2018 USA	Cohort	149 vs 64	<u>*Anterolateral thigh pedicle flap phalloplasty + full length urethroplasty + vaginectomy*</u> n=64 Total complications: 28 (43.8) p=0.09 Urethral complications: 21 (32.8) p=0.19 Meatal stenosis 3 (4.7) p=0.25 Urethral stricture 14 (21.9) p=0.16 Urethral fistula 14 (21.9) p=0.02 Other complications: 15 (23.4) p=0.03 Rectal injury 0 Partial loss 5 (7.8) p=0.17 Hematoma 2 (3.1) p=0.86 Dehiscence 6 (9.4) p=0.03 Abscess 3 (4.7) p=0.64 No sensation 1 (1.6) p=0.90	<u>*Radial forearm flap (RFF)phalloplasty + full length urethroplasty + vaginectomy*</u> n=149 Total complications 47 (31.5) Urethral complications : 36 (24.2) Meatal stenosis 14 (9.4) Urethral stricture 21 (14.1) Urethral fistula 15 (10.1) Other complications : 17 (11.4) Rectal injury 1 (0.7) Partial loss 5 (3.4) Hematoma 4 (2.7) Dehiscence 3 (2.0) Abscess 5 (3.4) No sensation 2 (1.3)	The main drivers for choice of procedure were BMI, patients' goals and desire to avoid donor site morbidity.	+	-	-

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Fang 1994 Republic of China	Cohort	56	*RFF phalloplasty + neourethra ("tube in tube")* n=28 (first series) Flap necrosis 7 Fistula 22 Stricture 4 Urethrolithiasis 1 Hair growth 3 Infection 4 40/56 could stand voiding, had tactile sensation	*RFF phalloplasty + neourethra with tubed vaginal mucosa graft* n=28 (second series) Flap necrosis 0 Fistula 16 Stricture 3 Urethrolithiasis 1 Hair growth 1 Infection 3	Groups based on different procedures in different time periods	?		
Kim 2010 South Korea	Retro-spective cohort	70	*RFF phalloplasty + urethroplasty;* n=38 Fistula 14 (36.8%)	*RFF phalloplasty +Modified urethroplasty,* labium minoral flap and the smaller U-shaped flap from the anterior wall of the vagina for the cylindrical shaped urethra, *with vaginal flap* n=32 Fistula 7 (21.9%)		+	-	-

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Massie 2017 USA	Retro-spective cohort	224	*Phalloplasty+vaginectomy* n=215 All complications 76 (35) Urethral complications 58 (27) Meatal stenosis 17 (8) Urethral stricture 36 (17) Urethral fistula 30 (14) Other complications 32 (15) Rectal injury 1 (0.5) Partial loss 10 (5) Hematoma 6 (3) Dehiscence 9 (4) Abscess 8 (4) No sensation 2 (1) Scrotal complication 1 (0.5) *Anterolateral thigh + vaginectomy* n=64 All complications 28 (44) Urethral complications 21 (33) Other complications 15 (23) *RFF phalloplasty + vaginectomy* n=149 All complications 47 (32) Urethral complications 36 (24) Other complications 17 (11)	*Phalloplasty only* n=9 All complications 6 (67) Urethral complications 6 (67) Meatal stenosis 2 (22 Urethral stricture 4 (44) Urethral fistula 5 (56) Other complications 0 (0) Rectal injury 0 (0) Partial loss 0 (0) Hematoma 0 (0) Dehiscence 0 (0) Abscess 0 (0) No sensation 0 (0) Scrotal complication 0 (0) *Anterolateral thigh flap only* n=3 All complications 1 (33) Urethral complications 1 (33) Other complications 0 (0) *RFF phalloplasty only* n=6 All complications 5 (83) Urethral complications 5 (83) Other complications 0 (0)		+	-	-

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Weyers 2006 Belgium	Cohort	105	*Vaginectomy + phalloplasty + total hysterectomy, n=69* Serious complications 4 (5.8) Reintervention (any reason) 9 (13) Transfusion needed 24 (34.7) Textiloma perineal 2 (2.9) Hematoma 8 (11.6) Reintervention for perineal hematoma 3 (4.3) Urinary infection 3 (4.3) Urinary stenosis (10 (14.5) Total patients with fistula 28 (40.6) Urinary fistula temporary 18 (26.1) Urinary fistula permanent 15 (21.7) Inguinal opening 2 (2.9) Suprapubic skin necrosis 1 (1.4)	*Vaginectomy + phalloplasty, n=36* Serious complications 0 (0) Reintervention (any reason) 5 (13.8) Transfusion needed 6 (16.7) Textiloma perineal 0 (0) Hematoma 3 (8.3) Reintervention for perineal hematoma 3 (8.3) Urinary infection 3 (8.3) Urinary stenosis (4 (11.1) Total patients with fistula 13 (36.1) Urinary fistula temporary 8 (22.2) Urinary fistula permanent 7 (19.4) Inguinal opening 1 (2.8) Suprapubic skin necrosis 0 (0)				
Leriche 2008 France	Case series	56	*RFF phalloplasty* Total complications 14 (25) Flap loss 3 Cephalic vein thrombosis 1 Arterial ischaemia 1 Infection 5 Distal limited necrosis 2 Haematoma 2 Total Prosthesis and urethra complications 29 (55) Urinary fistula requiring perineal urethrostomy 7 Urinary fistula with conservative treatment 8 Urinary retention 3 Prosthesis change 8 Prosthesis explantation 3					

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Monstrey 2005 Belgium	Case series	81	<u>*RFF phalloplasty*</u> Partial Flap failure 2 (2.4%) Total Flap failure 1 (1.2%) Pulmonary embolism 2 (2.4%) Anastomotic re-exploration 16 (19%) Partial skin graft failure 2 (2.4%) Wound healing problems at the recipient site 18 (22%) Nerve compression 2 (2.4%) Urinary complications (total) 34 (42%) Fistulas 17 (21%) Strictures 26 (32%)					
Wirthmann 2017 Germany	Case series	229	<u>*RFF phalloplasty*</u> Hematoma in groin area 33 (14.2) Vascular insufficiency 26 (11.2) (Arterial 13, venous 5, arterial + venous 5) Delayed wound healing 39 (16.8) Total flap failure 7/232 (3) Partial flap necrosis 2 (0.9) Revision surgery Urethral fistulas and strictures 387 (mean 1.3 revision/patient) Persisting urethral fistulas 4 (1.7)					

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Doornaert 2011 Belgium	Case series	306	*RFF phalloplasty* **Flaprelated complications:** Anastomotic revision 36 (11.3) Complete flaploss 3(0.9) Marginal partial necrosis 23 **Urological complications:** Fistula, no reop 53 (16.7) Stricture, no reop 20 (6) Fistula/stricture reop 54 (17) Erectile prosthesis (n=143) complications 59 (41) **Various complications:** Minor pulmonary embolism 3 (0.9) Regrafting defect arm 9 (2.8) Nerve compression 2 (0.6) Delayed wound healing 33 (10.4)					
Garaffa 2010 UK	Case series	115	*RFF phalloplasty* Stage 1,2,3 with 3 months interval **Complications stage 1:** Acute arterial thrombosis 2 Acute venous thrombosis 3 Phallus loss 3 (2.6) Partial skin necrosis 12 (10.4) Infection 5 (4.3) Contracture 4 (3.4) Meatal stenosis w/wo fistulas 9 (7.8) Compartment syndrome hand 1 **Complication stage 2:** Hematoma 2 (2.4) Strictures 9 (10.7) Fistula 20 (23.8)					

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Zielinski 1999 Poland	Case series	127	*Phalloplasty with lateral groin flap* n=127 Oedema and venous congestion 14 (11) Hematoma 4 (3.1) Infection 7 (5.5) Lymforrhagia 4 (3.1)					
Djordjevic 2013 Serbia	Cohort	207	*Metoidioplasty BM+clitoral skin flap* n=49 Voiding standing 88%, p <0.05 Neophallus 5.2 cm (4-9.2) Minor complication 17 (34.7), p>0.05 Fistula 7 (14.3) p<0.05 Stricture 3	*Metoidioplasty BM+labial skin flap* n=158 Voiding stand 93% Neophallus 5.8 cm (4.7-10) Minor comp 42 (26.6) Fistula 9 (5.69) Stricture 3	BM= buccal mucosa Minor complication =no reop required			
Stojanovic 2017 Serbia	Case series	79	*Metoidioplasty* **Hysterectomy+colpectomy** 11 (14): Abdominal conversion 2 Perineal cyst (vaginal mucosa) 9 **Mastectomy** 6 (7.6): Breast hematoma 1 Nipple graft necrosis 3 Hypertrophied scars 2 **Metoidioplasty** 11 (14): Urethral fistula 4 Urethral stricture 3 Urethral diverticulum 1 Testicular implant rejection or displacement 3 Blood transfusion 1 (1.2)		Complications reviewed only for patients undergoing metoidioplasty+GAS one stage procedure			

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Hage 2006 The Netherlands	Cohort	70	<u>*Metoidoioplasty*</u> n=23 Fistula 9 Stricture 9 Loss testicular implant 11	<u>*Metoidoioplasty+scrotoplasty*</u> n=47 Fistula 17 Stricture 16 Loss testicular implant 14				
Vukadinovic 2014 Serbia	Case series	97	<u>*Metoidioplasty*</u> n=97 Dribbling and spraying during voiding 17 (17.5) Urethral strictures 2 (2) Fistula 6 (6.2) Testicular displacement 2 (2.1%)					
Van de Grift 2017c The Netherlands	Cohort	21	<u>*Phalloplasty, all types*</u> n=15 <u>Urinary complications</u> Urethral stricture 12 (80) Fistula 5 (33.3) Recurrent urinary tract infection 4 (26.7) Spraying 2 (13.3) <u>Flap complications</u> Dehiscence 9 (60) Partial necrosis 5 (33.3) <u>Donor site complications</u> Partial necrosis 4 (26.7) Edema 2 (13.3) Pain 1 (6.7)	<u>*Metoidioplasty*</u> n=6 <u>Urinary complications</u> Urethral stricture 2 (33.3) Fistula 0 Recurrent urinary tract infection 0 Spraying 0 <u>Flap complications</u> Dehiscence 5 (83.3) Partial necrosis 1 (16.7) <u>Donor site complications</u> (No donor site with this procedure)		+	-	-
Selvaggi 2009 Belgium	Case series	240	<u>*Scrotoplasty*</u> Hematoma 1 (0.41) Wound dehiscence 11 (4.58)					

Project: Gender dysphoria
Appendix 4.1.4 Trans men (FtM)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Falcone 2018 Italy	Case series	247	<u>*RFF phalloplasty*</u> n=157 + <u>*infra umbilical pubic flap phalloplasty*</u> n=90 Infection 21(8.5) Mechanical failure 38 (15.4		Single cylinder n=208 Two cylinder n=39 n=140 (56.6%) had original implant in place, 20 months M FU =mean follow-up			
Hoebecke 2010 Belgium	Case Series	129	<u>*Penile prosthesis insertion*</u> Infection 22 (11.9) Protrusion 15 (8.1) Leak 17 (9.2) Dysfunction 24 (13.0) Malposition 27 (14.6)					

Project: Gender dysphoria
Appendix 4.1.5 Trans men (FtM)
Outcome variable: **Re-operation**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Mastectomy								
Cregten-Escobar 2012 The Netherlands	Cohort	202	<u>*Mastectomy Without skin resection*</u> n=19 Reop corrections: Nipple and areolar: PAR 18.6% vs ISR-FNG 3.3%, p <0.05 Scar revision: ISR-PN 20.0% vs ISR-FNG 8.0%, p<0.05 Chest contouring: PSR 54.7% vs ISR-FNG 23.3%, p<0.05 ISR-PN 50% vs ISR-FNG 23.3%, p<0.05	<u>*Periareolar skin resection (PAR)*</u> n=43 Acute tot nr reop per breast: PAR 0.44 vs. ISR-FNG 0.26, p <0.05 <u>*Inframammary skin resections (ISR)*</u> n=140 Mastectomy ISR : pedicled nipple graft (PNG) (n=130) Free nipple graft (FNG) (n=150) reop lower in FNG akute reop due to hematoma (21% in surgery without skin resection compared to 9% overall)		+	-	?
McEvenue 2017 Canada	Cohort	679	<u>*Circumareolar incision*</u> 15/104 (14.4) Contour revision 1 (1.0) Nipple revision/reduction 12 (11.5) Hematoma 2 (1.9) Scar revision 0 (0.0)	<u>*Free nipple graft*</u> 61/575 (10.6) Contour revision 42 (7.3) p<0.008 Nipple revision/reduction 5 (0.9) p<0.001 Hematoma 9 (1.6) p=0.679 Scar revision 10 (1.7) p=0.374		+	-	+
Bluebond Lagner 2017 USA	Cohort	109 vs 186	<u>*Circumareolar incision*</u> Per patient 33/109 (30.2) No. of revisions 71 Direct excision 17 (23.9) p=0.019 Liposuction 11 (15.5) p=0.661 Scar revision 2 (2.8) p=0.155 Conversion 1 (1.4) p=0.234 NAC revision 13 (18.3) p=0.188	<u>*Free nipple graft*</u> Per patient 34/186 (18.2) No. of revisions 100 Direct excision 10 (10.0) p=0.019 Liposuction 13 (13.0) p=0.661 Scar revision 8 (8.0) p=0.155 Conversion 0 (0.0) p=0.234 NAC revision 11 (11.0) p=0.188		+	-	?

Project: Gender dysphoria
Appendix 4.1.5 Trans men (FtM)
Outcome variable: **Re-operation**

* + No or minor problems
? Some problems
- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Knox 2017 Korea	Cohort	101	<u>*Concentric circular mastectomy n=46*</u> Scar revision 2 (2.2) Contour correction 23 (25) NAC revision 32 (34.8)	<u>*Free nipple graft N=55*</u> Scar revision 9 (8.2) Contour revision 9 (8.2) NAC revision 1 (0.9)		+	-	-
Berry 2012 UK	Case series	92	<u>Periareolar incision, standard or extended,</u> n=11 <u>*Free nipple graft, n=79*</u> Axillary dog-ear 10 (10.9) Nipple shave 2 (2.2) Liposuction 1 (1.1) Scar revision 1 (1.1) Flap thinning/contour 2 (2.2)		The reopereations are not defined per each group of intervention			
Monstrey 2008 Belgium	Case series	70	<u>*Concentric circular mastectomy*</u> 20/70 (28.6) *2nd operation (1st reoperation)* liposuction 10 scar revision 14 skin resection 8 nipple reduction 4 areola reshaping 4 fat grafting 1 tattoo 1 *3rd operation (2nd reoperation)* liposuction 2 scar revision 3					
Wolter 2015 Germany	Case series	81	<u>*Inferior pedicled mammoplasty*</u> Secondary revision: Scar revision 4 Contour revision 13 NAC revision 2					

Project: Gender dysphoria
Appendix 4.1.5 Trans men (FtM)
Outcome variable: **Re-operation**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Hysterectomy/oophorectomy								
Weyers 2008 Belgium	Case series	83	*Hysterectomy* 1/83 (1.2) Revision of hematoma					
Genital surgery								
Fang 2018	Cohort	56	*RFF phalloplasty* First cases 28 with "tube-in-tube Complications for reop: Flap necrosis 7 Fistula 22 Stricture 4	*RFF phalloplasty* The later cases 28 neouretra with tubed vaginal mucosal graft Flap necrosis 0 Fistula 16 Stricture 3		+	-	-
Garaffa 2010 UK	Case series	115	*RFF phalloplasty* Acute arterial thrombosis 2 (1.7), Pale/cold phallus reop Acute venous thrombosis 3 (2.6), Phallus removed reop Partial skin necrosis 12 (10.4), 3 patient reop Meatal stenosis w/wo fistulas 9 (7.8), reop with buccal mucosal graft Strictures 9 (10.7%), one/two stage reop with buccal mucosal graft					
Doornaert 2011 Belgium	Case series	306	*RFF phalloplasty* Flaprelated compl: Anastomotic Revision 36 (11.3) Fistula/stricture reop 54 (17) Erectile prosthesis n143, 59 (41) Regrafting defect arm 9 (2.8)					
Wirthman 2017 Germany	Case series	229	*RFF phalloplasty* Revision for delayed wound healing 32 (13.8) Revision for urethral fistulas and strictures 387 (mean 1.3 revision/patient) Persisting fistula 4 (1.7), after up to 6 reop (2-6) and >20 years					

Project: Gender dysphoria
Appendix 4.1.5 Trans men (FtM)
Outcome variable: **Re-operation**

* + No or minor problems
? Some problems
- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Hage 2006 The Netherlands	Cohort	70	*Metoidioplasty* n=23 Fistula 9 Strictures 9 Loss testicular implants 11, reop 10	*Metoidioplasty+scrotoplasty* n=47 Fistula 23, reop local skin flap Strictures 16, 2w-4.8 yr, 16 reop Loss testicular implants 14, reop 21		+	-	-
Stojanovic 2017 Serbia	Case series	473	*Metoidioplasty+GAS, n=79* Reoperations caused by complications 18/79 (22.8) Hysterectomy+colpectomy 9 (11.3) Perineal cyst (vaginal mucosa) 9 Mastectomy 1 (1.2) Breast hematoma 1 Metoidioplasty 8 (10.1) Urethral fistula 2 Urethral stricture 2 Urethral diverticulum 1 Testicular implant rejection or displacement 3		Original cohort study, re-op reported for one group only.			
Hoebecke 2010 Belgium	Case Series	129	*Penile prosthesis insertion* Replacement of prosthesis due to complication 41 (32) 9 needed a second revision 5 needed a third revision 1 patient needed a fourth revision					

RFF= Radial forearm flap, GAS= Genital affirmation surgery

Project: Gender dysphoria
Appendix 4.2.1 Trans women (MtF)
Outcome variable: **Quality of life**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results: Intervention n (%) or mean (SD)	Results: Control n (%) or mean (SD)	Comments	Directness *	Study limitations *	Precision *
Facial feminisation surgery (FFS)								
Ainsworth 2010 USA	Cross-sectional	247	Mean (SD) FFS (n=28) 50 (8.9) FFS+ GRS (n=47) 49.2 (7.5)	Mean (SD) No surgery (n=147) 39.5 (7.3) p<0.05	SF 36 version 2 Mental component summary Quality of Life 0-100 In general population; mean 48.9 (SD 10)	+?	-	?
Breast augmentation No studies								
Genital surgery								
Ainsworth 2010 USA	Cross-sectional	247	Mean (SD) GS (n=25) 49.3 (9.5) FFS+ GS (n=47) 49.2 (7.5)	Mean (SD) No surgery (n=147) 39.5 (7.3) p<0.05	SF 36 version 2 Quality of Life Mental component summary 0-100 In general population; mean 48.9 (SD 10)	+?	-	?
Lawrence 2003 USA	Case series	232	*Vaginoplasty with penile skin inversion and sensate clitoroplasty* Improved QoL Mean 7.9 (SD 2.6) range -2; 10 Improved QoL LS n (%) 10 97 (42) >8 137 (59) 0 to -10 8 (3)		Postop mailed questionnaire Improved Quality of life related to GS, Likert scale (-10, most worsening possible, 10 most improvement possible)			
Lawrence 2006 USA	Case series	232	*Vaginoplasty with penile skin inversion and sensate clitoroplasty* Improvement in QoL *Additional surgery* compared with no additional surgery Any additional surgical procedure (n=189) ns Labioplasty (n=179) ns p=0.08 *Complications* Pain in vagina or genitals present absent 6.6 (3.0) 8.0 (2.5) p<0.05		Postoperatively mailed questionnaire on SRS Likert scale (-10, most worsening possible to 10, most improvement possible) QoL was significantly related to 1/7 complications registered			

GS= Genital Surgery

Project: Gender dysphoria
Appendix 4.2.2 Trans women (MtF)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results: Intervention 1 n (%)	Results: Intervention 2 n (%)	Comments	Directness *	Study limitations *	Precision *
Facial feminisation surgery								
Ainsworth 2010 USA	Cross-sectional study	247	*Facial feminisation surgery (FFS)* n= 75 Mean (SD) 76 (17.7) *p< 0.01*	*No FFS* n=172 44.3 (15.7)	FFS outcome evaluation score (0-100). Satisfaction in physical, emotional and social domains after plastic surgery	+?	-	?
Bellinga 2016 Spain	Case series	200	*Rhinoplasty + forehead reconstruction n=150* *Rhinoplasty+lip-lift n=24* *Rhinoplasty+forehead reconstruction+lip-lift n=21* *Rhinoplasty only n=5* Level of femininity (%) 1 2 3 4 5 preop/ 13 63 20 4 0 postop 0 0 30 46 24 Aesthetic improvement/satisfaction (%) postop 2 4 22 46 26		Nose Feminisation Scale (NFS); level of femininity 1–5 (very masculine-very feminine) Aesthetic improvement/satisfaction 1-5 (nose is worse- result exceptional)	+?	-	-
Capitán 2014 Spain	Case series	172	*Frontonasal-orbital recontouring procedures +osteotomy of the anterior wall of the frontal sinus* Satisfaction Index 1 2 3 4 5 n (%) 0 (0) 1 (0.6) 14 (8.1) 45 (26.2) 112 (65.1)		Satisfaction index 1-5 (completely dissatisfied-completely satisfied) No measurements preoperatively	-	-	-
Breast augmentation								
Kanhai 2000 The Netherlands	Case series	107	*Mammaplasty- augmentation (performed simultaneously with vaginoplasty in 85 patients)* Further op Satisfied with surgery 80 (75) 12/80 (15%) Unhappy with surgery 27 (25) 5/27 (19%)		Anonymous posted questionnaire Reasons for dissatisfaction: Breasts too big, breasts too small, pain.			
Smith 2005 The Netherlands	Case series	52	*Mammaplasty- augmentation* Satisfied 34 (65.4) Not completely satisfied 15 (28.8) Dissatisfied 3 (5.8)		Postoperative questionnaire and questions on satisfaction with the result			
Van der Grift 2017b The Netherlands	Case series	81	*Mammaplasty -augmentation* n=33 Missing data Selfreported satisfaction Mammoplasty 7 (21) 25 (96)					

Project: Gender dysphoria
Appendix 4.2.2 Trans women (MtF)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	**Intervention 2** n (%)				
Genital surgery								
Buncamper 2017 The Netherlands	Cohort	100	*Penile inversion vaginoplasty without full- thickness skingraft* (FTG-) n= 68 Follow up >1 year n=28 Aesthetic outcome Mean (SD) Patients (n=26) 7.9 (1.4) Surgeons (n=20) 7.7 (0.8) ns FSFI total score (n=41) Patients all 17.2 (7.9) Patients sex active (n=32) 20.4 (6.0) p=0.13 FGSIS total Patient 21.9 (5.1) p=0.75 Overall satisfaction and Functional outcome (n=32) Completely satisfied 20 (63%) Partially satisfied 9 (28%) Dissatisfied 3 (9%) p=0.59	*Penile inversion vaginoplasty with full- thickness skingraft* (FTG+) n= 32 Follow up >1 year n=15 Aesthetic outcome Mean (SD) Patients (n=12) 8.6 (1.3) Surgeons (n= 9) 7.6 (0.9) FSFI total score (n=17) Patients 16.3 (11.1) Patients sex active (n=10) 23.9 (7.5) FGSIS total Patient 21.4 (5.7) Overall satisfaction and Functional outcome (n=13) Completely satisfied 6 (46%) Partially satisfied 5 (38%) Dissatisfied 2 (15%)	Aesthetic outcome scale 1-10 Patient/ surgeon FTG-/ FTG+ Female Sexual Function Index (FSFI) Six domains, total score max 36, Sexual dysfunction <=26.55 in biological women Female genital Self- Image Scale (FGSIS) Seven questions, total score 7-28 Higher score more positive Overall satisfaction and Functional outcome	+	?	?
Van Noort 1993 The Netherlands	Cohort	27	*Penile +scrotal skin flap vaginoplasty (PSSFV)* n=16 Satisfied/very satisfied Cosmetic result 8 (62) Vaginal width 10 (77) Vaginal depth 8 (62) Sexual intercourse 10 (77) Orgasm 11 (85)	*Penile skin flap vaginoplasty (PSFV)* n= 11 Satisfied/very satisfied Cosmetic result 9 (100) Vaginal width 4 (44) Vaginal depth 4 (44) Sexual intercourse 6 (67) Orgasm 7 (78) p>0.05	Standardised interviews PSFV (n=9/11) PSSFV (n=13/16), Physical investigations PSFV n=8/11 PSSFV n= 8/16	+	-	-

Project: Gender dysphoria
Appendix 4.2.2 Trans women (MtF)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Hess 2014 Germany	Case series	119	*Penile inversion vaginoplasty* n=102 Overall satisfied with life Score 1- 3 7 (6.9) 4- 7 39 (38.2) 8-10 56 (54.9) Aesthetic outcome of surgery n= 94 Very satisfied 36 (38.3) Satisfied 34 (36.2) Mostly satisfied 21 (22.3) Dissatisfied 2 (2.1) Very dissatisfied 1 (1.1) Functional outcome of surgery n=93 Very satisfied 32 (34.4) Satisfied 35 (37.1) Mostly satisfied 18 (19.4) Dissatisfied 6 (6.5) Very dissatisfied 2 (2.2) Able to achieve orgasm n=75 Easily 19 (20.9) Usually easily 39 (42.9) Rarely easily 17 (18.7)		LS=Likert scale 1-10 (very dissatisfied- very satisfied) Overall satisfied			
Kanhai 2016 The Netherlands	Case series	50	*Penile inversion vaginoplasty with neo-clitoroplasty in combination with a sensate vagina pedicled-spot-plasty* Sexual sensibility 15 weeks after surgery In clitoris 41 (82) In the sensate pedicled-spot 31 (62)					

Project: Gender dysphoria
Appendix 4.2.2 Trans women (MtF)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Lawrence 2003 USA	Case series	232	*Penile- inversion vaginoplasty and sensate clitoroplasty* Overall Happiness with GAS result: mean 8.7 (1.6) range 0-10 Happiness with Result n % Likert scale 10 95 41 >8 199 86 <= 5 20 9 Predictor variable pre/ postop Happiness with Result Number of significant surgical complications -0.37 p<0.0001 Functional Index 0.49 p<0.0001		Postoperatively mailed questionnaires Likert scale 0-10 (very unhappy-very happy) Functional Index Each of 19 physical and functional outcome variables (vaginal size, genital touch and erotic sensation, pain, urine leakage etc) was rated by Likert scale (0-10). FI= Mean of numerical responses Spearman rank-order correlations between post-operative predictor variables and Happiness with GAS			

Project: Gender dysphoria
Appendix 4.2.2 Trans women (MtF)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Lawrence 2006 USA	Case series	232	*Penile- inversion vaginoplasty and sensate clitoroplasty* Mean (SD) range Overall happiness with genital sexual function 7.8 (2.4) 0-10 Overall happiness with genital surgery result 8.7 (1.6) 0-10 Additional surgery and association with Happiness with sexual function GAS result Any additional surgical procedure (n=189) ns ns Labioplasty (n=179) ns ns Complications Mean (SD) Mean (SD) Vaginal stenosis present at all times 5.9 (3.2) 6.8 (3.1) absent " " " 8.0 (2.2) p< 0.001 8.9 (1.3) p<0.0001 Clitoral necrosis present 5.0 (3.5) 6.8 (1.9) absent 7.9 (2.2) p<0.001 8.8 (1.6) p<0.001 Pain in vagina or genitals present 6.0 (3.2) 7.1 (2.9) absent 8.0 (2.2) p<0.001 8.9 (1.4) p<0.0001 Other complications present 6.5 (3.3) 7.9 (2.7) absent 8.0 (2.1) p<0.01 8.8 (1.4) p<0.01		Postoperatively mailed questionnaires Likert scale 0-10 (very unhappy- very happy) Complications of genital surgery and overall measures of satisfaction. All versus the complication- absent condition *t-test*			
Morrison 2015 USA	Case series	83	*Rectosigmoid neocolporhaphy (vaginoplasty)* Outcome reported n= 21 Appearance 4.67 Sexual function 4.24 Overall satisfaction 4.67 Ability to achieve orgasm n= 44 43 (98%)		Patientreported outcomes Likert scale LS 1- 5			
Smith 2005 The Netherlands	Case series	67	*Vaginoplasty* Satisfied 47 (70.1) Not completely satisfied 15 (22.4) Dissatisfied 5 (7.5)		Postoperative questionnaire and Questions on satisfaction with result			

Project: Gender dysphoria
Appendix 4.2.2 Trans women (MtF)
Outcome variable: **Satisfaction**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Tavakkoli Tabassi 2014 Iran	Case series	112	*Penile inversion vaginoplasty* Satisfaction: 96 (86) Dissatisfaction: 16 (14)		Appearance and function. Vaginal depth (n=10), appearance (n=6)			
Van der Grift 2017 b The Netherlands	Case series	81	*Vaginoplasty* n= 71 Missing data Selfreported satisfaction Vaginoplasty 16 (23) 53 (96)					
Wagner 2010 Germany	Case series	50	*Penile inversion vaginoplasty* Aesthetic results: Satisfied: 45 (90) Dissatisfied: 5 (10) Depth of the vagina: Satisfied: 40 (80) Dissatisfied: 10 (20) Achieving clitoral orgasm: 35 (75)		Dissatisfied with the appearance of labia majora.			
Wierckx 2014 Belgium	Case series	214	*Vaginoplasty* More spontaneous desire in women who had undergone vaginoplasty compared to waiting list p=0.002 Experience of complication was not associated with sexual desire scores.		Hypoactive Sexual Desire Disorder (HSDD) defined as never/rarely-experience spontaneous or responsive sexual desire the past month, and causing personal or relational distress.			

Project: Gender dysphoria
Appendix 4.2.3 Trans women (MtF)
Outcome variable: **Regret, retransition**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Facial feminisation surgery No studies								
Breast augmentation No studies								
Genital surgery								
Van Noort 1993 The Netherlands	Cohort		*Penile +scrotal skin flap vaginoplasty (PSSFV)* n=16 0/13	*Penile skin flap vaginoplasty (PSFV)* n= 11 0/9	Regrets genital surgery Structured interview PSSFV 13/16 PSFV 9/11			
Lawrence 2003 USA	Case series	232	*Penile- inversion vaginoplasty and sensate clitoroplasty* No consistent regret 232 (100) Regret sometimes 15 (6)* Disappointing physical or functional outcomes of surgery 8 (53) Familial or social problems 5 (33) Retransition/ Reversion 2 (1) living part time as a man Predictor variable pre/ postop and correlation to Absence of Regret Number of significant surgical complications (r) -0.17 p<0.01 Functional Index FI (r) 0.28 p<0.001		Mailed questionnaire after genital surgery. *All patients had explanatory comments Retransition/ Reversion to living as a man from fulltime as a man – fulltime as a woman. A positive Absence of Regret measure was created. Functional Index (FI:mean of numerical responses) Each of 19 physical and functional outcome variables (vaginal size, genital touch and erotic sensation, pain, urine leakage etc) was rated by Likert scale (0-10). Spearman rank-order correlations of pre- and post-operative predictor variables and Absence of regret after genital surgery			

Project: Gender dysphoria
Appendix 4.2.3 Trans women (MtF)
Outcome variable: **Regret, retransition**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Lawrence 2006 USA	Case series	232	*<u>Penile- inversion vaginoplasty and sensate clitoroplasty</u>* No regret 232/232 (100) Sometimes 15/232 (6)* Association between: -any additional surgical procedure (n=189) and regret ns -any complication and sometimes regret ns *Frequency of achieving orgasm with masturbation* after GAS and association with regret sometimes p=0.064 Association with Absence of Regret, X^2 *Physical and functional outcomes of GAS* Vaginal width 9.0 p<0.01 Vaginal lubrication 7.8 p<0.01 Vaginal hair 9.1 p<0.01 Touch sensation at vaginal introitus 4.10 p<0.05 Erotic sensation in vagina 9.2 p<0.01 Erotic sensation in clitoris 21.2 p<0.001 Pain in or around clitoris 8.7 p<0.01		Mailed questionnaire after genital surgery *All patients had explanatory comments *Frequency of achieving orgasm* Ability to achieve orgasm with masturbation scale 1-5 (never- almost always) Fisher- Freeman- Halton test Physical and functional outcomes of genital surgery Likert scale (0-10) Associations with Absence of regret is by logistic regression, *df*=1			

Project: Gender dysphoria
Appendix 4.2.4 Trans women (MtF)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention 1 n (%)	Intervention 2 n (%)				
Facial feminisation surgery								
Capitan 2017 Spain	Case series	65	<u>*Hairline analysis, Forehead reconstruction, Simultaneous hair transplant*</u> Paraesthesia in scalp region (all recovered in 3 m) 0 (0) Postsurgical oedema (all cured by manual lymphatic drainage) 0 (0)					
Spiegel 2011 USA	Case series	63+49+56=168	<u>*Feminising forehead cranioplasty (island technique)*</u> n=49 Excessive mobility of a bony fragment resulting from nonunion 3 (6)		pneumosinus dilatans frontalis			
Breast augmentation No studies								
Genital surgery								
Bucci 2014 Italy	Cohort	217 vs 65	<u>*Vaginoplasty*</u> (bilateral orchiectomy, removal of corpora cavernosa, creation of the urethrostomy, neovaginoplasty, and creation of neoclitoris with preservation of neurovascular bundles and neovulvoplasty)			-		
			<u>*(2 sutures)*</u> n=217 Prolapse 8 (12.3)	<u>*(4 sutures)*</u> n=65 Prolapse 9 (4.1)				
Buncamper 2016 The Netherlands	Cohort	405 vs 70	<u>*Penile Inversion Vaginoplasty (no full-thickness skin graft)*</u> n=405 Major complication: 38 (9.4) Minor complication: 228 (56.3) Long-term complication Major: 72 (17.8) Minor: 54 (13.3)	<u>*Penile Inversion Vaginoplasty (with full-thickness skin graft)*</u> n=70 Major complication: 4 (5.7) Minor complication: 30 (42.9) Long-term complication Major: 9 (12.8) Minor: 9 (12.8)				
Falcone 2017 UK	Case Series	69	<u>*Penoscrotal vaginoplasty*</u> Total postop complication 15 (21.7) Vaginal atresi 2 (2.9) Vaginal stenosis 4 (5.8) Urethral meatus stenosis 9 (13)					
Gaither 2017 USA	Case Series	330	<u>*Penile inversion vaginoplasty*</u> Total postop complication 95 (28.7) Granulation formation 24 (7.3)					

Project: Gender dysphoria
Appendix 4.2.4 Trans women (MtF)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
			Wound separation 17 (5.2) Rectivaginal fistulas 3 (0.9) Vesiconeovaginal fistula 3 (0.9) Required second operation 30 (9) (labioplasty 90%, urethral reconstruction 21%)					
Goddard 2007 UK	Case Series	222	*Penectomy* Infection 15 (6.5) Post op bleeding 7; 5 uretrha/2clitoris (3.2%) Skin flap necrosis 6 (2.7%) Vaginal prolapse 4 (1.8%) Deep vein thrombosis 2 (0.5%) Urethral stenosis 36 (18.3%) (42 urethral dilatation, 8 meatotomy)					
Huang 1995 USA	Case Series	121	*Vaginoplasty* Major complication: 18 (14.8) Minor complication: 1 (0.8)		Incomplete reporting of complication			
Jarolim 2009 Czech Republic	Case series	121 + 8	*Vaginoplasty* I: Penile Inversion (n=121) II: Sigmoidovaginoplasty (n=8) **Perioperative Complications** Perioperative rectal damage 2 (1.5) **Short term complication** Bleeding urethra 6 (4.5) Temporary urinary retention 7 (5.2) Healing by secondary intention 7 (5.2) **Long term complication** Stenosis of neovagina 7 (5.2) Stenosis of neourethra 6 (4.5) Folliculitis of the neoclitoris 3 (2.2) Urinary stress incontinence 2 (1.5)					

Project: Gender dysphoria
Appendix 4.2.4 Trans women (MtF)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Karim 1995 The Netherlands	Case series	200	*Penile skin Vaginoplasty* Urethral stenosis 7 (3.5) Rectal vaginal fistula 1 (0.5) Partial obliteration 2 (1) Colocolpo neopoiesis 2 (1) Clitoryplasty 1(0.5) Corpus spongiosum resection 1(0.5) Labia correction 10 (5)					
Krege 2001 Germaany	Case series	66	*Vaginoplasty* Meatal stenosis 7 (5) Severe wound infection 6 (4) Rectal lesion 3 (2) Necrosis of the glans 3 (2) Vaginal prolapse 2 (1) Necrosis of the distal urethra 1 (0.6) Lesion of the external urethral sphincter 1 (0.6) Urethral fistula 1 (0.6)					
Lawrence 2006 USA	Case series	232	*Vaginoplasty* Vaginal stenosis 19 (8) Vaginal stenosis during arousal 15 (6) Misdirected urinary stream 77 (33) Urethral stenosis 9 (4) Clitoral necrosis 8 (3) Pain in vagina or genitals 20 (9) Other complications 27 (12)					
Perovic 2000 Serbia	Case series	85	*Inverted penile skin flap vaginoplasty* Rectovaginal fistula 1 Vaginal shrinkage 2 Introitus stenosis 6 Stenosis of urethral meatus 1 Urethral prolapse 2 Posterior vaginal wall rupture 1					

Project: Gender dysphoria
Appendix 4.2.4 Trans women (MtF)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Raigosa 2015 Spain	Case series	60	<u>*Vaginoplasty*</u> Major complications: 4 (6.7) (neovaginal stricture, rectovaginal fistula) Minor complications 13 (21.7) (urethral stenosis, wound dehiscence, minor bleeding)					
Reed 2011 USA	Case series	250	<u>*Vaginoplasty*</u> n=250 Rectal perforation 7 (2.8) Bleeding 6 (2.4) Urethral vaginal fistula 2 (0.8) Inadequate depth 5 (2) Elevated posterior commissure 14 (5.6) Urethral spongiosum rest 20 (8) Urethral meatus stenosis 15 (6) Scars, dehiscence 30 (12) Minor vag. Prolapse 5 (2) Major vag. Prolapse 1 (0.4) Clitoral necrosis 2 (0.8) Anterior elevation of vulvar plate 10 (4) Vaginal slough 2 (0.8) Vaginal stenosis 3 (1.2) Labial hematoma 10 (4) Revisions 8 (3.2)					
Sigurjonsson 2015 Sweden	Case series	205	<u>*Vaginoplasty twostage penile inversion*</u> Bleeding requiring reoperation 22 (11) Wound infection 20 (10) Wound dehiscence 4 (2) Clitoral flap necrosis 0 (0) Rectovaginal fistula 4 (2) Pulmonary emboli 2 (1) DVT 0 (0) Mortality 0 (0)					

Project: Gender dysphoria
Appendix 4.2.4 Trans women (MtF)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Rossi Neto 2012 Germany	Case series	332	*Vaginoplasty* **Genital complications:** Stricture of vaginal introitus 50 (15) Residual corpora tissue 50 (15) Vaginal stricture 40 (12) Loss of vaginal depth 27 (8) Vaginal segment necrosis 10 (3) Dyspareunia 7 (2) Partial clitoris necrosis 7 (2) Vaginal prolapse 3 (1) Clitoral pain 3 (1) **Urinary tract:** Obstructive voiding disorder 133 (40) Stricture recurrence 50 (15) Dribbling 27 (8) Transitory urinary retention 17 (5) Meatal edema 17 (5) Transitory urinary incontinence 13 (4) Urethral fistula 13 (4) Distal urethral necrosis 3 (1) **Gastrointestinal events:** Rectal injury 10 (3) Bowel atony 5 (1.5) Defecation discomfort 2 (0.6) Rectocele 1 (0.3) **Wound healing disorders:** Minor wound healing disorders 110 (33) Local abscesses 17 (5) Subcutaneous hematoma 13 (4) Blood transfusion 7 (2) Inguinal hernia 3 (1) Compartment syndrome 1 (0.3) Inguinal lymphocele 1 (0.3) Genital pain 10 (3)				

Project: Gender dysphoria
Appendix 4.2.4 Trans women (MtF)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Spehr 2007 Germany	Case series	500	<u>*Vaginoplasty*</u> Stenosis of the meatus 43 (8.6) Compartment syndrome 6 (1.2) Rectum perforation 5 (1) Late onset abscess 5 (1) Arm plexus lesion 2 (0.4) Vaginal contraction 1 (0.2) Recto-vaginal fistula 1 (0.2) Torn gastrocnemius muscle 1 (0.2) Peridural block 1 (0.2)					
Tavakkoli Tabass 2014 Iran	Case series	112	<u>*Vaginoplasty with scrotal flap*</u> Scrotal flap necrosis and shrinkage 4 (3.6) Vaginal shrinkage 4 (3.6) Bulging anterior vaginal wall 1(0.9) Excessive labial skin 3 (2.7)					
Wagner 2010 Germany	Case series	50	<u>*Vaginoplasty*</u> Shrinkage of the neovagina 5 (10)					

Project: Gender dysphoria
Appendix 4.2.4 Trans women (MtF)
Outcome variable: **Complications**

* + No or minor problems
? Some problems
\- Major problems

Author year country	**Study design**	**Number of patients n=**	**Results**		**Comments**	**Directness ***	**Study limitations ***	**Precision ***
			Intervention 1 n (%)	**Intervention 2** n (%)				
Morrison 2015 USA	Case series	83	*<u>Rectosigmoid neocolporaphy</u>* Total complications 48 (57.8) Complications requiring surgery 45 (93.8% of total complications) <u>Short-term complications</u> (<1 yr) 23 (27.7) Protrusion 5 (6.1) Urinary obstruction 2 (2.5) Stricture/stenosis 16 (20.0) Rectovaginal fistula 2 (2.4) Urethral fistula 1 (1.2) Abdominal pain 2 (3.8) Bowel obstruction 1 (1.2) Other 4 (4.8) <u>Long-term complications</u> (>1 yr) 27 (32.5) Infection 2 (2.4) Protrusion 13 (15.6) Prolapse 2 (2.4) Urinary obstruction 1 (1.2) Stricture/stenosis 18 (22.5) Colitis 2 (2.5) Urethral fistula 1 (1.2) Bowel obstruction 3 (3.6) Other 8 (9.6)					

Project: Gender dysphoria
Appendix 4.2.5 Trans women (MtF)
Outcome variable: **Re-operation**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention	Control				
Facial feminisation surgery No studies								
Breast augmentation No studies								
Genital surgery								
Buncamper 2016 The Netherlands	Case series	405 + 70	*Penile Inversion Vaginoplasty* Revision vaginoplasty 14 (2.9%) due to neovaginal stenosis. Meatotomy 46, meatusstenos Introital plasty 12, introital stenosis. Minor surgery 18, partial prolaps. Labia correction 160 (34%)		Original cohort study compared with and without full-thickness skin graft. Here reported as a case series.			
Karim 1995 The Netherlands	Case series	200	*Penile skin Vaginoplasty* Urethral stenosis 7 (3.5) Rectal vaginal fistula 1 (0.5) Partial obliteration 2 (1) Colocolpo neopoiesis 2 (1) Clitoryplasty 1 (0.5) Corpus spongiosum resection 1 (0.5) Labia correction 10 (5)					
Raigosa 2015 Spain	Case series	60	*Vaginoplasty* Secondary esthetic revision surgery 13 (21.7)					
Rossi Neto 2012 Germany	Case series	332	*Vaginoplasty* Vaginal prolaps 4 (1) Stricture 23 (7) Residual corpora tissue 50 (15) Meatal stenosis (Y-V plastic reconstruction) 132 (40) Urethral injury 7 (2) Neomeatus bleeding 5 (1.5) Rectal injury 8 (2.4) Compartment syndrome fasciotomy 1 (0.3)					

Project: Gender dysphoria
Appendix 4.2.5 Trans women (MtF)
Outcome variable: **Re-operation**

* + No or minor problems
? Some problems
- Major problems

Author year country	Study design	Number of patients n=	Results		Comments	Directness *	Study limitations *	Precision *
			Intervention	Control				
Spehr 2007 Germany	Case series	500	<u>*Vaginoplasty*</u> Rectal perforation 5 Recto vaginal fistula 1					
Wagner 2010 Germany	Case series	50	<u>*Vaginoplasty*</u> Bleeding with operative revision 2 (4) Shrinkage of neovagina correction 5 (10) Anterior vaginal wall recorrection 2 (4)					
Hage 2000 The Netherlands	Case series	390	<u>*Vaginoplasty*</u> Vulva corrections 86/390 (22)		130 reoperations on 86 patients			
Morrison 2015 USA	Case Series	83	<u>*Rectosigmoid neocolporaphy*</u> 45 (54)		Of 48 complications, 45 required surgery			

Project: Gender dysphoria

Appendix 5
Ethical aspects

The effect of the intervention on health	
Q1: Health: How does the intervention effect patients' health in terms of quality of life and life-length (including adverse effects)?	The effect of a surgical intervention which aims to align patients' body with the gender identity is foremost defined by patient satisfaction. The patients value the impact of the available interventions on health and quality of life extremely positive, even when experiencing adverse effects that might cause disabilities. For example, a patient might well accept donor site morbidity (following harvesting of the radial forearm flap), or some urinary complications (e.g. urinary infections and fistulas) if these are compensated by a successful penile reconstruction, which suggests that the patient subjectively values the positive outcomes of the reconstructive organ as more important than the negative outcomes. In fact, rather than perceiving negative outcomes of the surgery, the patients might regard these simply as sequelae. The patients are well aware of possible complications before the surgery. The success of the operation is determined by the patient's personal judgement, rather than by objective data measured by healthcare professionals. Indeed, more patient reported outcomes (PROM) are used and there is more effort trying to make patient's judgement measurable and comparable. However, there is a lack of validated PROM questionnaires for this specific group of patients and treatments. Certainly, there are patients that regret the interventions, either because the interventions are not fulfilling, post-operatively, what were the patient´s pre-intervention's expectations, at both functional and social level, or because of a major failure of the intervention.
Q2: Knowledge gaps: If there is lack of scientific evidence for the effect of the intervention, are there ethical and/or methodological problems with future research in order to strengthen this evidence.	Scientific evidence is lacking for all the different interventions and outcomes. The (limited) evidence also fails in the methodology used: there are no double-blind randomized studies, numbers are often small, and outcome measures vary; finally, the multitude of different interventions and the heterogeneity of the patients make comparisons difficult. Cultural disparities due to differences in legislation and demands from society limit transferability. At the same time, there are no principled ethical reasons for why the methodology could not be improved. Here it is important to note, that even if there is a strong preference from patients to undergo treatment, such preferences should not hinder well-designed studies where some patients act as control group. There are also issues in merit to research ethics, especially concerning intervention in the pediatric population. One example is puberty suppression therapy in children and adolescents. Introducing therapy or performing surgery with irreversible effects despite a lack of evidence is expose an already vulnerable population to known as well as unknown risks.
Q3: Degree of severity: What degree of severity has the condition the intervention is supposed to treat?	Transsexualism is a condition, which affects many parts of patients' life and may often cause long-lasting difficulties in work life and interpersonal relations. Suicide rates are considerably higher than in the normal population. The severity of the condition may motivate higher risk taking by the patient as well as more extended resources. The severity of the condition is also extremely variable. Some individuals, identifying themselves as 'transsexual', 'transgender', and 'gender nonconforming individuals', might not present gender dysphoria, and therefore they would not request any interventions. Other individuals present some degree of dysphoria, which might be reduced or eliminated following the chosen intervention's plan. Yet other individuals may experience dysphoria that no intervention can eliminate In spite of the intervention, these individuals may commit suicide. There is no instrument that mental health care professionals can use in order to assess the degree of dysphoria and/or foresee the effects of interventions on the degree of dysphoria.
Q4: Third parties: How does the intervention affect the health of third parties?	As gender dysphoria is connected to the sense of identity, and gender identity is intervening in most parts of the daily life, and all along the life span, the wellbeing of patients' has an impact on his/her family and on other relations. The transition process, therefore, demands different adjustments from third parties; these third parties are represented by those who are in close relationships (as family, friends, work colleagues), and by other parts of the society. Counseling can be needed also for third parties.

Project: Gender dysphoria

Appendix 5
Ethical aspects

Summary: How is the benefit/risk – ration for the intervention (given the answers of Q1-Q4)?	Gender dysphoria is a pathological condition that is affecting many areas of life and the groups affected show a high degree of vulnerability. Hence, in its more severe forms gender dysphoria might motivate higher risk-taking. Many patients value the effects of the interventions extremely positive, even when taking complications into account. There is effectively a clear and positive impact of having ones identity affirmed by the body representation. However, the scientific evidence on the value of the surgical intervention is limited, and it often fails in methodology. There is therefore an urgent demand for research.
Q5: Equality and justice: Is there a risk that access to the intervention violates the Human Dignity principle or the Swedish Discrimination Act?	In general, aspects like gender or sexual identity should not result in unequal treatment within the health-care system. Lack of policies may lead to arbitrariness and unjust decisions. As evidence is lacking, , decisions are taken based on health care professionals' expertise. There is always a possibility that judgement may be biased, and final decisions could possibly cause discrimination among individuals. It has been claimed that non-binary individuals have more difficulties to receive surgical interventions, and that different assessment teams decide differently. Removal of the Swedish law demanding for sterilization, in order to change the civil status, implies an increase in equal treatment. The Swedish health-care system is a needs-based and not a rights-based health-care system. This implies that it is the need of the patient (as considered by health-care professionals) and not the demand of patients, that should guide whether treatment is warranted or not. There are many cases where assessment is difficult and there can be conflicts between patient, surgeon and assessment teams. This might be the case when, e.g., patients' requests are borderline with aesthetic surgery, as for adjustments and revisions, when healthcare professionals have to decide to (re)-operate or not. To assess the need of the patient it is essential to understand how the patients condition impacts on his/her ability to live a good life in the society at hand. In order to avoid inequality and bias from professionals, there should be a careful assessment. One question is whether one procedure could be replaced by another, less extensive procedure. Given there is a definitied need and within restrictions of resources and professional responsibility (concerning things like exposing patients to risks etc.) – patients preferences for treatment should be accorded with. In gender affirmation surgery, as the patients expectations vary in many ways there is the question of fitting the procedure to the patient. To opt for a too limited set of procedures could in fact lead to discrimination because the expectations of some patients may be met, but other patients would be offered a procedure less fitted for these individuals. A procedure that is well fitted for one person could be a matter of misuse by the other. At the same time, when being prioritized in relation to other interventions within the healh-care system, it is more difficult to assess a reasonable resource use for these interventions since it is likely to vary depending on severity and the effects of the intervention. However, it can be said, that given the relatively high severity of the condition, and the fact that studies show a high degree of satisfaction post-intervention – it will probably not be given a low priority. However, developed research resulting in an even better match between need and intervention could result in an even more fair and effective resource use.

Project: Gender dysphoria

Appendix 5
Ethical aspects

The compatibility of the intervention with ethical values	
Q6: Autonomy: Can the intervention affect patients' and significant others participation in decisions and their ability to make informed and relevant decisions about the intervention?	Indeed, autonomy is put at stake. Patients are vulnerable both in relation to the (healthcare and society) system, and in relation to the suffering itself, generating a 'wishful thinking' in the patients, as described by Caplan and Purves (2017) in merit to patients requiring non-life rescuing transplantations. In fact, as Caplan and Purves note when discussing life-improving transplantations versus life rescuing transplantations, many other life-improving surgeries widely offered today, as reconstructive (as well as cosmetic procedures) impose a risk of death from anesthesia or surgical complications such as lethal infections. Yet these procedures are widely offered and chosen. Though it is important for patients to understand risks, before undergoing potentially dangerous procedures, banning whole categories of procedures on grounds of healthcare professionals' concern about patients' misunderstanding, goes much further than present practice does or should. The psychiatric assessment before being accepted for surgery is often perceived by patients as a too long. As Swedish health care is based on individual needs, and not on the right to treatments, there is a demand on the side of the care giver to ground the recommendations on adequate knowledge about the patient. There is also an explicit duty to make certain the patient has received information about and understood the effects and consequences of the interventions. As the surgical interventions in some cases are complex and carry considerable risks for complications, the information needed must take time in order to allow for proper consideration. The care giver needs to make sure that the patient understands the consequences, and that the surgical intervention can meet the expectations, without causing any extraordinary risks. As the procedures are not mandatory, but rather a list of possible options, it may lead to a situation where patients let them self be guided by wishful thinking: If I do this or that surgery I will have a better quality of life. But you cannot exercise true autonomy, if based on dreams and non-realistic ideas.
Q7: Privacy: How does the intervention affect patient's and significant others' physical and personal privacy?	Gender dysphoria touches on many private and intimate issues in the care situation. Poor knowledge within health care about the special needs of transgender individuals causes misunderstandings that can be emotionally painful for the patient. The issue of privacy leads, again, to discussing human rights. According to Niveau, Ummel and Harding (1999), the civil status is essential to the dignity of individuals because it affirms their membership in a community and constitutes a strong element of social life. As explained by Niveau, Ummel and Harding (1999), in fact, the discrepancy between physical appearance and civil status is obliging transsexuals 'to reveal and explain their health status in various everyday situations'. In these situations, the transsexual citizens need to show documents proving the treatments received, thereby having their rights for privacy violated. Those transsexual citizens who, in Europe, have been appealing to the European Court of Human Rights, claimed that the affirmation of one's gender in the society, without a corresponding change of civil status, had to be considered as 'inhuman' and 'degrading', thus violating the Article 3 of the same European Court of Human Rights (Niveau, Ummel & Harding, 1999).

Project: Gender dysphoria

Appendix 5
Ethical aspects

Q8: Cost effectiveness: Is the balance between the cost and effects of the intervention reasonable?	As simply as a figure, there is no evidence on the cost-effectiveness of each single treatment that could be provided to transsexual individuals. The ethical problem is extended to what should be considered as 'effectiveness', and how to prioritize amongst procedures that are not life-rescuing. In a previous paper (Selvaggi, Kolby & Elander, 2017) entitled 'Prioritization for plastic surgery procedures aimed to improve Quality of Life: case examples and moral considerations', principles were discussed that can be used as a guide for health professionals in order to revise and create policies for plastic surgery patients presenting with non-life-threatening conditions. It was concluded that a specific anatomical feature (measurements of function) should not be used as an indicator of patient's well-being/QoL in order to identify the worst-off, and that prioritization of the provision of health care should be grounded on some plausible measure of how much a specific patient can be expected to benefit from a treatment. Policies which do not track these principles in any reliable way can cause discrimination. In circumstances when the effectiveness of a specific treatment is unproven, professionals should not make assumptions based on their own values.
Summary: Is the use of the intervention compatible with ethical values (given the answers of Q5-Q8)?	The use of intervention might indeed be compatible with ethical values and there are no principled reasons against gender affirmation surgery. On the contrary, values of equality, autonomy and privacy support intervention. However, to arrive a whether intervention for a specific individual is motivated based on individual need, effect of intervention and a reasonable resources use – more research is needed. There is lack of scientific knowledge on objective and validated instruments to identify the worse-off and those who can expect to benefit the most of a specific intervention; therefore, it is not unlikely that healthcare professionals and policy makers might take wrong choices both when approving a specific individual for treatment, and when preparing a policy. Awaiting such scientific development, due to the extreme distress experienced by many transsexual individuals, it is ethically motivated to provide treatments to selected individuals, rather than a moratorium and, subsequently, not treating those whose dysphoria is likely to be eliminated following the treatment. Especially, since given the degree of need and the effect of treatment evidenced in this report, gender affirmation surgery does not seem to be the first candidate for rationing, i.e. it should not be prioritized on the lower range within the health-care system. However, it is recommended that all such interventions are carefully monitored over time, preferably within a research project. Such monitoring shoud include measuring the outcomes of the interventions to determine the amount of benefit received by a specific individual in comparison to other individuals. Also developing measures for assessing the degree of need or severity of the condition in order to aid in prioritizing different interventions and enable a continued discussion about what should be publicly and privately financed, respectively. Since prioritizing treatment in Sweden is based on assessing the need, effect of treatment and cost-effectiveness and there is no explicit legal ground for not offering cosmetic treatment per se – apparently cosmetic treatment should not be denied *prima facie*. However, to the extent such treatment is offered, it should be consistent with the grounds for offering similar treatment for other patient groups.
Structural factors that can affect the use and consequences of the intervention	
Q9: Resources and organisation: Are there resource- or organizational limitations that can affect who will get access to the intervention or that can lead to less access to other care if the intervention is used?	Indeed, today there is a gap between policy and evidence, and a gap between policy and practice. These gaps are inevitably causing an unjust distribution of the resources, and a possible waste of resources. The research proposed on transgender patients, grounded on the moral obligation to do *just* for the society, will result in extensive information specific on costs and, therefore, resources needed for providing highly prioritized health-care, and the resources wasted when providing less prioritized health-care. Comparisons can be made with other group of patients and diagnosis.

Project: Gender dysphoria

Appendix 5
Ethical aspects

Q10: Professional values: Can values within the affected care professions influence the use of the intervention and thereby lead to unequal access?	Transgender care include somatic and mental care. Being a multidisciplinary field, outcomes are valued differently, and in this case the surgery is done in order to get psychological effects. The matter may appear difficult to professionals with less knowledge about transgender care, and may even provoke emotional reactions that affects professionalism. As said, professionals should not make assumptions only based on their own personal values. In order to better understand the pathology, and to provide compassionate care to transsexual patients, as well as to further implement into the society principles of equality and respect, educational programs (such as: LGBTQ certifications, rotations at units specifically treating transsexual individuals, or web-based educational tools) should become mandatory for every health care professional involved in the care of these patients. In this way, a fair access to health care anywhere in the system is promoted. Equally important, following implementation of these educational tools, transsexual individuals will more likely be treated with dignity. Respecting the patient as an equal member of the community helps the patient with his/her self-affirmation and connectedness with society and strengthens identity and reduces gender dysphoria.
Q11: Stake holder interests: Are there stake holder interests that can influence the use of the intervention and thereby lead to unequal access?	It is important that politicians and managers within the health care system are well informed of the needs of transsexuals, as this group is growing in numbers and care must be adapted accordingly. Crowding effects may turn up in different disciplines of the care of transsexuals, due to a lack of resources or competence. In some areas private health care providers, may add to an unequal access as they find transsexual people a niche for profit opportunity. Inequality in care and access to care is often discussed in transsexual communities. The assessment, as such, is also described as an obstacle to care, and there are worries that different subgroups may be unjustly discriminated. There are also worries amongst health care professionals that the critique from the patients' proponents is not representative for the entire group, but is the voice of the stronger at the expense of the less well spoken individuals. Recent political or authority initiatives might be interpreted as giving patients with gender dysphoria a right to undergo certain interventions, however, it is important to remind ourselves that these patients should be treated equally and according to need as any other patient within the health-care system.
Summary: Are there reason to believe that an equal access to the intervention (or other care interventions) can be affected (given the answers to Q9-Q11)?	Up too few years ago, transsexual patients' access to intervention was unequal. More specifically, till 2013 transsexual patients were obliged by the Swedish law to be sterilized in order to change their civil status. That law has now been recognized as against the individual human rights, and could be considered as 'inhuman' and 'degrading'. Following the implementation of the new Swedish law, and the publication of the Swedish Department of Health and Welfare Guidelines on the knowledge and treatment of transsexual individuals, access to healthcare has become easier.
Long-term ethical consequences	
Q12: Long-term consequences: Can the use of the intervention result in more long-term consequences?	Long-term consequences has yet to be established. A risk with using interventions lacking in evidence is the risk of a backlash in trust if it turns out there are negative effects of the interventions. Given the history and available evidence of gender affirmation surgery, we do not have strong reasons to believe such a backlash would occur. A possible exception could be if gender affirmation surgery is performed on adolescents, which might indicate a restrictive approach. A possible long term consequence to be observant on is the risk of negative attitudes towards patients with gender dysphoria and the extensive interventions if the resources constraint of the health-care system will be further emphasised. That is, when health-care will have to be rationed, underlying discriminatory attitudes towards people of a different gender or sexual orientation might cause a strong negative attitude towards these interventions. The health-care system then needs to develop its argumentation in defence of such interventions.

Project: Gender dysphoria

Appendix 5
Ethical aspects

Overall summary	
How can the ethical aspects regarding the intervention be summarised? Does this summary indicate that the intervention should be modified or that there should be special requirements associated with offering the intervention?	In conclusion, the provision of gender affirmative treatment for transsexual patients is ethically justified in selected individuals, as there is currently no other effective way than changing the body to relieve transsexualism. Exactly which treatment is provided should be based on a careful assessment of the individuals' need as long as it is consistent with available resources and in line with professional responsibility not to expose patients to undue risks. Individual assessment might result in the conclusion that what is otherwise considered to be cosmetic or enhancing interventions, might still be warranted in this case. However, if such treatment is normally not offered within the health-care system, demands of consistency implies that it should be possible to show the greater need or better effect in this individual. This treatment should be performed within research projects, and not as standard clinical practice using innovative concepts and innovative, and state-of-the-art medical and surgical treatments. Given the lack of evidence about outcomes, it is essential that prospective patients are carefully assessed and given extensive information in order to understand the potential consequences of intervention. When treating transsexual patients, special care and consideration should be given, since this is a group of vulnerable individuals,. This is especially important when considering to offer children and adolescents treatments with unclear benefit and risk, when, e.g., suppressing the puberty . Finally, a series of mandatory educational tools regarding care of individuals with gender dysphoria should, for ethical reasons, be implemented within the health care system for its professionals.

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA

HTA

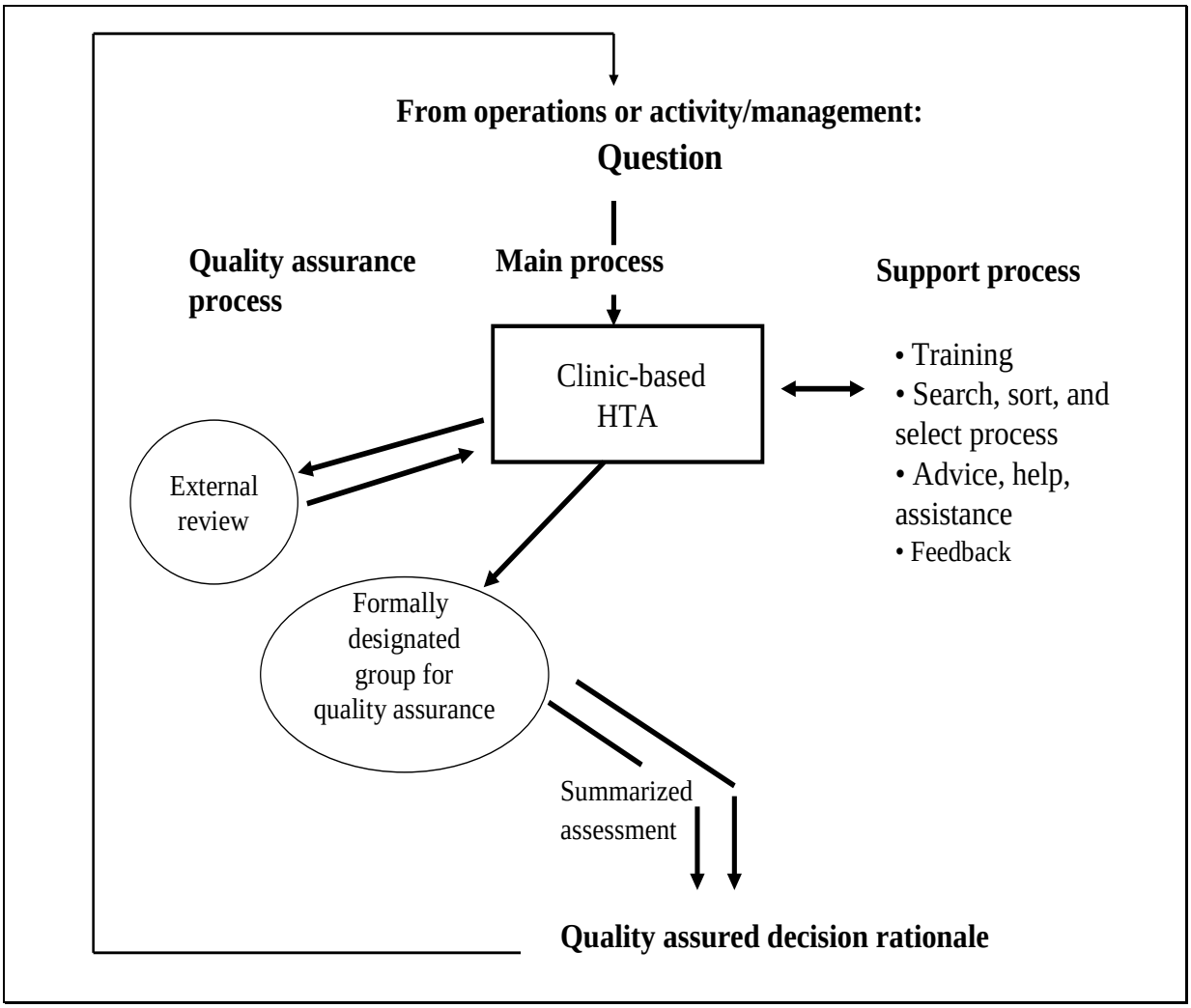
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Sahlgrenska Universitetssjukhuset, HTA-centrum
Röda Stråket 8, 413 45 Göteborg
www.sahlgrenska.se/hta-centrum