

December 9, 2024

In early 2023, staff of the Health Evidence Review Commission (HERC) worked with contractors to develop a report containing a review of evidence related to health outcomes for gender-affirming treatments. Months later (June 2023), the Oregon Legislature passed House Bill 2002 to require broad coverage of medically necessary gender-affirming treatments when prescribed, “in accordance with accepted standards of care,” and regardless of the coverage named in the Oregon Health Plan’s Prioritized List of Health Services. When it became clear the bill would become law, OHA ceased development of this report because the law would supersede HERC’s authority. OHA is releasing this incomplete, draft report, due to public interest. There is no plan to use this report to support any policy change affecting OHP coverage or the Prioritized List.

Receipt of Gender-affirming Medical Interventions

DRAFT for VbBS & HERC Meetings, August 9, 2023

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BACKGROUND

This section includes contextual information regarding medical interventions for gender-affirming care including definitions, estimates of the prevalence of gender incongruence in Oregon, the array of treatment modalities, barriers to access and utilization, along with clinical considerations.

Overview

Since 2015, the Oregon Health Plan has provided coverage for hormonal therapies and a selection of gender affirming surgeries for transgender individuals provided they met criteria in alignment with guidance from the World Professional Association for Transgender Health (WPATH) Standards of Care, Version 7.^{1,2} Over the 8 years since that decision, the research science, public discussion, and national policy landscape regarding care for transgender individual has continued to evolve. Additionally, in 2022, WPATH released the latest update to the Standards of Care, now in Version 8.³ This review aims to summarize the impacts of a selection of gender affirming medical interventions on mental health and quality of life outcomes for individuals with gender incongruence.

Definitions

Transgender and gender diverse (TGD) represents a wide spectrum of individuals identifying as a gender other than from that designated at birth.⁴ Gender, which varies across societies and cultures, is a construct of roles or behaviors associated with female or male without biological basis.⁴ The [National Institutes of Health](#) (NIH) provides definitions for Sex, Gender, and Sexuality that are relevant for this review.⁴ A sample of definitions include the following:⁴

- “Gender: Socially constructed roles, behaviors, activities, and/or attributes that a given society associates with being a woman, man, girl, or boy, as well as relationships with each other. As a social construct, gender varies from society to society and can change over time.
- Gender expression: how one chooses to convey one’s gender identity through behavior, clothing, and other external characteristics.
- Gender identity: An individual’s sense of being a man, woman, boy, girl, genderqueer, nonbinary, etc. This identity is not necessarily visible to others.
- Gender non-conforming: A person whose gender expression is not consistent with the societal or cultural norms expected of that gender.
- Nonbinary: A nonbinary person identifies outside of a gender binary by seeing themselves as neither a man nor or woman. Nonbinary people are part of the trans community.
- Transgender: A transgender person is someone who identifies with a gender other than the one that was assigned to them at birth.
- Sexual and gender minorities: Includes, but are not limited to, individuals who identify as lesbian, gay, bisexual, asexual, transgender, Two-Spirit, queer, and/or intersex.”

Over time, diagnostic frameworks have shifted from one of psychopathologizing TGD individuals (e.g., people with gender identify disorder) to one descriptive of the impact of gender incongruence on mental health (e.g., gender dysphoria) as in the 5th edition of the Diagnostic and Statistical Manual (DSM-V).⁵ Acknowledging the stigma from prior classifications and that not all TGD individuals experience dysphoria, the International Classification of Disease (ICD), 11th edition, uses gender incongruence within conditions related to sexual health.⁶

Additional important background on language, health, disparities, evolutions in care, and future directions for research are described by numerous review articles.⁷⁻¹⁰ We encourage the reader to review these additional resources for more details.

While a distinct population, individuals with disorders of sexual development have overlapping but distinct needs to the TGD population.¹¹ Differences of sexual development, also referred to as intersex conditions, encompass persons with ambiguous genitalia at birth, chromosomal variants, or hormonal conditions (e.g., congenital adrenal hyperplasia).¹¹ Prevalence varies by cause with estimates ranging from 1:200 for hypospadias or cryptorchidism, 1:14:000 births for congenital adrenal hyperplasia (in 46, XX individuals) to 1:100,000 births for androgen insensitivity syndrome (in 46, XY individuals).¹¹

Throughout this review we strive to use the NIH definitions, however several of the included studies use older language to describe this population or employ non-specific terminology (i.e. gender affirming surgeries) for procedures. We use TGD to include the spectrum of transgender, nonbinary, and gender non-conforming individuals in background and discussion, but use the language of the studies (e.g., trans man or men; trans woman or women; nonbinary) when appropriate in the findings. We attempt to specify surgical procedures (e.g., labiaplasty, vulvoplasty, vaginoplasty) when they are specifically reported rather than the more general category of gender affirming procedures or surgeries.

The Transgender Population in Oregon and the US

Demographics

In 2022, the Williams Institute of the UCLA School of Law updated their national report, “How Many Adults and Youth Identify as Transgender in the United States”,¹² using the Centers for Disease Control and Prevention’s Behavior Risk Factor Surveillance System (BRFSS) and the Youth Risk Behavior Survey ([YRBS] an annual survey of high school students).¹² The 2022 report incorporated data from the 2017-2020 BRFSS along with the 2017 and 2019 YRBS (as the 2021 did not assess gender identify).¹² Not all states use the additional components of the BRFSS and YRBS that include questions on sexual orientation or gender identify.^{13,14} The specific questions asked of individuals are as follows:

- BRFSS: “Do you consider yourself to be transgender?” If yes, then asks “Do you consider yourself to be (1) male to female, (2) female to male, or (3) gender nonconforming”.¹⁴
- YRBS: “Some people describe themselves as transgender when their sex at birth does not match the way they think or feel about their gender. Are you transgender?” with responses including “No, I am not transgender”, “Yes, I am transgender”, “ I am not sure if I am transgender” or “I do not know what this question is asking”.¹³

Table 1 summarizes national and Oregon data obtained from these reports. Compared to prior reports, overall the percentage of transgender adults remains stable.¹² The proportion of youth identifying as transgender increased from 10% (2016 to 2017 edition) to 18% (2017 to 2019 edition).¹² Notably, 2017 was the first year YRBS asked youth if they are transgender, this addition expanded the pool of individuals surveyed and the increase in prevalence should be interpreted in light of the change in survey technique.¹² The BRFSS added relevant questions in 2014.⁷

Table 1. Population Estimates of Transgender Individuals

Abridged from [Herman, Flores, & O'Neill; 2022](#)

Age (% n)	13 to 17	18 to 24	25 to 64	65+	All Adults (18 +)
Oregon	1.18%	1.57%	0.52%	0.35%	0.59%
	2,900	5,700	11,500	2,700	19,990
US Overall	1.43%	1.31%	0.45%	0.52%	0.52%
	300,100	398,900	766,500	171,700	1,337,100

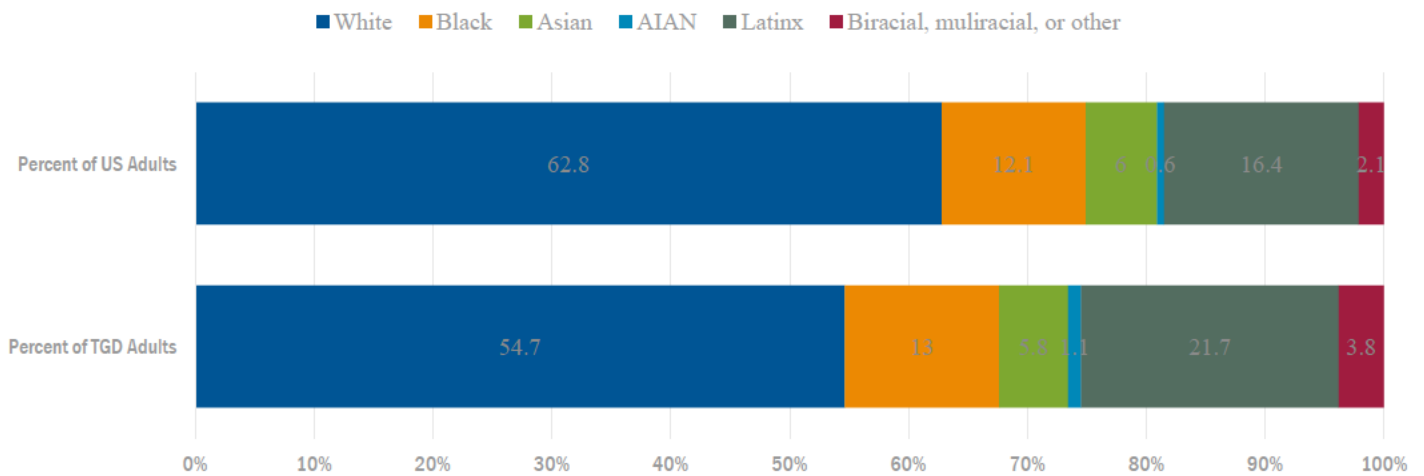
Data from Kaiser Permanente in Georgia, Northern and Southern California also analyzed trends in TGD individuals seeking care from 2006 to 2014 with steadily increasing numbers of TGD individuals each year, with the greatest in proportions in the Northern California region.¹⁵ Over the time period, the ratio of trans men to trans women shifted from 1:1.6 in 2006 to 1:1 in 2014.¹⁵ This shift was greater among youth (< 18 years), 1:1 in 2006 to 1.8:1 in 2014.¹⁵

While historically undercounted in surveys or studies,¹⁶ the number of TGD persons identifying a nonbinary or gender non-confirming continues to increase. In a recent national phone survey from 2022, 6 in 10 transgender individuals report identifying a trans, gender non-confirming or trans, nonbinary.¹⁷

Findings from the BRFSS and YRBS report the US TGD population as more diverse compared to the overall US population (**Figure 1**).¹² This is consistent across other national surveys (e.g., TransPop, US Transgender Survey) with the TGD population in the US younger and more racially diverse than the overall country.¹⁸

FIGURE 1. RACE AND ETHNICITY OF ADULT TRANSGENDER POPULATION COMPARED TO US

Abridged from [Herman, Flores, & O'Neill; 2022](#)



Reflecting the intersecting and additive effects of race, ethnicity and being TGD, mental health conditions are more common for TGD individuals compared to their cisgender peers.¹⁹ The odds of mental health distress and lifetime history of depression diagnosis are greater for TGD individuals compared to cisgender peers across Black, Hispanic, American Indian or Alaska Native, and other race and ethnic groups (table ###).¹⁹

TABLE ##.

Odds of Frequent Mental Distress for Transgender Compared to Cisgender Populations (Abridged from Robertson et al. 2021)¹⁹

Race/Ethnicity	White	Black	Hispanic	Asian	American Indian or Alaska Native	Other
Cisgender	1.00 (Reference)	aOR 0.75 (95% CI, 0.71 to 0.78)	aOR 0.58 (95% CI, 0.55 to 0.62)	aOR 0.56 (95% CI, 0.50 to 0.53)	aOR 1.23 (95% CI, 1.10 to 1.37)	aOR 1.32 (95%CI, 1.22 to 1.43)
Transgender	aOR 1.81 (95% CI, 1.49 to 2.21)	aOR 1.35 (95% CI, 0.91 to 2.00)	aOR 1.20 (95% CI, 0.77 to 1.86)	aOR 1.17 (95% CI, 0.56 to 2.43)	aOR 8.06 (95% CI, 2.03 to 32.00)	aOR 3.15 (95% CI,1.78 to 5.59)

Note: all analyses adjusted for age, sex, partnership status, presence of a child in the household, health insurance status, usual source of care, state of residency, survey year, educational attainment, and household income.¹⁹

Abbreviations: aOR: adjusted odds ratio; CI: confidence interval.

Overall, more TGD individuals report their health as fair or poor compared to cisgender individuals (26.2% vs. 14.7%) with more poor health days per month (7.9 vs. 4.4) compared to cisgender individuals.¹⁸ Rates of mental health distress are greatest for transgender American Indian or Alaska

Native adults (aOR 8.06; 95% CI 1.49 to 2.21) and transgender adults of other or multiple races and ethnicities (aOR 3.15; 95% CI 1.06 to 12.32) compared to White, cisgender individuals after adjusting for socioeconomic factors.¹⁹

The absence of gender identity information on vital statistics or national data (e.g., death certificates, drivers license, census, police records) prevents accurate estimation of disparities, including health outcomes, crime victimization, mortality, completed suicide, and other causes of death in a systematic way at a national level.²⁰ Cross-sectional or single point in time surveys using nonsystematic convenience samples generally report higher rates of suicide attempt or suicidal ideation than those collected from BRFSS and other probability-weighted methods.²¹

In reviews of large electronic health records, suicide rates for the TGD population exceed those of their cisgender peers.^{22,23} In an analysis from the Veterans Health Administration (VHA) of data collected from 1999 to 2016, the overall risk of suicide was doubled for the TGD population compared to that for cisgender population, nearly tripled for young adults, and 9-fold higher for older adults:²²

- Overall: Adjusted hazard ratio (aHR) 2.77; 95% CI 1.88 to 4.09
- 18 to 39 years: aHR 3.35; 95% CI, 1.30 to 8.60
- ≥ 65 years: aHR 9.48; 95% CI 3.88 to 23.19

These findings align with those from the STRONG cohort (Study of Transition Outcomes and Gender) which uses outcome data from 3 Kaiser Permanente Health regions and includes individuals under 18 and an overall larger number of trans men than the VHA study above.²³ Over an average of 4.5 years of follow-up for trans women and 4.1 years for trans men, the crude rate of suicide attempt was 3.0 (95% CI: 2.5 to 34.) and 4.8 (95% CI: 4.2 to 5.5) per 100,00 person-days, respectively.²³ Compared to individuals age over 45, the highest risk for suicide was in the 3 to 17 age group (HR 7.33; 95% CI, 4.32 to 12.43).²³ The rate for those age 18 to 25 years and those 26 to 35 years was similar to the outcome rates reported in the VHA study (HR 3.25; 95% CI, 1.84 to 5.75; HR 2.82; 95% CI 1.53 to 5.20, respectively).²³

Gender Affirming Medical Interventions

Interventions for the TGD population include a spectrum of services individualized to the needs of the person, with additional services offered to their families or social support persons.³ Services include psychosocial support, medical therapies (e.g., hormonal treatments), or surgical procedures. Psychosocial interventions for families aim to increase factors protective for TGD youth and may include education or resources to parents or caregivers.²⁴ While psychosocial supports to TGD individuals may work to alleviate **alleviate** distress and foster resiliency or community.²⁴ While hormone therapy in isolation is out of scope for this report, Wittlin and colleagues provide a table of studies on hormone treatment in youth that demonstrate improvements in psychosocial functioning, depression symptoms, and decrease in suicidality.²⁴ A recent systematic review on hormone therapy observed increased quality of life, decreased depression and anxiety for adults.²⁵

This review focuses on additional interventions beyond hormonal therapies, including surgical, dermatological, or vocal therapies. Version 8 of the WPATH Standards of Care summarizes potential

interventions for TGD individuals (Appendix E of the original guideline) and is included in **Appendix X** of this document.³

Briefly, these include interventions to revise facial features (e.g., brow, hair line, nose, cheek, lip, jaw, or chin), vocal cord surgery, the removal or addition of breast tissue, the removal of testes or uterus (with or without removal of the ovaries), and the creation of labia, vulva, vagina or penis.³ Additional interventions include hair removal, speech therapy, and body contouring (e.g., removal or addition of fatty tissue or implants to hips and buttocks).³ Surgical procedures can occur in a staged fashion or at one time depending on the combination (e.g., orchiectomy and vaginoplasty).

Access and Equity

TransPop, a national probability-based sampling phone survey from 2019, observed that despite similar rates of insurance coverage, TGD respondents were statistically less likely to report a usual site of care (60.7% vs. 76.4%; p value $<.001$), lower satisfaction with care (81.8% vs. 88.4%; p value $<.05$), and higher rates of care avoidance due to cost (32.5% vs. 14.6%; p value $<.001$) compared to cisgender individuals.¹⁸ Half (55.9%) of TGD respondents reported a transgender-related health care provider, with nonbinary respondents less like compared to trans men or trans women. Compared to an earlier survey, the US Transgender Survey (from 2015), TransPop did not observe significant changes in insurance status, care avoidance due to cost, or having a transgender-related health care site.

In a 2023 national survey of TGD individuals from the Kaiser Family Foundation, nearly 50% reported discrimination in health care settings including interacting with providers with very limited knowledge of caring for TGD individuals.¹⁷

While TGD individuals continue to report lower access to care and high rates of interactions with providers untrained in their care, guidelines recommend (and insurance companies as a result require) the medical community, specifically a mental health provider, to assess TGD individuals for readiness for care and complete a letter of readiness.⁸ This requirement is commonly known as gatekeeping and is without an equivalent experience for cisgender individuals seeking to obtain medical procedures.⁸ In their 2022 scoping review on readiness assessment for gender-affirming surgery, Amengual and colleagues synthesized the evolution of WPATH guidance across all 8 versions in terms of letter writing requirements, diagnosis, and training requirements of providers **(Potential Figure ##)**.⁸

POTENTIAL FIGURE ##. COMPARISON OF WPATH REQUIREMENTS OVER TIME

WPATH Standards of Care around Gender Affirming Medical and Surgical Treatments Over Time

Standard of Care Version	Version 1	Version 2	Version 3	Version 4	Version 5	Version 6	Version 7	Version 8
Letter Writer Requirements	Must be Licensed Psychologist or Psychiatrist	<ul style="list-style-type: none"> •Minimum Master Degree Clinical Behavioral Scientist •One letter must be from doctorate level •Demonstrated competence in psychotherapy, sex therapy, and gender identity disorders 				<ul style="list-style-type: none"> •Masters degree or Equivalent •Competence in DSMV or ICD10 •Ability to create differential for Gender Dysphoria (GD) •Competency in Psychotherapy and in assessing and treating GD •CME in GD 		<ul style="list-style-type: none"> •At least masters degree •Competent in ICD •Can perform psychosocial assessment •Able to assess capacity to consent •Experience in Gender Dysphoria/Incongruence •Interdisciplinary team preferred
General Requirements for All Treatments	<ul style="list-style-type: none"> •Age of Majority •Patient should express understanding of risks and benefits 			<ul style="list-style-type: none"> •DSM III-R Diagnosis of Transsexualism 	<ul style="list-style-type: none"> •DSM IV diagnosis of Gender Identity Disorder • Further consolidation of Gender ID during RLT or Psychotherapy •Progress on solving problems in life 		<ul style="list-style-type: none"> •Persistent, well documented Gender Dysphoria (DSM V) or ICD-10 Transsexualism •Capacity to make informed Decision •If significant medical or mental health concerns are present, they must be reasonably well-controlled. 	<ul style="list-style-type: none"> •A single opinion from a professional who has competencies in these assessments •Physical health, Mental Health and Substance abuse disorders that interfere with patient's ability to provide informed consent are treated first •Patient is abstinent from tobacco/nicotine • Persistent well documented Gender Dysphoria/Incongruence
Requirements for Hormones	<ul style="list-style-type: none"> •At least 3 months RLT 	<ul style="list-style-type: none"> •The initiation of hormonal sex reassignment shall be preceded by recommendation for such hormonal therapy, made by a clinical behavioral scientist. 			<ul style="list-style-type: none"> •At least 3 months of documented RLT or Psychotherapy* •Indications that hormones will be used responsibly 		<ul style="list-style-type: none"> •If significant medical or mental health concerns are present, they must be reasonably well-controlled. 	
Requirements for Top Surgery	<ul style="list-style-type: none"> •Hormonal sex reassignment should precede surgical sex reassignment as its effects (patient satisfaction or dissatisfaction) may indicate or contraindicate later surgical sex reassignment. •Primary CBS must obtain peer review 				<ul style="list-style-type: none"> •At least 12 months of continuous hormone therapy 	<ul style="list-style-type: none"> •Do not need hormones prior to surgery •Breast Augmentation •Hormones recommended but not required 	<ul style="list-style-type: none"> •Persistent well documented Gender Dysphoria/Incongruence 	
Requirements for Bottom Surgery	<ul style="list-style-type: none"> •The clinical behavioral scientist making the primary recommendation in favor of genital (surgical) sex reassignment shall have known the patient, in a psychotherapeutic relationship, for at least 6 months prior to making said recommendation. That clinical behavioral scientist should have access to the results of psychometric testing (including IQ testing of the patient) when such testing is clinically indicated. •Genital sex reassignment shall be preceded by a period of at least 12 months during which time the patient lives full-time in the social role of the genetically other sex. 				<ul style="list-style-type: none"> •At least 12 months of RLT •Psychotherapy not absolute requirement, but mental health provider may require •Second letter required, must be by doctorate level provider 	<ul style="list-style-type: none"> •Interdisciplinary team approach recommended •2 Providers can sign single letter (in place of 2 separate letters) •1 letter should be comprehensive psychosocial assessment, second letter can be more brief 	<ul style="list-style-type: none"> •Hysterectomy or Orchiectomy •12 continuous months of hormone therapy as appropriate to the patient's gender goals (unless hormones are not clinically indicated for the individual) •Metoidioplasty, Phalloplasty or Vaginoplasty •Above + 12 continuous months of living in a gender role that is congruent with the patient's identity. 	<ul style="list-style-type: none"> •Gonadectomy •Reproductive Options have been discussed •At least 6 months of gender affirming hormones or gonadal suppression
Requirements for Other Surgeries	At least 6 months RLT	Not Commented on				<ul style="list-style-type: none"> •No referral from Mental health provider required, but can be helpful 		

* = SOCS these are absolute requirements, in version 6 providers can prescribe hormones without this criteria being met if it is in the service of harm reduction

Critical and Important Outcomes

Intro paragraph needed with guidance from the HERC team regarding origin of these outcomes

The prioritized outcomes for this rapid review include death from suicide or suicide attempt, gender dysphoria, depression or anxiety symptoms, suicidal ideation, quality of life, experience of discrimination or stigma, withdrawal from care or request for revision for non-aesthetic reasons.

Mental Health Outcomes

Disparities in mental health for the TGD community are well documented as described earlier. Relevant outcomes for mental health include suicide (both completed events and attempts), depression, suicidal ideation, and anxiety. Suicide and related outcomes can be identified by vital statistics, health record review for diagnoses or treatments, standardized assessments, or self-report. Multiple validated scoring

tools exist for depression (which can also inventory suicidal ideation) and anxiety symptom assessment. **Table XXX** includes a high level overview of validated commonly used scoring tools.²⁶

Table XXX. Examples of Validated Tools for Anxiety and Depression Assessment

Abridged from the American Psychological Association²⁶

Tool	Valid Age Range
Beck Depression Inventory (BDI)	Ages 13 to 80
Center for Epidemiologic Studies Depression Scale (CES-D)	Ages 6 through adulthood
Patient Health Questionnaire (PHQ-9)	General adult population
Behavioral Assessment System for Children (BASC)	Ages 2 to 21
Child Behavior Checklist (CBCL)	Ages 6 to 18
Children’s Depression Inventory	Ages 7 to 17, includes parent, teacher, and self-report components
Children’s Depression Rating Scale (CDRS)	Ages 6 to 18

Patient-reported Outcome Measures

Several systematic reviews (SRs) highlight the variation in use of patient-reported outcome measures (PROMS) across gender affirming surgeries.²⁷⁻²⁹ Many PROMS are ad hoc researcher developed questions or simple “yes/no” questions regarding satisfaction.^{28,29} Unfortunately, many PROMS are not validated in the TGD population nor for the interventions of interest for this review. In their 2021 SR, Clennon and colleagues inventory PROMS across 158 articles in GAS literature.²⁷ Only half of studies used a validated tool (51%), and of those using a validated tool, approximately only a third were validated in the TGD population.²⁷ The review also highlights the low levels of patient engagement in PROM development (8.2%).²⁷

Table XXX, abridged from Clennon and colleagues, provides a summary of commonly used tools validated in the general populations, but not in TGD populations.²⁷ Additional reviews highlight the challenges in interpretation of these tools following gender affirming genital surgeries.³⁰ For example, the female sexual function index (FSFI) was developed in sexually-active heterosexual cisgender female populations to assess sexual function, with higher scores reflecting greater sexual functioning (scoring range is 2 to 36).³¹ Scores below 26.55 reflecting clinically significant sexual dysfunction.^{30,31} However, the FSFI is also commonly used to assess TGD individuals following vaginoplasty.³⁰ While many meet the FSFI cut off for sexual dysfunction, they also report high sexual function post-operatively highlighting the need for specific validated tools in this population.³⁰ There are ongoing efforts to improve PROMS for gender affirming care including the GENDER-Q³² and the Operated Male-to-Female sexual function index.

Table XXX. Validated QOL Assessments Used in Transgender or Gender Diverse Populations

Abridged from Clennon et al., 2021

General QOL	General Psychosocial	Gender Dysphoria	Aesthetic	Voice Function	Genital Function
UCSF Gender QOL	Allgemeiner Depressions-Skala	Body Image Scale	Body-Q Chest	Voice Handicap Index	Operated Male-to-Female Sexual function index
	Essen Resource Inventory	Utrecht Gender Dysphoria Scale	Patient and Observer Scar Assessment Scale	Transgender Self-Evaluation Questionnaire	Self-evaluation of vaginoplasty
	Depression Anxiety Stress Scale	Transgender Congruence Scale	Vancouver Scar Scale	Trans Woman Voice Questionnaire	

Withdrawal from Treatment or Request for Revision for Non-aesthetic Indications

The decision to withdrawal from gender affirming treatment or request a revision after surgical intervention (for non-aesthetic reasons) may reflect an array of reasons including lack of access to care or other barriers to continued care, substance misuse, other worsening mental health conditions or regret.³³

Regret after surgical procedures (not specific to gender affirming care) is common with estimates of 1 in 7 individuals across a wide range of procedures (including cancer resections), and to up to 1 in 5 older adults following spine surgery.^{34,35}

Regret after gender affirming surgery could potentially worsen an individual's health or quality of life and warrants research to identify the prevalence and risk factors and ensure adequate services in longer term time periods.^{36,37} Societal stigma, family pressures, and other external factors are associated with the decision to de-transition, along with reports of inadequate support post-operatively, and surgical complications.^{38,39}

In one of the earliest studies on regret, based on the clinical practice of a single provider and a literature review from 1993, the prevalence of regret was reported to be 1 to 1.5% for trans women, and 0 to < 1% for trans men. The author noted that many regrets were temporary.³⁷ In updated work from Kuiper and Cohen-Kettenis in 1998, based on their prior research and interviews with a small cohort of individuals with regret, they proposed more expansive definitions based on role reversal or expression of feelings:³⁹

- Clear regret: openly expressed, role reversal either surgically or returning to former gender role
- Regret uncertain: do not reverse gender role, but disappointed with their result, or might consider a different surgery
- Regret: role reversal without expressing feelings of regret, happy with their decision, consider themselves transgender, but live as former gender
- Regret assumed by others: Unfavorable social circumstances or psychological disturbances with concern from others (e.g., family, clinicians) that despite the patient not expressing regret, that regret may be a factor

These older research frameworks of “regret” do not include the growing population of non-binary or gender non-conforming individuals.^{16,17}

The report of withdrawal from treatment or request for revision may be determined from chart review, self-report, or clinic or national registries. Studies may also only report regret without additional details. As there is no single, validated tool to assess regret studies may use single item questions, review chart records or registries for surgeries to return to prior gender, or qualitative interviews.

Clinical Guidelines

HERC Team.

Also referred to as facial gender surgery or facial feminization surgery, facial confirming surgery was not deemed medically necessary in the WPATH Standards of Care, 7th edition.⁴⁰ In a systematic review and evidence-based consensus guidelines from the International Facial Gender Symposium in 2022, the authors used a 1999 framework from Stanford University on medical necessity including decision authority, purpose, scope, evidence, and cost effectiveness to review the role of Facial Gender Confirmation Surgery.⁴¹ The guideline framed FGCS as an important component of GAC in terms of ability to treat internal distress or distress from social rejection and violence.⁴¹ The authors also comment, without specific evidence, on the anecdotal reports from high volume surgeons of a phase of depression following facial surgery that can last days to weeks and is likely multifactorial in origin, highlighting the need for longer term follow-up for these patients.⁴¹

Aim of This Report

This rapid review aims to summarize the impact of gender-affirming interventions on outcomes related to quality of life, mental health (e.g., depression, suicidality), withdrawal from treatment (not related to aesthetic or cosmetic outcomes), and request for revision (for non-cosmetic revisions) for the TGD population in light of new guidance on interventions following the release of WPATH Standards of Care, 8th edition.

METHODS

The following section summarizes the overall scope of this review, including Key Questions (KQs), inclusion and exclusion criteria, and a brief overview of the methods used to conduct the review. Additional information regarding methods can be found in [Appendix A](#).

Key Questions

KQ1. What is the overall impact of receiving gender-affirming medical interventions for adults in this population?

KQ2. What is the overall impact of receiving gender-affirming medical interventions for adolescents in this population?

KQ3. Does the overall impact of access to gender-affirming medical interventions vary by

- a. Sex assigned at birth
- b. Age of initiation of gender-affirming medical intervention(s)
- c. Types of interventions available to patients in the study

Study Eligibility Criteria

Table ## summarizes the framework used to inform study selection for this rapid evidence review. See Appendix A for more detailed information.

TABLE ##: Scoping Framework

CATEGORY	INCLUDED	EXCLUDED
POPULATION	Adults and adolescents who are transgender or gender diverse (regardless of hormone therapy status) who seek gender-affirming medical intervention(s)	
INTERVENTION(S)	Gender-affirming medical interventions, including any combination of medication, speech therapy, physical therapy, behavioral health care, hair removal or surgical procedures selected based on patient's needs	Services related to fertility preservation or infertility treatment, medication therapy alone (e.g., puberty blocking medications, cross sex hormones)
COMPARATORS	No gender affirming medical interventions, delayed (waitlist) care, primary care and behavioral care without other interventions, medication therapy alone, population averages	
OUTCOMES	<p>Critical: Death from suicide, suicide attempt, gender dysphoria^a</p> <p>Important: Depression or anxiety using validated scales, suicidal ideation, QOL outcomes using validated scales^b, discrimination or experience of stigma, withdrawal from treatment, revision for reasons other than aesthetic dissatisfaction</p>	<p>Considered but not selected: Medication complications, physical or social de-transition, procedure-related complications, satisfaction</p>

STUDY DESIGNS

-SRs of RCTs or comparative cohort studies;
-RCTs;
-Registries from national databases or large datasets (i.e., > 300 individuals)

Case reports, case series, cross-sectional analyzes, registries of under 300 individuals

Selection of studies based on methodological rigor by outcome; sample size threshold may be adjusted based on search results

FOLLOW-UP

Outcome reported at ≥ 12 months after receipt of initial intervention

Outcome reported at < 12 months after receipt of initial intervention

Notes.^a Gender dysphoria when measured as an outcome rather than a medical diagnosis. ^b Validated quality of life (QOL) assessments to the transgender or nonbinary population are limited, many studies use validated QOL tools broadly applicable but may not capture fully the extent of impacts to transgender individuals.

Abbreviations: QOL: quality of life; RCTs, randomized controlled trials; SRs: systematic reviews.

Methods Overview

To answer the KQs, we searched multiple clinical evidence databases (i.e., Ovid MEDLINE, Ovid APA PsycInfo, Cochrane Databases of Systematic Reviews) on April 21, 2023, for published studies evaluating outcomes for gender-affirming medical interventions. We also hand searched the journals: Annals of LGBTQ Public and Population Health, the International Journal for Transgender Health (and its former title the International Journal for Transgenderism), and Transgender Health. Reference lists of included studies were reviewed for published studies and searches in Google Scholar were also conducted. To meet eligibility criteria, studies had to be available in English, include follow-up of at least 12 months, and be published 2000 or later. Two reviewers independently examined abstracts and full-text articles for inclusion. Disagreements were resolved through consensus or by a third reviewer. Full search strategies are available in Appendix A.

We summarized findings from eligible studies by intervention.

EVIDENCE REVIEW

The following results section organizes findings by KQs (i.e., adults, adolescents) then by outcomes

Within each outcome, results are summarized by intervention.

The original search identified 2,854 publications of which 2,608 were unique. After dual review by title and abstract, 230 underwent full text review. Ultimately we identified 29 SRs and 5 cohort studies and

summarized findings from 11SRs and 3 cohorts with extractable data.^{28-30,36,40-67} For inclusion in this review we prioritized SRs with reproducible search strategies, clear inclusion and exclusion criteria, use of comparative or longitudinal studies, and extractable data. **Figure XX** is a PRISMA diagram that displays the flow of citations from search to inclusion.⁶⁸

FIGURE XXX

PRISMA 2020 flow diagram.⁶⁸

Several SRs only summarized the outcomes reported by individuals studies in narrative form without any extractable data, or outcomes from a non-validated tool, were not comparative, or not longitudinal in nature.^{28,29,43,44,46-49,53,55-57,59,60,63,64} Three publications were included in more recent SRs.^{51,62,66} We did not fully cross reference each individual study across the multiple SRs so there is a potential for the same study to be included in multiple SRs.

We identified 10 SRs in adults on gender affirming surgeries (4 SRs, 1 cohort), facial confirmation surgery (2 SRs), breast augmentation (1 SR), vaginoplasty (1 SR), and vocal interventions (2 SRs) in adults.^{30,36,40-42,50,52,54,58,61,65} We did not identify any SRs with extractable data for phalloplasty. We identified 1 SR on mental health in adolescents which only summarized data narratively, but given the absence of any other sources meeting inclusion we provide the findings of their narrative review.⁴⁵ Two cohort studies on mastectomy in adolescents with smaller sample sizes (< 300) were also included given the absence of any other sources for this intervention in this age group. **Table XXX** provides an overview of included studies by intervention and outcome.

The current search did not identify any studies reporting outcomes of discrimination or experience of stigma after gender affirming interventions.

TABLE XXX

Overview of Summarized Studies

INTERVENTIONS	Death from Suicide or Suicide Attempt	Gender Dysphoria	Depression or Anxiety Symptoms	Quality of Life	Withdrawal or Revision
ADULTS					
Gender Affirming Surgeries	n 1 SR,			n 1 SR	n 1 SR
Gender Affirming Hormones and Surgery	n 1 cohort				
Gender Affirming Genital Surgery			n 1 SR		
Breast Augmentation					n 1 SR
Facial Gender Confirmation Surgery				n 2 SRs	

INTERVENTIONS	Death from Suicide or Suicide Attempt	Gender Dysphoria	Depression or Anxiety Symptoms	Quality of Life	Withdrawal or Revision
Vaginoplasty				n 1 SR	
Endoscopic Glottoplasty				n 1 SR	
Speech Therapy				n 1 SR	
ADOLESCENTS					
Gender Affirming Hormones and Surgery*			n 1 SR		
Mastectomy		n 2 cohorts			

Note: *all individuals underwent surgery at ≥ 18 years of age

Adults

Death from Suicide or Suicide Attempt

Gender Affirming Surgery

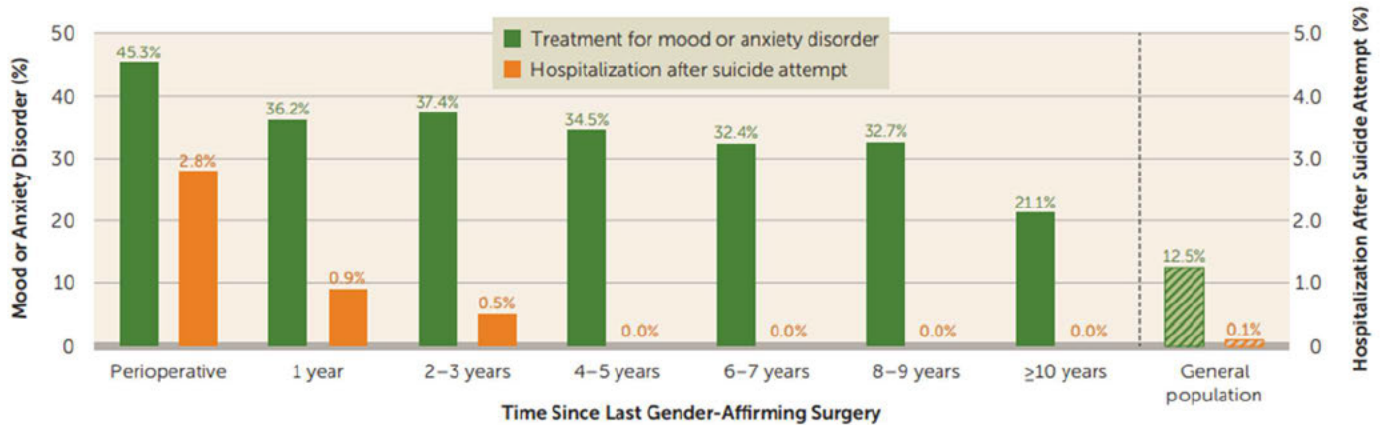
In their SR of studies published through 2015, Marshall and colleagues also only identified 1 longitudinal, comparative study from 2011 on suicide or non-suicidal self-injury after gender affirming surgery (surgical details not specified) from Sweden (from 2011).⁵² Rates of suicide deaths and attempts for the transgender population (n = 324) exceeded those from a population cohort matched by age and birth sex or reassigned sex.⁵² Suicide deaths for transgender individuals were 2.7% compared to 0.1% for matched controls; with suicide attempts also higher (7.9% vs. 1% matched controls).⁵² No statistical analysis was reported.⁵² The authors of the SR highlight many potential factors for this observed relationship including isolation, experience of victimization, depression, or lack of social support that may precede surgery and persist following it, along with inadequate support post-surgery from the healthcare system.⁵² The authors of the SR did not include details about whether the original study attempted to address potential confounding factors (e.g., pre-existing depression, severe depression).⁵²

Gender Affirming Hormone and Surgery

Branstrom and Pachankis analyzed mental health utilization including for care after suicide attempt by time since treatment or surgery for a national cohort of individuals with gender incongruence from 2005 to 2015 in Sweden, compared to remaining population of Sweden.⁶⁵ Surgical intervention categories included breast or chest surgery, surgery of the reproductive organs, laryngeal, or dermatological options.⁶⁵ Of the overall cohort of 2,697 individuals with gender incongruence, 1,885 (70%) received hormone treatment, 1,018 (37.9%) received surgical treatment, and of those receiving surgery 97% also received hormone treatment.⁶⁵

Compared to the national population without a diagnosis of gender incongruence (N = 9,744,645), individuals with a diagnosis of gender incongruence remained more likely to receive care and treatment for mood or anxiety disorder and to be hospitalized after suicide attempt in the year 2015.⁶⁵ However, when comparing rates over time, at 4 to 5 years post- surgery the rate of hospitalization for suicide is similar or lower compared to the general population.⁶⁵

FIGURE 1. Prevalence of treatment for mood or anxiety disorders (health care visit or antidepressant or anxiolytic prescription) and hospitalization after suicide attempt in 2015 among individuals with a gender incongruence diagnosis, by number of years since last gender-affirming surgery



In an analysis of the subgroup who received surgery, the odds of mental health treatment receipt was reduced as time from surgery increased (aOR 0.92; 95% CI: 0.87 to 0.97; *p* value not reported).⁶⁵ However, the effect of surgery on suicide attempt in the single year of 2015 was not statistically significant (aOR 0.87; 95% CI: 0.61 to 1.24; *p* value not reported).⁶⁵ The authors note the small number of suicide attempts resulting in hospitalization (22 in the year 2015) for this population.⁶⁵ Analyses were adjusted for age, gender, education, income, urbanity, and country of birth.⁶⁵

In reaction to several letters to the editor, the authors completed additional analyses for those with gender incongruence receiving and not receiving surgery.⁶⁵ There was no statistical difference in terms of health care utilization, prescriptions, nor suicide attempts.⁶⁵

Depression or Anxiety Symptoms

Gender Affirming Genital Surgery

The current search did not identify any SRs reporting depression symptom outcomes. In a SR of studies published through June 2015, Millet and colleagues identified 5 longitudinal studies reporting on anxiety symptoms after gender affirming genital surgery (surgical details not specified).⁵⁴ Nearly all studies (4 of the 5) used the same tool (Symptom Checklist Revised (SCL-90-R)).⁵⁴ The SCL-90-R assesses severity of psychological symptoms (e.g., anxiety, depression, phobia, somatization, psychoticism) with higher scores reflecting greater symptom severity.⁶⁹ Table XXX summarizes the impact of gender affirming genital surgery on anxiety symptoms. Anxiety symptoms improved (3 studies from 1 to 4 years post-surgery), and worsened (1 study at 6 months post-surgery).⁵⁴ The remaining study, using a different tool (i.e., State-Trait Anxiety Inventory), observed improvements for trans men, but worsening symptoms for trans women at year post-surgery.⁵⁴ The authors highlight the younger age of participants in this study (median age pre-CHT was 13.6, post-surgery was 20.7) compared to the other studies where average ages ranged from 23 to 59 years.⁵⁴ No statistical analysis was reported for any of the included studies.⁵⁴

TABLE XXX.

Anxiety Symptoms following Gender Affirming Genital Surgery⁵⁴

Studies using SCL-90-R	Participants	Anxiety Symptom Severity
Smith et al., 2001 The Netherlands	21 TG: TW 8, TM 13 1–4 years post	pre-GCGS vs. post-: 15.8 vs. 12.0
Smith et al., 2005 The Netherlands	222 TG: 146, TW 76 TM 1–4 years post	pre-CHT vs. post-GCGS: 15.0 vs. 13.0
Heylens et al., 2014 Belgium	57 TG :46 TW, 11 TM 1 to 12 months post	pre-CHT vs. post GCGS: 17.0 vs. 13.5
Ruppín & Pfafflin et al., 2015 Germany	71 TG: 35 TW 36 TM 13 years post	pre-CHT vs. post-GCGS: 0.47 vs. 0.18

Abbreviation: GCGS: gender confirming genital surgery; CHT: cross sex hormone treatment; SCL-90: Symptom Checklist Revised; TM: trans man; TW: trans woman.

Withdrawal from Treatment or Non-aesthetic Revision

Gender Affirming Surgeries

The current search did identify SRs reporting specific information on withdrawal from treatment. Revisions for reasons other than aesthetics were also not well described. We did identify a recent SR (from studies published through 2020) on regret that provided insights into this concept.³⁶ In a SR with meta-analysis of studies published through May 2020, 27 studies provided data on regret after gender affirming surgery.³⁶ The included studies represent data from 7,928 individuals.³⁶ In studies providing additional details, 2,578 underwent masculinizing procedures, 5,136 feminizing surgeries, the remainder reflecting studies pooling all gender affirming procedures together.³⁶ Follow-up ranged from 0.8 years to 9 years after surgery.³⁶ Assessment of regret, as there is no validated tool, included single questions with limited responses (e.g., yes, sometimes, no, all the time, most certainly, most likely, definitely not) or semi-structured interviews.³⁶

Across the entire cohort of individuals undergoing gender affirming surgeries of any type, regret was identified in 77 persons (12 trans men, 57 trans women, 8 not-specified) who reported it sometimes or always of the 7,928 total population included across the studies.³⁶ The most common reason for regret was difficulty, dissatisfaction, or acceptance of life in the new gender role. **Table XXX** provides the overall estimate and estimates by type of surgery.³⁶ The overall pooled estimate across all gender-affirming surgeries was 1% (95% CI, < 1% to 2%) which aligns with historical estimates.³⁶

The authors performed a sensitivity analysis removing studies with small sample sizes, and the overall estimate for regret after gender-affirming surgeries did not change.³⁶ The authors also identified a potential for publication bias and used techniques (e.g., trim and fill method) to assess the impact of missing publications on their overall estimate through use of an additional 14 hypothetical studies without change in the overall estimate.³⁶

The authors highlight findings from the qualitative interviews of individuals with regret commonly noting challenges after surgery in acceptance from friends and families or social networks driving their regret.³⁶

TABLE XXX

Estimates of Regret after Gender-affirming Surgeries (from Bustos et al., 2021)³⁶

	Regret
After gender-affirming surgery (any type)	1% (95% CI, <1% to 2%; I2 = 75.1%)
After masculinizing surgeries	<1% (95% CI, <1% to <1%, I2 = 28.8%)
After feminizing surgeries	1% (95% CI, <1% to 2%, I2 = 75.5%)
After vaginoplasty	2% (95% CI, <1% to 4%, I2 = 41.5%)
After mastectomy	<1% (95% CI, <1 to <1%, I2 = 21.8%)

Abbreviations; CI: confidence interval; GAS: gender affirming surgery

Breast Augmentation

Sijben and colleagues report on revision for non-aesthetic reasons following breast augmentation from a cohort of 527 trans women or nonbinary individuals from a single center in the Netherlands as part of a SR.⁵⁸ Completion of genital gender-affirming surgery was high in this cohort (96.8%).⁵⁸ Over a median of 11.2 years of follow-up, only 5 individuals reported regret with their transition (0.94%).⁵⁸ Of those with regret, three opted for implant removal, one underwent removal due to implant rupture prior to report of regret, and one had expressed regret, but did not undergo removal.⁵⁸

Quality of Life

Gender Affirming Surgery

In their SR of studies published through 2017 on quality of life after GAS for trans women, Weinforth and colleagues report on comparative findings from 6 studies (2 prospective pre-surgery vs. post-surgery, 4 postoperative compared to cisgender women controls) using the SF-36, WHOQOL-100, and a German tool, the Fragebogen zur Lebenszufriedenheit (FLZ).⁶¹ Quality of life after surgery for trans women using the SF-36 statistically improved in the multiple components of the tool in 2 studies (authors of the SR report *p* values only).⁶¹ In 2 studies using the WHOQOL-100, statistically significant improvements in sexual activity, psychological domains, and social relationship were observed post operatively compared to preoperatively (*p* values also only reported).⁶¹ The authors also observed statistically significant decreases in physical health and independence post-operatively.⁶¹ In 1 study, postoperative trans women were no different compared to cisgender women in sexual activity (65.85 vs. 66.28; *p* value > .05), body image (64.64 vs. 65.47; *p* value > .05), and quality of life scores (67.87 vs. 69.49; *p* value > .05) using the WHOQOL-100.⁶¹ Using the FLZ, postoperative trans women also scored similarly to the cisgender population in terms of health.⁶¹ The authors of the SR note high heterogeneity across studies and a median drop-out rate of 56% (range 12 to 77%).⁶¹

The current search did not identify any SRs on QOL specific to trans men after interventions or in nonbinary or non-conforming populations.

Facial Gender Confirmation Surgery

The search identified two SRs (1 from 2016, 1 from 2022) on QOL outcomes after facial gender confirmation surgery (also known as facial feminization surgery).^{40,41} While the more recent SR from Coon and colleagues also includes the 2017 SR by Berli et al., each provides different extractable data so are both included.^{40,41}

In a SR of studies published through 2016 prepared for the 8th edition of the WPATH Standards of Care, the authors note the use of a standardized, validated QOL assessment was rare.⁴⁰ One study included in their review provided QOL outcomes using the FFS Outcome Score.⁴⁰ The FFS Outcome score ranges from 0 (lower) to 100 (better) and includes questions across physical, emotional, and social aspects of life following surgery.⁴⁰

Compared to trans women undergoing gender affirming surgery without facial feminization or no surgical intervention, recipients of facial confirming surgery (alone or with other surgical affirming procedures) reported greater QOL (FFS Outcome Score 76 ± 17.7 vs. 44.3 ± 15.7 ; $p < 0.01$).⁴⁰ The authors of the SR list additional studies reporting QOL outcomes, but do not include extractable data that could be summarized in this rapid review.⁴⁰

In the 2022 SR on facial gender confirmation surgery, the authors identified the above study and 1 newer publication reporting comparative outcomes before and after facial gender confirmation surgery using the FFS Outcome Score, which went from 48.0 ± 12.3 pre-operatively to 76.5 ± 14.6 at long-term (at least 6 months) follow up (statistical analysis not reported).⁴¹

Vaginoplasty

In an SR of studies published through 2020, sexual function quality of life using the FSFI (7 studies) compared to a single study with scores from cisgender women.³⁰ While the assessments were obtained post-operatively, the authors do not make clear the follow-up time.³⁰ The authors note the limitations of the FSFI in the TGD population, specifically its use in sexually inactive individuals.³⁰ They report out FSFI findings for each study without any statistical analysis.³⁰ Overall, the total scores were lower (worse) for the TGD than the comparator study of cisgender women.³⁰ When the comparison is limited to only sexually active individuals, the FSFI scores improve for TGD, but still are below those reported among cisgender women.³⁰ The authors note that the FSFI may not be appropriate to use to assess sexual function in this population as many individuals report high function overall even if their FSFI scores are low or are not currently sexually active.³⁰

Endoscopic Glottoplasty

In a SR of studies on endoscopic glottoplasty published through XXX, the authors identified 14 cohort studies ($n = 566$ individuals) with mean follow-up of 15.6 months.⁴² The included studies reported voice-related quality of life (6 studies) using the Voice Handicap Index-30, and additional 2 used the Transgender Self Evaluation Questionnaire (TSEQ).⁴² In studies using the voice handicap index, 2 observed statistically significant improvements, however only 1 went below the threshold for minimal vocal disorder.⁴² In the 2 studies using the TSEQ both observed statistically significant reductions postoperatively (less psychosocial functioning impact). No meta-analysis was performed for voice-quality of life outcomes.⁴²

Speech Therapy

In a SR of studies on voice therapy for trans women published through XX, 3 studies report outcomes using validated tools.⁵⁰ The TSEQ was used in 2 studies, and the Transsexual Voice Questionnaire (TVQ) in 1 study, with the remaining 11 studies not reporting relevant outcomes to this review.⁵⁰ The number of sessions across studies ranged from 5 to 90.⁵⁰ No study performed statistical analysis.⁵⁰ The authors note in the 2 studies using the TSEQ participants improved in 1 study, from a score of 106 to 53 (out of a

possible score of 120; lower being better) at 2 months after ending therapy but in the other study, there was not sufficient data (only 4 of 25 completed the survey).⁵⁰ In the study using the TVQ, scores also improved (from 100/120 to 81/120) post therapy.⁵⁰

Adolescents or Youth

We did not identify any SRs with extractable data on gender affirming medical interventions among adolescents and youth. Given that paucity of data, we summarize the findings from a single identified SR (that includes narrative reports from 2 longitudinal cohorts) and 2 separate individual cohorts with smaller sample sizes (< 300 individuals) reporting outcomes of mental health and a component of gender dysphoria, chest dysphoria.^{70,71}

Mental Health Outcomes

Gender Affirming Hormones and Surgery

In an SR of studies published through 2016 reporting mental health outcomes for transgender youth, the authors identified 2 studies providing longitudinal mental health outcomes.⁴⁵ The first cohort followed Dutch youth (n = 55) through diagnosis, hormone therapy (at ≥ 16 years), and 1 year after gender affirming surgery (occurred ≥ 18 years of age). The authors of the SR report that outcomes “steadily improved” on the Children’s Global Assessment Scale, Child/Adult Behavioral Checklist, and the Youth/Adult self-report.⁴⁵ None of the youth reported regret.⁴⁵ The second cohort study followed children in the US who self-identified as TGD and who under the age of 13, prior to any medical or surgical intervention, all socially transitioned (n = 73). Compared to their cisgender siblings and a cohort of peers, rates of depression and anxiety were statistically no different.⁴⁵

Chest Dysphoria or Gender Dysphoria

Two studies report on chest dysphoria, a component of gender dysphoria. In the initial publication of this novel assessment tool, researchers at a single center in the US developed a scale to assess chest dysphoria, in trans male youth aged 14 to 25.⁷¹ Chest dysphoria scoring ranges from 0 to 51 (higher scores equating to more distress).⁷¹ The authors reported outcomes for those who underwent chest reconstruction (i.e., mastectomy) compared to similar aged patients at the clinic who had not yet completed surgery.⁷¹ Trans male youth with a history of chest reconstruction reported less distress than those not undergoing surgery (mean 3.3 vs. 29.6; *p* value <.001).⁷¹

In a subsequent study at a different center, outcomes from 36 post-surgical patients were compared to 34 matched controls (average age 18 for both groups).⁷⁰ At 3 months post-surgery the chest dysphoria scores were also lower for the surgical group (3.8 vs. 30.5; no statistical analysis reported).⁷⁰ This study also reported outcomes using the Transgender Congruence Scale (TCS). The TCS assesses gender acceptance and congruence with higher scores reflecting greater congruence.⁷² At 3 months the TCS scores were higher for the surgery group (44.4) compared to the control (36.9).⁷⁰

Evidence Summary and Limitations

This review prioritized the inclusion of methodologically robust systematic reviews on interventions for gender affirming care in the TGD population to identify the overall impact of these components of gender affirming care. Table XXX provides a cross walk across summarized studies by outcome and specific intervention for both key questions.

TABLE XXX

Overview of Summarized Studies

INTERVENTIONS	Death from Suicide or Suicide Attempt	Gender Dysphoria	Depression or Anxiety Symptoms	Quality of Life	Withdrawal or Revision
ADULTS					
Gender Affirming Surgeries	Unclear			Beneficial	Uncommon (~1%)
Gender Affirming Hormones and Surgery	May improve over time				
Gender Affirming Genital Surgery			Likely beneficial		
Breast Augmentation					Uncommon (< 1%)
Facial Gender Confirmation Surgery				Beneficial	
Vaginoplasty				Mixed	
Endoscopic Glottoplasty				Beneficial	
Speech Therapy				Beneficial	
ADOLESCENTS					
Gender Affirming Hormones and Surgery*			Likely beneficial		
Mastectomy		Beneficial			

Note: *all surgeries occurred at 18 years or older and included outcome is mental health broadly

KQ1: Adults

The current search identified 10 SRs in adults with robust methodologies and extractable data, with each SR reporting at least 1 relevant outcome, including suicide or suicide attempt, anxiety, quality of life, and withdrawal from treatment, request for surgical revision, or regret. None of the included SRs reported on depression, suicidal ideation, or experience of discrimination or stigma.

Death from suicide or suicide attempts remain higher for the TGD population from 1 SR (which found only 1 longitudinal study) while in 1 national registry, over time after surgery rates of suicide or suicide attempts are similar to the overall population.

Overall, there is a trend of improvement in anxiety and quality of life, after gender affirming surgeries overall and in SRs of specific interventions (e.g., facial confirmation, vocal treatments). While rates of withdrawal from treatment or request for revision were not commonly reported, rates of regret were low after gender affirming surgery (1%) and breast augmentation (< 1%).

The absence of benefit to quality of life after vaginoplasty may be limited by the lack of a validated tool in this population and use of a cisgender validated tool to assess outcomes.

The low rates of regret following a complicated and prolonged road to achieve treatment to address gender incongruence likely augments the scarcity of long term outcomes for mental health outcomes following surgical interventions.

KQ2: Adolescents

Mental Health Outcomes

As gender affirming surgeries are rare in adolescents, the search only identified 1 SR on mental health outcomes after gender affirming surgeries that occurred when the individuals were over 18 but their treatment course (e.g., counseling, hormones) started earlier. Overall, in 2 longitudinal cohorts who had experienced chest surgery, mental health outcomes were improved.

Review Limitations

Longitudinal, comparative data in this population is scarce in this population and early studies exclude important confounders, particularly for outcomes like suicide. Practice patterns and research methodologies have changed over time so earlier cohorts may use older tools or definitions not in current use, limiting comparisons over time. Many of the authors of the included SRs addressed the methodological limitations of this body of literature, including small sample sizes, reliance on small cohorts or case series, absence of randomized controlled trials, variable length of follow-up, lack of standardized assessment tools or reporting standards, and the use of PROMs not validated in this population. Many authors highlight the need for greater standardization in outcome reporting.^{40,44,55}

Additionally, this body of literature largely takes place in high income countries, with less economic, racial, and ethnic diversity compared to the US. Many of the European centers require extensive (e.g. months to years) of evaluation and counseling prior to receipt of services. The outcomes of studies from clinics with waitlists or prolonged evaluation procedures may reflect a healthier, more motivated, or more socially supported population which could be at lower risk of both procedural and psychosocial complications.

Not all studies specifically address the inclusion of non-binary or gender diverse individuals, a growing proportion of the TGD population.^{16,17} Future work is needed to understand the impact of gender affirming interventions on this specific population.

While several SRs pooled all gender affirming surgery together, for the purpose of this review that may be more applicable to the key questions as the aim was to assess the overall impact of gender affirming interventions. Future work will review the specific procedural complications from individual interventions or surgeries.

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APPENDIX A. METHODS

Key Question Methods

Search Strategy

We conducted searches in several clinical bibliographic databases to identify relevant publications; registry studies needed to be conducted in a country deemed as Very High Human Development by the United Nations.⁷³ All database searches were run on April 21, 2023. We limited the search to peer-reviewed publications in English published since January 1, 2000. Search strategies for the individual databases appear below.

We also hand searched 3 topic specific journals: Annals of LGBTQ Public and Population Health, the International Journal for Transgender Health (and its former title the International Journal for Transgenderism), and Transgender Health. Reference lists of included studies were also reviewed for published studies and searches in Google Scholar were also conducted.

Ovid MEDLINE(R) ALL <1946 to April 20, 2023>

- 1 *Gender Dysphoria/ 796
- 2 (gender-dysphor* or gender-varian* or gender-incongru* or gender-nonconform* or gender-nonconform* or gender-minorit* or gender-questioning).ti,ab,kf. 5020
- 3 (gender* adj1 (dysphor* or varian* or incongru* or nonconform* or non-conform* or atypical or minorit* or questioning or fluid* or expansi*)).ti,ab,kf. 5335
- 4 *transgender persons/ 5563
- 5 (transgender* or transsexual* or transexual* or genderqueer or trans-gender* or trans-sexual* or gender-queer or gender-variant or two-spirit person* or nonbinary or non-binary or trans-person* or transperson* or trans-people* or transpeople*).ti,ab,kf. 14727
- 6 (trans adj2 (person* or people* or individual* or m?n or wom?n)).ti,ab,kf. 1383
- 7 (trans-m?n or trans-wom?n or transm?n or transwom?n or transperson* or trans-person* or transpeople* or trans-people*).ti,ab,kf. 1757
- 8 (transfeminine or transmasculine or trans-feminine or trans-masculine).ti,ab,kf. 494
- 9 (bigender or bi-gender or pangender or pan-gender or genderfluid* or gender-fluid* or gender-expansi* or agender).ti,ab,kf. 218
- 10 ("male-to-female" or "female-to-male").ti,ab,kf. 158199
- 11 or/1-10 174306
- 12 ((confirm* or affirm* or reaffirm* or re-affirm* or reassignment or change or transition* or transform*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,kf. 42268
- 13 exp *Sex Reassignment Procedures/ 1027

- 14 ((sex-confirm* or sex-affirm* or sex-reaffirm* or sex-reassignment or sex-change or sex-transition* or sex-transform*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,kf. 612
- 15 ((gender-confirm* or gender-affirm* or gender-reaffirm* or gender-reassignment or gender-change or gender-transition* or gender-transform*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,kf. 1355
- 16 ((masculini* or masculi?ing or femini?ation or femini?ing or demasculi* or defemin*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,kf. 456
- 17 exp *Reconstructive Surgical Procedures/ 192344
- 18 (reconstructive adj2 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,kf. 27508
- 19 *Rhytidoplasty/ or (facelift* or face lift*).ti,ab,kf. 4160
- 20 (facial* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*)).ti,ab,kf. 7455
- 21 (face* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*)).ti,ab,kf. 2933
- 22 (brow* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or reconstruct* or refin*)).ti,ab,kf. 315
- 23 (forehead* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or reconstruct* or refin*)).ti,ab,kf. 479
- 24 *Rhinoplasty/ or rhinoplast*.ti,ab,kf. 11196
- 25 (nose* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or reconstruct* or refin*)).ti,ab,kf. 2136
- 26 *Genioplasty/ or genioplast*.ti,ab,kf. 1015
- 27 (chin* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*)).ti,ab,kf. 1794
- 28 *Laryngoplasty/ or (laryngoplast* or glottoplast* or thyroplast* or phonosurger*).ti,ab,kf. 1865
- 29 (Chondrolaryngoplast* or (trachea* adj2 shav*)).ti,ab,kf. 59
- 30 (neck* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct* or refin* or reconstruct*)).ti,ab,kf. 13322
- 31 *Body Contouring/ or (body contour* or body-contour* or chest contour* or chest-contour*).ti,ab,kf. 1921
- 32 (body* adj3 (masculini* or masculi?ing or femini?ation or femini?ing or defemini* or demasculi*)).ti,ab,kf. 79

- 33 *Lipectomy/ or (lipectom* or liposuction*).ti,ab,kf. 5330
- 34 (fat transfer* or fat graft*).ti,ab,kf. 4440
- 35 exp *mammoplasty/ or mamm?plast*.ti,ab,kf. or *Breast Implantation/ 17247
- 36 (breast adj2 (reconstruct* or augment* or reduc* or implant* or enhanc*).ti,ab,kf. 25589
- 37 exp *mastectomy/ or mastectom*.ti,ab,kf. 34469
- 38 (breast adj2 remov*).ti,ab,kf. 657
- 39 (chest* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*).ti,ab,kf. 3357
- 40 (genital* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*).ti,ab,kf. 2217
- 41 (vaginoplast* or neovagina*).ti,ab,kf. 1709
- 42 *Phalloplasty/ or *Penile Transplantation/ or *Penile Implantation/ or *Penile Prosthesis/ 1579
- 43 (phalloplast* or neophall* or glansplast* or glans-plast*).ti,ab,kf. 744
- 44 ((peni* or testic*) adj2 (prothes* or implant* or transplant*).ti,ab,kf. 1716
- 45 (inflat* adj2 prothes*).ti,ab,kf. 994
- 46 gluteal implant*.ti,ab,kf. 64
- 47 ((esthetic or aesthetic or cosmetic) adj2 (procedure* or surg* or service* or operation* or intervention*).ti,ab,kf. 9686
- 48 ((calf or calve or silicon* or pectoral or chin or nose or cheek) adj4 (implant* or augmentation* or prosthes*).ti,ab,kf. 7602
- 49 ((esthetic or aesthetic or cosmetic or collagen) adj2 inject*).ti,ab,kf. 1390
- 50 *Hair Removal/ 1475
- 51 (hair adj2 (remov* or reduc* or transplant*).ti,ab,kf. 3327
- 52 (epilation* or depilation* or electrolys*).ti,ab,kf. 8877
- 53 *voice training/ 1027
- 54 (voice* adj3 (training or retraining or coaching or therap* or masculini* or femini*).ti,ab,kf. 2067
- 55 (vocal* adj3 (training or retraining or coaching or therap* or masculini* or femini* or surg*).ti,ab,kf. 1212
- 56 *speech therapy/ or (speech adj2 therap*).ti,ab,kf. 8226
- 57 or/12-56 364499

- 58 11 and 57 5143
- 59 Health Services for Transgender Persons/ 196
- 60 ((gender* or gender nonconforming or gender-nonconforming or gender non-conforming or trans or transgender or nonbinary or non-binary) adj7 (confirm* or affirm* or reaffirm* or re-affirm* or identity-affirm* or identity-confirm* or identity-reaffirm*)).ti,ab,kf. 5425
- 61 (gender-confirm* or gender-affirm* or gender-reaffirm* or gender-reassignment or gender-change or gender-transition* or gender-transform*).ti,ab,kf. 3334
- 62 (sex-confirm* or sex-affirm* or sex-reaffirm* or sex-reassignment or sex-change or sex-transition* or sex-transform*).ti,ab,kf. 1442
- 63 or/59-62 7726
- 64 *Suicide/ or *Suicide, Attempted/ or *Suicide, Completed/ or *Resilience, Psychological/ or *Depression/ or *Self-Injurious Behavior/ or *Self Mutilation/ or *Stress, Psychological/ or *Anxiety Disorders/ or *Mood Disorders/ or *Depressive Disorder/ 285787
- 65 (suicide* or suicidal* or self-injur* or self injur* or cutting or self-mutilat* or self mutilat* or depressi* or anxiety).ti,kf. 324378
- 66 (regret* or detransition* or desist or desist?r* or desistance).ti,ab,kf. or (discontinu* or revers*).ti,kf. 144651
- 67 or/64-66 598325
- 68 11 and 67 7203
- 69 or/58,63,68 17824
- 70 (exp Animals/ not Humans/) or (baboon\$1 or bovine\$1 or canine\$1 or cat\$1 or chimpanzee\$1 or cow\$1 or dog\$1 or feline\$1 or fish or goat\$1 or hens or macque\$1 or mice or monkey\$1 or mouse or murine\$1 or ovine or pig\$1 or porcine or primate\$1 or sheep or rabbit\$1 or rat or rats or rattus or rhesus or rodent\$1 or zebrafish).ti.5563447
- 71 69 not 70 15170
- 72 Registries/ or (registry* or registries or database* or data center* or data warehouse*).ti,kf. 167793
- 73 ((regist* or population* or government* or nation* or region*) adj3 (data or study or studies or cohort)).ti,ab,kf. 472571
- 74 Follow-Up Studies/ 690985
- 75 ((long term or long-term or longterm or longitudinal) adj3 (cohort or follow-up)).ti,ab,kf. 97525
- 76 (((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or medline or psyclit or psychinfo or

(psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("cochrane database of systematic reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or Evidence Report: Technology Assessment*.jn. or ((review adj5 (rationale or evidence)).ti,ab. and review.pt.) or meta-analysis as topic/ or Meta-Analysis.pt. 680986

77 ((review or umbrella or evidence) adj2 (review* or synthesis)).ti,ab. 2109519

78 (Transgender or LGBT* or transsexual* or GLBT).jw. 1119

79 or/72-78 3510516

80 71 and 79 3452

81 limit 80 to (english language and yr="2013 -Current") 2514

82 "Africa South of the Sahara"/ or Africa, Central/ or Africa, Eastern/ or Africa, Northern/ or Africa, Southern/ or Africa, Western/ or Indochina/ or Melanesia/ or Sub-Saharan.ti. or Central Africa.ti. or East\$3 Africa.ti. or North\$3 Africa.ti. or South\$3 Africa.ti. or West\$3 Africa.ti. 57226

83 Afghanistan.ti. or Afghanistan/ or Albania.ti. or Albania/ or Algeria.ti. or Algeria/ or Angola.ti. or Angola/ or Antigua.ti. or Barbuda.ti. or "Antigua and Barbuda"/ or Armenia.ti. or Aremenia/ or Azerbaijan.ti. or Azerbaijan/ or Bangladesh.ti. or Bangladesh/ or Barbados.ti. or Barbados/ or Belize.ti. or Belize/ or Benin.ti. or Benin/ or Bhutan.ti. or Bhutan/ or Bolivia.ti. or Bolivia/ or "Bosnia and Herzegovina".ti. or "Bosnia and Herzegovina"/ or Botswana.ti. or Botswana/ or Brazil.ti. or Brasil.ti. or Brazil/ or Bulgaria.ti. or Bulgaria/ or Burkina Faso.ti. or Burkina Faso/ or Burundi.ti. or Burundi/ 176527

84 Cabo Verde.ti. or Cabo Verde/ or Cambodia.ti. or Cambodia/ or Cameroon.ti. or Cameroon/ or "Central African Republic".ti. or Central African Republic/ or Chad.ti. or Chad/ or China.ti. or China/ or Colombia.ti. or Colombia/ or Comoros.ti. or Comoros/ or Congo.ti. or Congo/ or Cote d'Ivoire.ti. or Ivory Coast.mp. or Cote d'Ivoire/ or Cuba.ti. or Cuba/ or "Democratic Republic of the Congo"/ or Djibouti.ti. or Djibouti/ or Dominica.ti. or Dominica/ or Dominican Republic.ti. or Dominican Republic/ 329372

85 Ecuador.ti. or Ecuador/ or Egypt.ti. or Egypt/ or El Salvador.ti. or El Salvador/ or Equatorial Guinea.ti. or Equatorial Guinea/ or Eritrea.ti. or Eritrea/ or Eswatini.ti. or Eswatini/ or Ethiopia.ti. or Ethiopia/ or Fiji.ti. or Fiji/ or Gabon.ti. or Gabon/ or Gambia.ti. or Gambia/ or Ghana.ti. or Ghana/ or Grenada.ti. or Grenada/ or Guatemala.ti. or Guatemala/ or Guinea.ti. or Guinea/ or Guinea-Bissau.ti. or Guinea-Bissau/ or Guyana.ti. or Guyana/ or Haiti.ti. or Haiti/ or Honduras.ti. or Honduras/ 144725

86 India.ti. or India/ or Indonesia.ti. or Indonesia/ or Iran.ti. or Iran/ or Iraq.ti. or Iraq/ or Jamaica.ti. or Jamaica/ or Jordan.ti. or Jordan/ or Kenya.ti. or Kenya/ or Kiribati.ti. or Kyrgyzstan.ti. or Kyrgyzstan/ or Laos.ti. or Laos/ or Lebanon.ti. or Lebanon/ or Lesotho.ti. or Lesotho/ or Liberia.ti. or Liberia/ or Libya.ti. or Libya/ 250890

87 Madagascar.ti. or Madagascar/ or Malawi.ti. or Malawi/ or Maldives.ti. or Mali.ti. or Mali/ or Marshall Islands.ti. or Mauritania.ti. or Mauritania/ or ((Mexico.ti. or Mexico/) not "New Mexico".ti.) or Micronesia.ti. or Moldova.ti. or Moldova/ or Mongolia.ti. or Mongolia/ or Morocco.ti. or Morocco/ or

Mozambique.ti. or Mozambique/ or Myanmar.ti. or Myanmar/ or Namibia.ti. or Namibia/ or Nauru.ti. or Nauru/ or Nepal.ti. or Nepal/ or Nicaragua.ti. or Nicaragua/ or Niger.ti. or Niger/ or Nigeria.ti. or Nigeria/ or North Korea.ti. or "Democratic People's Republic of Korea"/ or North Macedonia.ti. or "Republic of North Macedonia"/ 143146

88 Pakistan.ti. or Pakistan/ or Palau.ti. or Palau/ or Palestine.ti. or Papua New Guinea.ti. or Papua New Guinea/ or Paraguay.ti. or Paraguay/ or Peru.ti. or Peru/ or Philippines.ti. or Philippines/ or Rwanda.ti. or Rwanda/ or "Saint Kitts and Nevis".ti. or "Saint Kitts and Nevis"/ or Saint Lucia.ti. or Saint Lucia/ or "Saint Vincent and the Grenadines".ti. or "Saint Vincent and the Grenadines"/ or Samoa.ti. or Samoa/ or "Sao Tome and Principe".ti. or "Sao Tome and Principe"/ or Senegal.ti. or Senegal/ or Seychelles.ti. or Seychelles/ or Sierra Leone.ti. or Sierra Leone/ or Solomon Islands.ti. or Somalia.ti. or Somalia/ or South Africa.ti. or South Africa/ or South Sudan.ti. or South Sudan/ or Sri Lanka.ti. or Sri Lanka/ or Sudan.ti. or Sudan/ or Suriname.ti. or Suriname/ or "Syrian Arab Republic".ti. or Syria.ti. or Syria/ 141359

89 Tajikistan.ti. or Tajikistan/ or Tanzania.ti. or Tanzania/ or Timor-Leste.ti. or Timor-Leste/ or Togo.ti. or Togo/ or Tonga.ti. or Tonga/ or Tunisia.ti. or Tunisia/ or Turkmenistan.ti. or Turkmenistan/ or Tuvalu.ti. or Uganda.ti. or Uganda/ or Ukraine.ti. or Ukraine/ or Uzbekistan.ti. or Uzbekistan/ or Vanuatu.ti. or Vanuatu/ or Venezuela.ti. or Venezuela/ or Viet Nam.ti. or Vietnam.ti. or Vietnam/ or Yemen.ti. or Yemen/ or Zambia.ti. or Zambia/ or Zimbabwe.ti. or Zimbabwe/ 101388

90 "low* and middle* income countries".ti. 5972

91 or/82-90 1267054

92 81 not 91 2367

APA PsycInfo <1806 to April Week 3 2023>

1 *Gender Dysphoria/ or *Gender Identity Disorder/ 1068

2 (gender-dysphor* or gender-varian* or gender-incongru* or gender-nonconform* or gender-nonconform* or gender-minorit* or gender-questioning).ti,ab,id. 4775

3 (gender* adj1 (dysphor* or varian* or incongru* or nonconform* or non-conform* or atypical or minorit* or questioning or fluid* or expansi*)).ti,ab,id. 5403

4 *Transsexualism/ or *Transgender/ or *Gender Nonconforming/ or *Gender Nonbinary/ or *Two-Spirit/ 7955

5 (transgender* or transsexual* or transexual* or genderqueer or trans-gender* or trans-sexual* or gender-queer or gender-variant or two-spirit person* or nonbinary or non-binary or trans-person* or transperson* or trans-people* or transpeople*).ti,ab,id. 16887

6 (trans adj2 (person* or people* or individual* or m?n or wom?n)).ti,ab,id. 1248

7 (trans-m?n or trans-wom?n or transm?n or transwom?n or transperson* or trans-person* or transpeople* or trans-people*).ti,ab,id. 3837

8 (transfeminine or transmasculine or trans-feminine or trans-masculine).ti,ab,id. 242

- 9 (bigender or bi-gender or pangender or pan-gender or genderfluid* or gender-fluid* or gender-expansi* or agender).ti,ab,id. 380
- 10 ("male-to-female" or "female-to-male").ti,ab,id. 69552
- 11 or/1-10 87920
- 12 ((confirm* or affirm* or reaffirm* or re-affirm* or reassignment or change or transition* or transform*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,id. 13246
- 13 *Gender Reassignment/ or *Sex Change/ 572
- 14 ((sex-confirm* or sex-affirm* or sex-reaffirm* or sex-reassignment or sex-change or sex-transition* or sex-transform*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,id. 480
- 15 ((gender-confirm* or gender-affirm* or gender-reaffirm* or gender-reassignment or gender-change or gender-transition* or gender-transform*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,id. 437
- 16 ((masculini* or masculi?ing or femini?ation or femini?ing or demasculi* or defemin*) adj3 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,id. 110
- 17 *Plastic Surgery/ 512
- 18 (reconstructive adj2 (procedure* or surg* or service* or operation* or intervention*)).ti,ab,id. 291
- 19 (facelift* or face lift*).ti,ab,id. 28
- 20 (facial* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*)).ti,ab,id. 357
- 21 (face* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*)).ti,ab,id. 531
- 22 (brow* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or reconstruct* or refin*)).ti,ab,id. 33
- 23 (forehead* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or reconstruct* or refin*)).ti,ab,id. 1
- 24 rhinoplast*.ti,ab,id. 59
- 25 (nose* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or reconstruct* or refin*)).ti,ab,id. 29
- 26 genioplast*.ti,ab,id. 2
- 27 (chin* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*)).ti,ab,id. 172

- 28 (laryngoplast* or glottoplast* or thyroplast* or phonosurger*).ti,ab,id. 35
- 29 (Chondrolaryngoplast* or (trachea* adj2 shav*).ti,ab,id. 4
- 30 (neck* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct* or refin* or reconstruct*).ti,ab,id. 96
- 31 (body contour* or body-contour* or chest contour* or chest-contour*).ti,ab,id. 31
- 32 (body* adj3 (masculini* or masculi?ing or femini?ation or femini?ing or defemini* or demasculi*).ti,ab,id. 146
- 33 (lipectom* or liposuction*).ti,ab,id. 35
- 34 (fat transfer* or fat graft*).ti,ab,id. 15
- 35 mamm?plast*.ti,ab,id. 38
- 36 (breast adj2 (reconstruct* or augment* or reduc* or implant* or enhanc*).ti,ab,id. 568
- 37 *mastectomy/ or mastectom*.ti,ab,id. 1039
- 38 (breast adj2 remov*).ti,ab,id. 24
- 39 (chest* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*).ti,ab,id. 52
- 40 (genital* adj3 (surger* or femini* or masculi* or defemini* or demasculi* or remodel* or refin* or reconstruct*).ti,ab,id. 322
- 41 (vaginoplast* or neovagina*).ti,ab,id. 90
- 42 (phalloplast* or neophall* or glansplast* or glans-plast*).ti,ab,id. 64
- 43 ((peni* or testic*) adj2 (prothes* or implant* or transplant*).ti,ab,id. 200
- 44 (inflat* adj2 prothes*).ti,ab,id. 103
- 45 gluteal implant*.ti,ab,id. 0
- 46 ((esthetic or aesthetic or cosmetic) adj2 (procedure* or surg* or service* or operation* or intervention*).ti,ab,id. 787
- 47 ((calf or calve or silicon* or pectoral or chin or nose or cheek) adj4 (implant* or augmentation* or prothes*).ti,ab,id. 79
- 48 ((esthetic or aesthetic or cosmetic or collagen) adj2 inject*).ti,ab,id. 15
- 49 (hair adj2 (remov* or reduc* or transplant*).ti,ab,id. 156
- 50 (epilation* or depilation* or electrolys*).ti,ab,id. 68
- 51 (voice* adj3 (training or retraining or coaching or therap* or masculini* or femini*).ti,ab,id. 1202

52 (vocal* adj3 (training or retraining or coaching or therap* or masculini* or femini* or surg*)).ti,ab,id. 398

53 *speech therapy/ or (speech adj2 therap*).ti,ab,id. 6607

54 or/12-53 25723

55 11 and 54 1802

56 ((gender* or gender nonconforming or gender-nonconforming or gender non-conforming or trans or transgender or nonbinary or non-binary) adj7 (confirm* or affirm* or reaffirm* or re-affirm* or identity-affirm* or identity-confirm* or identity-reaffirm*)).ti,ab,id. 2921

57 (gender-confirm* or gender-affirm* or gender-reaffirm* or gender-reassignment or gender-change or gender-transition* or gender-transform*).ti,ab,id. 1604

58 (sex-confirm* or sex-affirm* or sex-reaffirm* or sex-reassignment or sex-change or sex-transition* or sex-transform*).ti,ab,id. 846

59 or/56-58 4399

60 *"Suicide (Attempted)"/ or *Parasuicide/ or *Suicide/ or *Attempted Suicide/ or *Suicidality/ or *Suicidal Ideation/ or *Non-Suicidal Self-Injury/ or *Self-Injurious Behavior/ or *Self-Inflicted Wounds/ or *Self-Mutilation/ 40603

61 *Unipolar Depression/ or *Late Life Depression/ or *Major Depression/ or *Recurrent Depression/ or *Treatment Resistant Depression/ 121059

62 *Anxiety Disorders/ or *Generalized Anxiety Disorder/ or *Chronic Mental Illness/ or *"Mental Disorders due to General Medical Conditions"/ or *Body Dysmorphic Disorder/ 21592

63 *"Resilience (Psychological)"/ or *"Stress and Trauma Related Disorders"/ or *Psychological Stress/ or *Social Stress/ 10014

64 (suicide* or suicidal* or self-injur* or self injur* or cutting or self-mutilat* or self mutilat* or depressi* or anxiety).ti,id. 304190

65 (regret* or detransition* or desist or desist?r* or desistance).ti,ab,id. or (discontinu* or revers*).ti,id. 25094

66 or/60-65 348083

67 11 and 65 425

68 or/55,59,67 5440

69 (exp Animals/ not Humans/) or (baboon\$1 or bovine\$1 or canine\$1 or cat\$1 or chimpanzee\$1 or cow\$1 or dog\$1 or feline\$1 or fish or goat\$1 or hens or macque\$1 or mice or monkey\$1 or mouse or murine\$1 or ovine or pig\$1 or porcine or primate\$1 or sheep or rabbit\$1 or rat or rats or rattus or rhesus or rodent\$1 or zebrafish).ti.389189

70 68 not 69 5266

71 (registry* or registries or database* or data center* or data warehouse*).ti,id.5785

72 ((regist* or population* or government* or nation* or region*) adj3 (data or study or studies or cohort)).ti,ab,id. 91118

73 Followup Studies/ 12396

74 ((long term or long-term or longterm or longitudinal) adj3 (cohort or follow-up)).ti,ab,id. 11656

75 (((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or medline or psyclit or psychinfo or (psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("cochrane database of systematic reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or Evidence Report: Technology Assessment*.jn. or Systematic Review/ or Meta Analysis/ 113525

76 ((review or umbrella or evidence) adj2 (review* or synthesis)).ti,ab. 411908

77 or/71-76 558335

78 70 and 77 623

79 limit 70 to ("0830 systematic review" or 1200 meta analysis or 1300 metasyntesis)73

80 or/78-79 626

81 limit 80 to ("0400 dissertation abstract" or "column/opinion" or "comment/reply" or dissertation or letter) 69

82 80 not 81 557

83 limit 82 to (english language and yr="2013 -Current") 332

Cochrane Database of Systematic Reviews (CochraneLibrary.com)

1 MeSH descriptor: [Gender Dysphoria] this term only 13

2 (gender-dysphor* or gender-varian* or gender-incongru* or gender-nonconform* or gender-nonconform* or gender-minorit* or gender-questioning):ti,ab 125

3 (gender* near/1 (dysphor* or varian* or incongru* or nonconform* or non-conform* or atypical or minorit* or questioning or fluid* or expansi*)):ti,ab 135

4 3 not 210

5 MeSH descriptor: [Transgender Persons] this term only 108

6 (transgender* or transsexual* or transexual* or genderqueer or trans-gender* or trans-sexual* or gender-queer or gender-variant or two-spirit person* or nonbinary or non-binary or trans-person* or transperson* or trans-people* or transpeople*):ti,ab 815

7 (trans near/2 (person* or people* or individual* or m?n or wom?n)):ti,ab 76

- 8 (trans-m?n or trans-wom?n or transm?n or transwom?n or transperson* or trans-person* or transpeople* or trans-people*):ti,ab 93
- 9 (transfeminine or transmasculine or trans-feminine or trans-masculine):ti,ab 9
- 10 (bigender or bi-gender or pangender or pan-gender or genderfluid* or gender-fluid* or gender-expansi* or agender):ti,ab 7
- 11 ("male-to-female" or "female-to-male"):ti,ab 651
- 12 (or 1-11) in Cochrane Reviews 5

Inclusion/Exclusion Criteria

CATEGORY	INCLUDED	EXCLUDED
POPULATION	Adults and adolescents who are transgender or gender diverse (regardless of hormone therapy status) who seek gender-affirming medical intervention(s)	
INTERVENTION(S)	Gender-affirming medical interventions, including any combination of medication, speech therapy, physical therapy, behavioral health care, hair removal or surgical procedures selected based on patient's needs	Services related to fertility preservation or infertility treatment, medication therapy alone (e.g., puberty blocking medications, cross sex hormones)
COMPARATORS	No gender affirming medical interventions, delayed (waitlist) care, primary care and behavioral care without other interventions, medication therapy alone, population averages	
OUTCOMES	<p>Critical: Death from suicide, suicide attempt, gender dysphoria^a</p> <p>Important: Depression or anxiety using validated scales, suicidal ideation, QOL outcomes using validated scales^b, discrimination or experience of stigma, withdrawal from treatment, revision for reasons</p>	<p>Considered but not selected: Medication complications, physical or social de-transition, procedure-related complications, satisfaction</p>

other than aesthetic dissatisfaction

STUDY DESIGNS

-SRs of RCTs or comparative cohort studies;
-RCTs;
-Registries from national databases or large datasets (i.e., > 300 individuals)

Case reports, case series, cross-sectional analyzes, registries of under 300 individuals

Selection of studies based on methodological rigor by outcome; sample size threshold may be adjusted based on search results

FOLLOW-UP

Outcome reported at ≥ 12 months after receipt of initial intervention

Outcome reported at < 12 months after receipt of initial intervention

Additional inclusion criteria: individual cohort registry studies needed to be conducted in a country deemed as Very High Human Development by the United Nations.⁷³

Additional exclusion Criteria: non-comparative, not in English, studies solely looking at the role of hormone treatment

We prioritized reviews with robust search methodologies (e.g., more than 2 databases) with clear inclusion and exclusion criteria and extractable data to report for this review. We also prioritized newer systematic reviews if 2 reviews met the prior criteria.

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This document was prepared by the Center for Evidence-based Policy at Oregon Health & Science University (Center). This document is intended to support Health Evidence Review Commission staff and their constituent decision-making bodies to make informed decisions about the provision of health care services. The document is intended as a reference and is provided with the understanding that the Center is not engaged in rendering any clinical, legal, business, or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers and authors involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

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