EXHIBIT 113

World Health Organization

Posted on 15 January 2024

Frequently Asked Questions (FAQ)

WHO development of a guideline on the health of trans and gender diverse people

15 January 2024

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1. Why is a technical guideline on the health of trans and gender diverse people needed?

- Trans and gender diverse people encounter specific challenges that negatively impact their access to quality health services, quality of life and life expectancy, violating their right to health and associated rights, such as the right to free, informed consent to medical interventions. This guideline has a specific focus on adults and will not address issues relating to children and adolescents.
- Trans and gender diverse people often face barriers to accessing health care services, including stigma and discrimination in health care settings. This can have serious impacts on their health. Many settings also lack policies to facilitate access to inclusive and gender affirming care. Trans and gender diverse people experience a high burden of mental health issues (including suicide) and often experience high levels of violence. Thus, there is an urgent need for the health sector to consider ways to provide more inclusive, acceptable and effective health care for trans and gender diverse people.
- This proposed guideline is guided by WHO's mandate to enable the attainment of the highest possible level of health and well-being for all.
- The guideline will reflect the principles of human rights, gender equality, universality and equity. It is aligned with and responds to WHO's mandate to work for all people, the effort to reach the furthest behind first, and a commitment to leave no one behind. The guideline also contributes to ensuring universal health coverage (UHC).
- Additionally, the guideline aims to contribute to reaching the goals of the 2015 Joint Statement of 14 UN agencies, including WHO, pledging to protect all people from discrimination and violence on the grounds of gender identity and/or gender expression, as well as the 2017 United Nations Joint Statement committing to eliminate discrimination in healthcare settings, including discrimination based on gender identity and gender expression.

2. Why is this guideline needed now?

- The midterm review of the Sustainable Development Goal (SDG) agenda, including SDG 3 "Ensure healthy lives and promote well-being for all at all ages", has brought renewed attention and commitment to the global goal of universal health coverage.
- This proposed guideline builds on more than 10 years of WHO work on trans and gender diverse people's health. This includes:
    - The International Statistical Classification of Diseases and Related Health Problems (ICD), which in its 11th edition included changes to reflect scientific understanding of sexual health, gender identity and gender incongruence. The ICD-11 was endorsed by WHO Member States in 2019 and published in January 2022.
    - Guidelines related to HIV, viral hepatis and sexually transmitted infections (STIs), which include good practice statements on the enabling environments that are essential to curb these epidemics among this disproportionately affected group of people.
    - Guidelines related to self-care interventions that recognize the importance of gender equality, rights in delivery of gender affirming care, and reducing discrimination.
- There is an increasing body of scientific evidence highlighting the unmet health needs of trans and gender diverse persons, due to stigma, discrimination, violence, and other human rights violations, including in the health care settings.
- Trans and gender diverse people are entitled to the full protection of their human rights, as specified in international human rights instruments. Human rights include, but are not limited to, the right to equal enjoyment of rights and non-discrimination; security of person and privacy; recognition and equality before the law; the right to the highest attainable standard of mental and physical health; education; employment and just and favourable conditions of employment; freedom of movement; peaceful assembly and association; freedom from arbitrary arrest and detention, and from cruel and inhumane treatment; and protection from violence. States have an obligation to ensure that the above rights are enjoyed without discrimination of any kind, including on grounds of race, language, national or social origin, political or other opinion, sex, age, religion, disability, marital status or other status. United Nations human rights treaty bodies have repeatedly held that sexual orientation, gender identity and sex characteristics are prohibited grounds of discrimination under international law.
- Some countries have laws, regulations, policies and practices that present barriers to equal access to health care for trans and gender diverse people. A number of countries criminalize gender identity in a de facto manner, by criminalizing cross-dressing or impersonation of the opposite sex. For trans and gender diverse people, the lack of legal gender recognition is a key barrier to access to health services, in addition to the full enjoyment of other rights, such as freedom of movement, and right to adequate housing, education and employment. Harmful practices include forced anal examinations, which are used to investigate or punish alleged same-sex behaviour between consenting men or transgender women. These legal barriers have

measurable, detrimental effects on the health of trans and gender diverse people, as shown by research.

3. What will the guideline cover?

- This guideline will review evidence of the impact of specific interventions and on that basis provide recommendations for enhancing the health of specifically, adult, trans and gender diverse people, , and their access and utilization of health services.
- Interventions to be assessed include:
  - the provision of gender affirming care services for trans and gender diverse adults in a clinical setting;
  - health workers' training and education approaches related to providing gender inclusive care for adults;
  - specific provisions of gender identity recognition laws, policies and administrative procedures that may affect the health and wellbeing of adult trans and gender diverse people; and
  - provisions of health policies aimed at facilitating gender inclusive health care for adults.
- The guidelines will also inform existing WHO recommendations that support health services and health workers in providing empathetic and evidence-based clinical care to trans and gender diverse people that addresses their needs, who experience interpersonal violence.

4. How was the scope decided?

- The scope was based on requests of some WHO Member States and on the outcomes of a stakeholder consultation held in 2022 with experts in transgender health and representatives from the affected communities from all WHO geographic regions. From the initial consultations, it was agreed that the scope should focus on adults and not on children/adolescents.

5. Why will the guideline only cover adults and not also children or adolescents?

- The scope will cover adults only and not address the needs of children and adolescents, because on review, the evidence base for children and adolescents is limited and variable regarding the longer-term outcomes of gender affirming care for children and adolescents.

6. What do we mean by 'trans and gender diverse people'?

- "Trans and gender diverse people" is an umbrella term for those whose gender identity, roles or expression do not conform to the norms and expectations traditionally associated with the sex assigned to them at birth; it includes people who are transsexual, transgender, or otherwise gender nonconforming or gender incongruent. Transgender people may self-identify as transgender, female, male, trans woman or trans man, transsexual or one of many other gender nonconforming identities. They may express their genders in a variety of masculine, feminine and/or androgynous ways.
- See WHO's frequently asked questions on health and sexual diversity for further information.

7. What are the definitions of gender affirming and gender inclusive care used in this guideline process?

- In line with the 11th edition of the WHO International Classification of Diseases and Related Health Problems (ICD-11), gender-affirming health care can include any single or combination of a number of social, psychological, behavioural or medical (including hormonal treatment or surgery) interventions designed to support and affirm an individual's gender identity. Of note, these new technical guidelines on the health of trans and gender diverse people will not consider surgical interventions.
- Gender inclusive care refers to gender diverse people's inclusion in, and access to, all forms of health care, free of stigma and discrimination, facilitated by health policy, laws and/or health interventions.

8. What is the timeline for this process?

- 2021: Establishment of an internal WHO steering group and the contracting of the first of two independent and experienced guideline methodologists to impartially guide the process, including the formulation of recommendations.
- 2022: A stakeholder consultation (including with Member States) was conducted to define the scope of this guideline, which led to the identification of the three areas of focus: service delivery approaches, health workforce training, and health policy. A detailed proposal for the guideline was submitted and approved by the WHO Guideline Review Committee.
- 2023: Evidence synthesis was initiated; the preliminary list and biographies of 14 proposed Guideline Development Group (GDG) members was published on the WHO website for public consultation; and an updated list of 21 proposed GDG members, with additions primarily of public health policy experts from Ministries of Health, was published for a further period of public consultation (extended until 2 February 2024). In December 2023, one member of the proposed GDG list asked to be removed due to scheduling conflicts.

9. **What are the criteria for selection of the GDG members?**

- The standard criteria for the selection of technical experts for the GDG include (a) technical expertise in the subject matter as defined in the scope of the approved guidelines proposal; (b) geographic representation; (c) gender diversity; (d) representatives of people affected by the guidelines; and (e) end users (i.e., people who will use the guidelines such as health policy makers and health professionals).
- In the specific case of this guideline, the following profiles were considered for the members of the GDG:

- expertise in gender affirming health care, health workforce, violence response, mental health, law, public health policy, and human rights;
- geographic representation;
- gender diversity;
- trans and gender diverse individuals (as subject matter experts and/or as representatives of those affected by the guidelines); and
- health policy-makers and health professionals working in the field of trans and gender diverse health (end users)

- All GDG members act in their own technical capacity and do not represent their affiliated organizations. Their work is unpaid.

10. How were the proposed GDG members selected for this guideline?

- The selection was informed by both participants of the stakeholder consultation meeting held in early 2022 and by WHO technical staff, including those in Regional Offices.
- The proposal for GDG composition has been approved by the WHO Guideline Review Committee.
- The proposed GDG membership along with relevant biographies was announced for rounds of public notice and comment, in line with WHOs policy for managing conflicts of interest of external experts, in June and December 2023. Following a wide-ranging set of feedback, WHO is further extending the submission of feedback on the GDG membership until 2 February 2024. All comments should be sent to hiv-aids@who.int by this deadline.

11. What are WHO normative guidelines?

- WHO guidelines aim to support Member States in implementing evidence-based interventions to update health policies and achieve health outcomes for populations. They do not constitute binding commitments and Member States choose whether to apply and adapt them to their context.

12. What is the process for developing WHO guidelines?

- The WHO guideline development strictly adheres to a robust and evidence-based process as detailed in the WHO handbook for guideline development and is overseen by an independent internal review Committee charged to ensure these processes are followed.
- The process includes the defining of the scope, the development of key research questions (using the PICO format), commissioning of systematic reviews of the literature by WHO looking at the impact of selected interventions on specific health outcomes and their risks and benefits. The results of these reviews are summarized and assessed for certainty or quality of evidence and risk of bias, using established and internationally recognized '*Grading of Recommendations Assessment, Development and Evaluation*' (GRADE) and the '*Confidence in the Evidence from*

Reviews of Qualitative Research' (GRADE-CERQual) methodologies; and a Guideline Development Group (GDG) of external experts is established.

- Standard criteria for the selection of technical experts for the GDG include (a) technical expertise in the subject matter that is defined in the scope of the approved guidelines proposal; (b) geographic representation; (c) gender diversity; (d) representatives of people affected by the guidelines; and (e) end users (i.e., people who will use the guidelines, such as health policy-makers and health professionals). Biographies are then made public for feedback before the GDG is finalized.
- Once the GDG is established, it is presented with the summarized results of the reviews addressing each research question as well as with evidence related to:
    - values and preferences of the users and beneficiaries of the recommendations;
    - feasibility of implementation with a focus in low- and middle-income countries;
    - economic implications (e.g. costs, cost-benefits, etc.); and
    - human rights and ethical implications.
- The GDG is systematically guided through the evidence-to-decision process by an independent methodologist, and decisions regarding the recommendations are reached by consensus.
- Once the recommendations are finalised by the GDG, they are subject to further external expert peer review, and the full guideline is subsequently submitted for review and approval by the WHO Guideline Review Committee, following the process outlined in the WHO handbook for guideline development.
- The time to development of a guideline varies depending on the scope, availability and volume of evidence and resources, but can take between 6 months and two years. All guidelines are subject to external peer review for accuracy and implement-ability.

13. **How are conflicts of interest of Guideline Development Group (GDG) members managed?**

- Conflicts of interests are managed following standard WHO procedures, notably its Declaration of Interest (DOI) policy for external experts. According to this policy, members of WHO Guideline Development Groups are required to declare any (intellectual or financial) interest that might affect their objectivity and independence and/or create an unfair or competitive advantage. They are screened through a series of background checks performed by the WHO Secretariat, and through a period of public notice and comment.
- Any significant disclosed interest identified through these processes is reviewed by the Secretariat (including as appropriate, in consultation with the WHO Office of Compliance, Risk Management and Ethics) to determine if a conflict of interest exists, and what, if any measures (ranging from conditional participation, partial or full exclusion) are required.

  WHO reserves the right to review the declaration of interests (DOIs) and if a new interest becomes apparent, WHO shall at all times manage that conflict of interest, including adjusting membership of a GDG.

EXHIBIT 114

Topic Brief: Treatments for Gender Dysphoria in Transgender Youth

Date: 1/8/2021
Nomination Number: 0928

Purpose: This document summarizes the information addressing a nomination submitted on July 17, 2020 through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: Youth who identify as transgender experience high rates of depression, anxiety, eating disorders, substance use disorders, and suicide ideation or attempts. There is a lack of current evidence-based guidance for the care of children and adolescents who identify as transgender, particularly regarding the benefits and harms of pubertal suppression, medical affirmation with hormone therapy, and surgical affirmation.

Program Decision:

The EPC Program will not develop a new systematic review because we found protocols for two systematic reviews that addresses portions of the nomination, and an insufficient number of primary studies exist to address the remainder of the nomination.

Key Findings

- We found a protocol for a systematic review that included key questions (KQs) that met the nominator's needs for KQ1 regarding pubertal suppression in transgender youth.
- For KQ 2 and 3, we found two protocols (one is the same as that for KQ1) for systematic reviews that partially address each of the two KQs, respectively. We did not find any studies addressing the parts of the KQs not addressed by these protocols.

Background

The term transgender refers to individuals whose gender identity persistently and consistently does not match their assigned sex.[1] An estimated 0.6 percent of adults[2] and 0.7 percent of youth ages 13 to 17 in the U.S. identify as transgender or "gender nonconforming." [3] Many transgender youth experience gender dysphoria, characterized as an impairment in peer and/or family relationships, school performance, and other aspects of life as a consequence of the discordance between their gender identity and assigned sex.[1] Transgender youth also experience high rates of depression, anxiety, eating disorders, and suicide.[4-6]

Gender affirmation is a complex interpersonal process of reflection, acceptance, social and legal recognition and medical interventions. Gender-affirming behavioral, social and medical interventions may improve psychological functioning in children and adolescents.[6] Available interventions include the following: 1) social affirmation (e.g., expressing one's asserted gender

through hairstyle, clothing, pronouns, name, etc.); 2) legal affirmation (e.g., name and gender officially reflected on legal documents); 3) medical affirmation (e.g., using cross-sex hormones in adolescents who have initiated puberty to facilitate the development of secondary sex characteristics of the sex the individual identifies with); and/or 4) surgical affirmation (e.g., surgical interventions to masculinize or feminize features).[1]

Gender-affirming health care is part of comprehensive primary care for many gender-diverse patients. There is a lack of current evidence-based guidance for the care of children and adolescents who identify as transgender, particularly regarding the benefits and harms of pubertal suppression, medical affirmation with hormone therapy, and surgical affirmation. While there are some existing guidelines and standards of care,[1, 7, 8] most are derived from expert opinion or have not been updated recently. A comprehensive evidence review is currently not available.

Scope

1. For children and adolescents who identify as transgender and have not initiated puberty, what are the benefits and harms of pubertal suppression?
2. For adolescents who identify as transgender and have initiated puberty, what are the benefits and harms of medical affirmation with hormone therapy?
3. For adolescents who identify as transgender and have initiated puberty, what are the benefits and harms of surgical affirmation?

Table 1. Questions and PICOs

Questions	1. Pubertal suppression	2. Hormone therapy	3. Surgical affirmation
Population	Children and adolescents who identify as transgender and have not initiated puberty	Adolescents who identify as transgender and have initiated puberty	Adolescents who identify as transgender and have initiated puberty
Interventions	Pubertal suppression	Medical affirmation with hormone therapy	Surgical affirmation
Comparators	No pubertal suppression	No intervention; Social affirmation only	No intervention; social affirmation with other medical affirmation (e.g., hormone therapy); social affirmation without medical affirmation

Questions	1. Pubertal suppression	2. Hormone therapy	3. Surgical affirmation
Outcomes	• Depression/anxiety, suicidality, distress/dysphoria, social interaction, quality of life • Medication effects (e.g., weight gain, height, decreased secondary sex characteristics, hot flashes, headache, bone density, fertility)	• Depression/anxiety, suicidality, distress/dysphoria, social interaction, quality of life • Estrogen effects (feminization, weight gain, mood swings, hot flashes, VTE, migraine, fertility, cancer risks), antiandrogen effects (feminization, hypotension, electrolyte abnormality, VTE), androgen effects (masculinization, cancer risks, hypertension, hyperlipidemia, vascular disease)	• Depression/anxiety, suicidality, distress/dysphoria, social interaction, quality of life • Surgical risks (e.g., infection, bleeding, poor healing of incisions, hematoma, seroma, necrosis, nerve injury, stenosis of the vagina, injury of the urinary tract, painful intercourse)

Abbreviations: PICOS=population, intervention, comparator, outcome; VTE=venous thromboembolism.

Assessment Methods

See Appendix A.

Summary of Literature Findings

We identified a protocol for a systematic review that covered KQ1,[9] protocols that partially covered KQ 1 and 2, and no primary literature to cover the portions of KQs 2-3 not covered by the protocols.

For KQ1, we identified a protocol for a systematic review[9] that included the following key questions that meet the nominator's needs:

- "For transgender adolescents, what are the long term effect of GnRH agonists compared to no treatment, in terms of surrogate outcomes, clinical outcomes, and harms?"
- "For transgender people, what are the effect of progesterones (cyproterone) compared to Medroxyprogesterone and other progesterones in terms of breast growth (adults), delay of puberty (children), and side effects?"
- "For transgender adolescents, what are the effects of suppressing puberty with GnRH agonists on quality of life?"

For KQ2, we found a protocol for a systematic review[9] that partially covered KQ2:

- "For transgender people, what are the psychological effects (including quality of life) associated with hormone therapy."
- "For transgender people, what are the effects of hormone therapy on metabolic syndrome?"
- "For transgender people, what are the effects of hormone therapy on fertility?"

We did not find any systematic reviews or protocols for systematic reviews for hormone effects such as cancer risks, hot flashes, or migraine, nor did we find any primary studies addressing

these remaining portions of KQ2. We did find 11 non-randomized controlled trial studies that either did not include a comparator group[10-17] or that included a comparator group that did not match the PICOs.[18-21] These studies were not included in our assessment of the feasibility of a systematic review, but are mentioned here as they are related and may be of interest.

For KQ3, we found a protocol for a systematic review that partially covered KQ3.[22] Specifically, it covered top, but not bottom surgery:

- "How does age affect the benefits and risks of top surgery for transmasculine individuals and gender nonconforming individuals assigned female at birth, particularly for those under age 18?"

- "How does age affect the benefits and risks of top surgery, particularly for those under age 18 for
transfeminine individuals and gender-nonconforming individuals assigned male at birth?"

We did not find any studies addressing the remainder of KQ3, namely, bottom, or genital, surgery.

Table 2. Literature identified for each KQ

Question	Systematic reviews (1/2018-1/2021)	Primary studies (1/2016-1/2021)
Question 1: Pubertal suppression	Total: 1 • PROSPERO protocol: 1	N/A
Question 2: Hormone therapy	Total: 1 • PROSPERO protocol: 1	Total: 0
Question 3: Surgical affirmation	Total: 1 • PROSERO protocol: 1	Total: 0

Abbreviations: KQ=key question; NA=not applicable; RCT=randomized controlled trial.

See Appendix B for detailed assessments of all EPC selection criteria.

Summary of Selection Criteria Assessment

There is a lack of current evidence-based guidance for care of children and adolescents who identify as transgender regarding the benefits and harms of pubertal suppression, medical affirmation with hormone therapy, and surgical affirmation. A systematic review is currently underway that addresses KQ1, and parts of KQs 2 and 3. There is insufficient evidence at this time to create a new systematic review that would inform the development of evidence-based guidance for the remainder of the nomination.

Please see Appendix B for detailed assessments of individual EPC Program selection criteria.

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Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years, January 7, 2018 - January 7, 2021, on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
  - AHRQ Evidence Reports https://www.ahrq.gov/research/findings/evidence-based-reports/index.html
  - EHC Program https://effectivehealthcare.ahrq.gov/
  - US Preventive Services Task Force https://www.uspreventiveservicestaskforce.org/
  - AHRQ Technology Assessment Program https://www.ahrq.gov/research/findings/ta/index.html
- US Department of Veterans Affairs Products publications
  - Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
  - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program https://www.healthquality.va.gov/
- Cochrane Systematic Reviews https://www.cochranelibrary.com/
- PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
- PubMed https://www.ncbi.nlm.nih.gov/pubmed/

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a limited literature search in PubMed from the last five years 1/7/2016 - 1/7/2021. We reviewed all identified titles and abstracts for inclusion and classified identified studies by question and study design to estimate the size and scope of a potential evidence review.

Search strategy
Ovid MEDLINE ALL 1946 to January 07, 2021
Date searched: January 8, 2021
1 Gender Dysphoria/ or Transgender Persons/ or Transsexualism/ or (F2M or M2F or "assigned female" or "assigned male" or "female-to-male" or (gender adj3 (dysphor* or minorit* or nonbinary or non-binary or nonconforming or non-conforming)) or "male-to-female" or transboy* or transfemale or trans-female or transfeminine or trans-feminine or transgender* or

trans-gender* or transgirl* or transmale or trans-male or transmasculine or trans-masculine or transsexual* or trans-sexual*).ti,kf. (20784)
2 Adolescent/ or Child/ or (adolescence or adolescent* or boy or boys or child* or girl or girls or juvenile* or paediatr* or pediatr* or prepubertal or pre-pubertal or prepubesc* or pre-pubesc* or pubesc* or pubertal or puberty or school or teen* or tween* or youth*).ti,ab,kf. or (adolescen* or child* or paediat* or pediat*).jw. (3984645)
3 Androgens/ or exp Estrogens/ or exp Gonadal Steroid Hormones/ or Hormone Replacement Therapy/ or Testosterone/ or ((gender adj3 (affirm* or confirm* or reassign*)) or androgen* or antiandrogen* or anti-androgen* or estradiol or oestradiol or estrogen* or oestrogen* or feminising or feminizing or "gonadotropin-releasing hormone" or GnRH or GnRHa or inhibit* or HRT or (hormon* adj3 (replac* or suppress* or therap* or treat*)) or progestin* or suppress* or testosteron*).ti,ab,kf. (3230286)
4 Sex Reassignment Procedures/ or Sex Reassignment Surgery/ or (((bottom or gender or genital) adj3 surger*) or clitoroplast* or genitoplast* or hysterectom* or labiaplast* or metoidioplast* or oophorectom* or orchiectom* or phalloplast* or (sex* adj3 reassign*) or vaginectom* or vaginoplast*).ti,ab,kf. (54867)
5 or/3-4 (3275183)
6 and/1-2,5 (1189)
7 6 not ((exp animals/ not humans/) or (animal* or canine* or crustacean* or dog or dogs or mice or monkey* or mouse or murine or primate* or rat or rats or rattus).ti. or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/) (847)
8 limit 7 to english language (791)
9 (systematic review or meta-analysis).pt. or (metaanal* or meta-anal*).ti,ab,kf. or ((systematic or evidence or integrat* or "mixed methods") adj3 (review or synthesis)).ti,ab,kf. (361026)
10 and/8-9 (6)
11 limit 10 to yr="2018 -Current" (6) <u>Systematic Review and Meta-analysis Results</u>
12 randomized controlled trials as topic/ or Clinical Trials, Phase III as Topic/ or Clinical Trials, Phase IV as Topic/ or Controlled Clinical Trials as Topic/ or ("randomized controlled trial" or "controlled clinical trial").pt. or (blind* or placebo* or random* or trial*).ti,ab,kf. (2138071)
13 and/8,12 (37)
14 limit 13 to yr="2016 -Current" (23) <u>Trial Results</u>
15 exp cohort studies/ or exp epidemiologic studies/ or (clinical study or observational study).pt. or (before-after or "case control" or "case series" or (control and (group* or study)) or cohort or cohorts or ((comparative or evaluation) adj (study or studies)) or observational).ti,ab,kf. (4289515)
16 and/8,15 (286)
17 limit 16 to yr="2016-Current" (181) <u>Observational Studies Results</u>
18 Focus Groups/ or Grounded Theory/ or "Interviews as Topic"/ or Qualitative Research/ or "Surveys and Questionnaires"/ (585616)
19 ("critical interpretive" or "critical race" or "critical realism" or "critical realist" or ethnograph* or "grounded theory" or phenomenolog*).ti,ab,kf,kw. (51085)
20 ("case study" or "content analysis" or descriptive or "focus group" or "focus groups" or interview* or "mixed design" or "mixed methods" or qualitative or questionnaire* or survey*).ti,ab,kf,kw. (1669770)
21 (attitudes or barriers or facilitators or experiences or perceptions or perspectives or preferences or values or viewpoints or views).ti,ab,kf,kw. (1845932)
22 or/18-21 (3290543)
23 and/8,22 (335)
24 limit 23 to yr="2016-Current" (226) <u>(Qualitative Studies Results)</u>

Ovid EBM Reviews - Cochrane Central Register of Controlled Trials November 2020
Date searched: January 8, 2021
1 Gender Dysphoria/ or Transgender Persons/ or Transsexualism/ or (F2M or M2F or "assigned female" or "assigned male" or "female-to-male" or (gender adj3 (dysphor* or minorit* or nonbinary or non-binary or nonconforming or non-conforming)) or "male-to-female" or transboy* or transfemale or trans-female or transfeminine or trans-feminine or transgender* or trans-gender* or transgirl* or transmale or trans-male or transmasculine or trans-masculine or transsexual* or trans-sexual*).ti. (897)
2 Adolescent/ or Child/ or (adolescence or adolescent* or boy or boys or child* or girl or girls or juvenile* or paediatr* or pediatr* or prepubertal or pre-pubertal or prepubesc* or pre-pubesc* or pubesc* or pubertal or puberty or school or teen* or tween* or youth*).ti,ab. or (adolescen* or child* or paediat* or pediat*).jw. (271417)
3 Androgens/ or exp Estrogens/ or exp Gonadal Steroid Hormones/ or Hormone Replacement Therapy/ or Testosterone/ or ((gender adj3 (affirm* or confirm* or reassign*)) or androgen* or antiandrogen* or anti-androgen* or estradiol or oestradiol or estrogen* or oestrogen* or feminising or feminizing or "gonadotropin-releasing hormone" or GnRH or GnRHa or inhibit* or HRT or (hormon* adj3 (replac* or suppress* or therap* or treat*)) or progestin* or suppress* or testosteron*).ti,ab. (164326)
4 Sex Reassignment Procedures/ or Sex Reassignment Surgery/ or (((bottom or gender or genital) adj3 surger*) or clitoroplast* or genitoplast* or hysterectom* or labiaplast* or metoidioplast* or oophorectom* or orchiectom* or phalloplast* or (sex* adj3 reassign*) or vaginectom* or vaginoplast*).ti,ab. (8156)
5 or/3-4 (170755)
6 and/1-2,5 (16)
7 6 not ((exp animals/ not humans/) or (animal* or canine* or crustacean* or dog or dogs or mice or monkey* or mouse or murine or primate* or rat or rats or rattus).ti.) (16)
8 limit 7 to yr="2016 -Current" (6)

Ovid PsycInfo 1806 to January Week 1 2021
Date searched: January 8, 2021
1 Gender Dysphoria/ or Transgender/ or Transsexualism/ or (F2M or M2F or "assigned female" or "assigned male" or "female-to-male" or (gender adj3 (dysphor* or minorit* or nonbinary or non-binary or nonconforming or non-conforming)) or "male-to-female" or transboy* or transfemale or trans-female or transfeminine or trans-feminine or transgender* or trans-gender* or transgirl* or transmale or trans-male or transmasculine or trans-masculine or transsexual* or trans-sexual*).ti. (15710)
2 (adolescence or adolescent* or boy or boys or child* or girl or girls or juvenile* or paediatr* or pediatr* or prepubertal or pre-pubertal or prepubesc* or pre-pubesc* or pubesc* or pubertal or puberty or school or teen* or tween* or youth*).ti,ab. or (adolescen* or child* or paediat* or pediat* or youth*).jw. (1123314)
3 ((gender adj3 (affirm* or confirm* or reassign*)) or androgen* or antiandrogen* or anti-androgen* or estradiol or oestradiol or estrogen* or oestrogen* or feminising or feminizing or "gonadotropin-releasing hormone" or GnRH or GnRHa or inhibit* or HRT or (hormon* adj3 (replac* or suppress* or therap* or treat*)) or progestin* or suppress* or testosteron*).ti,ab. (213738)
4 (((bottom or gender or genital) adj3 surger*) or clitoroplast* or genitoplast* or hysterectom* or labiaplast* or metoidioplast* or oophorectom* or orchiectom* or phalloplast* or (sex* adj3 reassign*) or vaginectom* or vaginoplast*).ti,ab. (1929)
5 or/3-4 (215040)
6 and/1-2,5 (494)

7 6 not (animal* or canine* or crustacean* or dog or dogs or mice or monkey* or mouse or murine or primate* or rat or rats or rattus).ti. (451)
8 limit 7 to english language (393)
9 limit 8 to ("0830systematic review" or 1200 meta analysis or 1300 metasynthesis) (3)
10 limit 9 to yr="2018 -Current" (3) Systematic Review and Meta-analysis Results
11 limit 8 to "0300 clinical trial" (0)
12 limit 11 to yr="2016 -Current" (0) Trial Results
13 limit 8 to ("0400 empirical study" or "0430 followup study" or "0450 longitudinal study" or "0451 prospective study" or "0453 retrospective study" or 1800 quantitative study or 2100 treatment outcome) (201)
14 limit 13 to yr="2016 -Current" (109) Observational Study Results
15 limit 8 to 1600 qualitative study (39)
16 limit 15 to yr="2016 -Current" (32) Qualitative Study Results

ClinicalTrials.gov
Date searched: January 8, 2021
EXPERT SEARCH MODE: (F2M OR M2F OR F-2-M OR M-2-F OR EXPAND[Concept] "assigned female" OR EXPAND[Concept] "assigned male" OR EXPAND[Concept] "female-to-male" OR gender dysphoria OR gender minority OR nonbinary OR non-binary OR nonconforming OR non-conforming OR EXPAND[Concept] "male-to-female" OR transboy OR transfemale OR trans-female OR transfeminine OR trans-feminine OR transgender OR trans-gender OR transgirl OR transmale OR trans-male OR transmasculine OR trans-masculine OR transsexual OR trans-sexual) AND (adolescence OR adolescent OR boy OR boys OR child OR girl OR girls OR juvenile OR paediatric OR pediatric OR prepubertal OR pre-pubertal OR prepubescent OR pre-pubescent OR pubescent OR pubertal OR puberty OR school OR teen OR tween OR youth) AND (gender affirming OR gender confirming OR gender reassignment OR androgen OR antiandrogen* OR anti-androgen OR estradiol OR oestradiol OR estrogen OR oestrogen OR feminising OR feminizing OR EXPAND[Concept] "gonadotropin-releasing hormone" OR GnRH OR GnRHa OR inhibit OR HRT OR hormone replacement OR suppression OR hormone therapy OR hormone treatment OR progestin OR testosterone OR bottom surgery OR gender surgery OR genital surgery OR clitoroplasty or genitoplasty OR hysterectomy OR labiaplast OR metoidioplasty OR oophorectomy OR orchiectomy OR phalloplast8 OR sex reassignment OR vaginectomy OR vaginoplasty) | Child | First posted from 01/01/2016 to 01/08/2020 (26)

clinicaltrials.gov link

Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the United States?	Yes
1b. Is the nomination a request for an evidence report?	Yes
1c. Is the focus on effectiveness or comparative effectiveness?	Yes
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	An estimated 0.6% of adults[2] and 0.7% of youth ages 13 to 17[3] in the United States identify as transgender or "gender nonconforming". While this may not be a large proportion of the population, it affects a vulnerable population.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, transgender individuals represent a vulnerable population. Transgender youth experience high rates of depression, anxiety, eating disorders, and suicide.[4-6]
2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, the cost to transition genders costs about $20,000 over two years.[24]
3. Desirability of a New Evidence Review/Absence of Duplication	
3. A recent high-quality systematic review or other evidence review is not available on this topic	No. We found one protocol for a systematic review that addresses KQ1. We found protocols that partially cover KQ 2 and 3.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes. There is a lack of current evidence-based guidance for care of children and adolescents who identify as transgender, particularly regarding the benefits and harms of pubertal suppression, medical affirmation with hormone therapy, and surgical affirmation. While there are some existing guidelines and standards of care, [1, 7, 8]most are derived from expert opinion or have not been updated recently.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes. There is a lack of current evidence-based guidance for care of children and adolescents who identify as transgender, particularly regarding the benefits and harms of pubertal suppression, medical affirmation with hormone therapy, and surgical affirmation. While there are some existing guidelines and standards of care, [1, 7, 8]most are derived from expert opinion or have not been updated recently.

Selection Criteria	Assessment
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	We did not find any studies addressing the remaining portions of KQ2 and 3 that were not covered by existing protocols.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; KQ=key question.

EXHIBIT 115

Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline

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*Cosponsoring Associations: American Association of Clinical Endocrinologists, American Society of Andrology, European Society for Pediatric Endocrinology, European Society of Endocrinology, Pediatric Endocrine Society, and World Professional Association for Transgender Health.

Objective: To update the "Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline," published by the Endocrine Society in 2009.

Participants: The participants include an Endocrine Society–appointed task force of nine experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The task force commissioned two systematic reviews and used the best available evidence from other published systematic reviews and individual studies.

Consensus Process: Group meetings, conference calls, and e-mail communications enabled consensus. Endocrine Society committees, members and cosponsoring organizations reviewed and commented on preliminary drafts of the guidelines.

Conclusion: Gender affirmation is multidisciplinary treatment in which endocrinologists play an important role. Gender-dysphoric/gender-incongruent persons seek and/or are referred to endocrinologists to develop the physical characteristics of the affirmed gender. They require a safe and effective hormone regimen that will (1) suppress endogenous sex hormone secretion determined by the person's genetic/gonadal sex and (2) maintain sex hormone levels within the normal range for the person's affirmed gender. Hormone treatment is not recommended for prepubertal gender-dysphoric/gender-incongruent persons. Those clinicians who recommend gender-affirming endocrine treatments—appropriately trained diagnosing clinicians (required), a mental health provider for adolescents (required) and mental health

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Abbreviations: BMD, bone mineral density; DSD, disorder/difference of sex development; DSM, Diagnostic and Statistical Manual of Mental Disorders; GD, gender dysphoria; GnRH, gonadotropin-releasing hormone; ICD, International Statistical Classification of Diseases and Related Health Problems; MHP, mental health professional; VTE, venous thromboembolism.

professional for adults (recommended)—should be knowledgeable about the diagnostic criteria and criteria for gender-affirming treatment, have sufficient training and experience in assessing psychopathology, and be willing to participate in the ongoing care throughout the endocrine transition. We recommend treating gender-dysphoric/gender-incongruent adolescents who have entered puberty at Tanner Stage G2/B2 by suppression with gonadotropin-releasing hormone agonists. Clinicians may add gender-affirming hormones after a multidisciplinary team has confirmed the persistence of gender dysphoria/gender incongruence and sufficient mental capacity to give informed consent to this partially irreversible treatment. Most adolescents have this capacity by age 16 years old. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to age 16 years, although there is minimal published experience treating prior to 13.5 to 14 years of age. For the care of peripubertal youths and older adolescents, we recommend that an expert multidisciplinary team comprised of medical professionals and mental health professionals manage this treatment. The treating physician must confirm the criteria for treatment used by the referring mental health practitioner and collaborate with them in decisions about gender-affirming surgery in older adolescents. For adult gender-dysphoric/gender-incongruent persons, the treating clinicians (collectively) should have expertise in transgender-specific diagnostic criteria, mental health, primary care, hormone treatment, and surgery, as needed by the patient. We suggest maintaining physiologic levels of gender-appropriate hormones and monitoring for known risks and complications. When high doses of sex steroids are required to suppress endogenous sex steroids and/or in advanced age, clinicians may consider surgically removing natal gonads along with reducing sex steroid treatment. Clinicians should monitor both transgender males (female to male) and transgender females (male to female) for reproductive organ cancer risk when surgical removal is incomplete. Additionally, clinicians should persistently monitor adverse effects of sex steroids. For gender-affirming surgeries in adults, the treating physician must collaborate with and confirm the criteria for treatment used by the referring physician. Clinicians should avoid harming individuals (via hormone treatment) who have conditions other than gender dysphoria/gender incongruence and who may not benefit from the physical changes associated with this treatment. (***J Clin Endocrinol Metab*** **102: 3869–3903, 2017)**

Summary of Recommendations

1.0 Evaluation of youth and adults

1.1. We advise that only trained mental health professionals (MHPs) who meet the following criteria should diagnose gender dysphoria (GD)/gender incongruence in adults: (1) competence in using the Diagnostic and Statistical Manual of Mental Disorders (DSM) and/or the International Statistical Classification of Diseases and Related Health Problems (ICD) for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)

1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or the ICD for diagnostic purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)

1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).

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1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 |⊕⊕◯◯)

1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 |⊕⊕⊕◯)

2.0 Treatment of adolescents

2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment, and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 |⊕⊕◯◯)

2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty. (2 |⊕⊕◯◯)

2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 |⊕⊕◯◯)

2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years. (1 |⊕⊕◯◯).

2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 |⊕◯◯◯)

2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment. (2 |⊕⊕◯◯)

3.0 Hormonal therapy for transgender adults

3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and the criteria for the endocrine phase of gender transition before beginning treatment. (1 |⊕⊕⊕◯)

3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment. (1 |⊕⊕⊕◯)

3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 |⊕⊕◯◯)

3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 |⊕◯◯◯)

4.0 Adverse outcome prevention and long-term care

4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every 3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 |⊕⊕◯◯)

4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 |⊕⊕◯◯)

4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 |⊕⊕◯◯)

4.4. We recommend that clinicians obtain bone mineral density (BMD) measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 |⊕⊕◯◯)

4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for non-transgender females. (2 |⊕⊕◯◯)

4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 |⊕◯◯◯)

4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

5.0 Surgery for sex reassignment and gender confirmation

5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically necessary and would benefit the patient's overall health and/or well-being. (1 ⊕⊕◯◯)

5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)

5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)

5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 ⊕◯◯◯)

5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 ⊕⊕◯◯).

5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 ⊕◯◯◯)

Changes Since the Previous Guideline

Both the current guideline and the one published in 2009 contain similar sections. Listed here are the sections contained in the current guideline and the corresponding number of recommendations: Introduction, Evaluation of Youth and Adults (5), Treatment of Adolescents (6), Hormonal Therapy for Transgender Adults (4), Adverse Outcomes Prevention and Long-term Care (7), and Surgery for Sex Reassignment and Gender Confirmation (6). The current introduction updates the diagnostic classification of "gender dysphoria/gender incongruence." It also reviews the development of "gender identity" and summarizes its natural development. The section on clinical evaluation of both youth and adults, defines in detail the professional qualifications required of those who diagnose and treat both adolescents and adults. We advise that decisions regarding the social transition of prepubertal youth are made with the assistance of a mental health professional or similarly experienced professional. We recommend against puberty blocking followed by gender-affirming hormone treatment of prepubertal children. Clinicians should inform pubertal children, adolescents, and adults seeking gender-confirming treatment of their options for fertility preservation. Prior to treatment, clinicians should evaluate the presence of medical conditions that may be worsened by hormone depletion and/or treatment. A multidisciplinary team, preferably composed of medical and mental health professionals, should monitor treatments. Clinicians evaluating transgender adults for endocrine treatment should confirm the diagnosis of persistent gender dysphoria/gender incongruence. Physicians should educate transgender persons regarding the time course of steroid-induced physical changes. Treatment should include periodic monitoring of hormone levels and metabolic parameters, as well as assessments of bone density and the impact upon prostate, gonads, and uterus. We also make recommendations for transgender persons who plan genital gender-affirming surgery.

Method of Development of Evidence-Based Clinical Practice Guidelines

The Clinical Guidelines Subcommittee (CGS) of the Endocrine Society deemed the diagnosis and treatment of individuals with GD/gender incongruence a priority area for revision and appointed a task force to formulate evidence-based recommendations. The task force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation group, an international group with expertise in the development and implementation of evidence-based guidelines (1). A detailed description of the grading scheme has been published elsewhere (2). The task force used the best available research evidence to develop the recommendations. The task force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of the recommendation, strong recommendations use the phrase "we recommend" and the number 1, and weak recommendations use the phrase "we suggest" and the number 2. Cross-filled circles indicate the quality of the evidence, such that ⊕◯◯◯ denotes very low–quality evidence; ⊕⊕◯◯, low quality; ⊕⊕⊕◯, moderate quality; and ⊕⊕⊕⊕, high quality. The task force has confidence that persons who receive care according to the strong recommendations will derive, on average, more benefit than harm. Weak recommendations require more careful consideration of the person's circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the

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values that the task force considered in making the recommendation. In some instances, there are remarks in which the task force offers technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the task force and their preferences; therefore, one should consider these remarks as suggestions.

In this guideline, the task force made several statements to emphasize the importance of shared decision-making, general preventive care measures, and basic principles of the treatment of transgender persons. They labeled these "Ungraded Good Practice Statement." Direct evidence for these statements was either unavailable or not systematically appraised and considered out of the scope of this guideline. The intention of these statements is to draw attention to these principles.

The Endocrine Society maintains a rigorous conflict-of-interest review process for developing clinical practice guidelines. All task force members must declare any potential conflicts of interest by completing a conflict-of-interest form. The CGS reviews all conflicts of interest before the Society's Council approves the members to participate on the task force and periodically during the development of the guideline. All others participating in the guideline's development must also disclose any conflicts of interest in the matter under study, and most of these participants must be without any conflicts of interest. The CGS and the task force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from commercial interests; grants; research support; consulting fees; salary; ownership interests [*e.g.*, stocks and stock options (excluding diversified mutual funds)]; honoraria and other payments for participation in speakers' bureaus, advisory boards, or boards of directors; and all other financial benefits. Completed forms are available through the Endocrine Society office.

The Endocrine Society provided the funding for this guideline; the task force received no funding or remuneration from commercial or other entities.

Commissioned Systematic Review

The task force commissioned two systematic reviews to support this guideline. The first one aimed to summarize the available evidence on the effect of sex steroid use in transgender individuals on lipids and cardiovascular outcomes. The review identified 29 eligible studies at moderate risk of bias. In transgender males (female to male), sex steroid therapy was associated with a statistically significant increase in serum triglycerides and low-density lipoprotein cholesterol levels. High-density lipoprotein cholesterol levels decreased significantly across all follow-up time periods. In transgender females (male to female), serum triglycerides were significantly higher without any changes in other parameters. Few myocardial infarction, stroke, venous thromboembolism (VTE), and death events were reported. These events were more frequent in transgender females. However, the quality of the evidence was low. The second review summarized the available evidence regarding the effect of sex steroids on bone health in transgender individuals and identified 13 studies. In transgender males, there was no statistically significant difference in the lumbar spine, femoral neck, or total hip BMD at 12 and 24 months compared with baseline values before initiating masculinizing hormone therapy. In transgender females, there was a statistically significant increase in lumbar spine BMD at 12 months and 24 months compared with baseline values before initiation of feminizing hormone therapy. There was minimal information on fracture rates. The quality of evidence was also low.

Introduction

Throughout recorded history (in the absence of an endocrine disorder) some men and women have experienced confusion and anguish resulting from rigid, forced conformity to sexual dimorphism. In modern history, there have been numerous ongoing biological, psychological, cultural, political, and sociological debates over various aspects of gender variance. The 20th century marked the emergence of a social awakening for men and women with the belief that they are "trapped" in the wrong body (3). Magnus Hirschfeld and Harry Benjamin, among others, pioneered the medical responses to those who sought relief from and a resolution to their profound discomfort. Although the term transsexual became widely known after Benjamin wrote "The Transsexual Phenomenon" (4), it was Hirschfeld who coined the term "transsexual" in 1923 to describe people who want to live a life that corresponds with their experienced gender vs their designated gender (5). Magnus Hirschfeld (6) and others (4, 7) have described other types of trans phenomena besides transsexualism. These early researchers proposed that the gender identity of these people was located somewhere along a unidimensional continuum. This continuum ranged from all male through "something in between" to all female. Yet such a classification does not take into account that people may have gender identities outside this continuum. For instance, some experience themselves as having both a male and female gender identity, whereas others completely renounce any gender classification (8, 9). There are also reports of individuals experiencing a continuous and rapid involuntary alternation between a male and female identity (10) or men who do not experience themselves as men but do not want to live as women (11, 12). In some countries, (*e.g.*, Nepal, Bangladesh, and Australia), these nonmale or nonfemale genders are officially recognized (13). Specific treatment protocols, however, have not yet been developed for these groups.

Instead of the term transsexualism, the current classification system of the American Psychiatric Association uses the term gender dysphoria in its diagnosis of persons who are not satisfied with their designated gender (14). The current version of the World Health Organization's ICD-10 still uses the term transsexualism when diagnosing adolescents and adults. However, for the ICD-11, the World Health Organization has proposed using the term "gender incongruence" (15).

Treating persons with GD/gender incongruence (15) was previously limited to relatively ineffective elixirs or creams. However, more effective endocrinology-based treatments became possible with the availability of testosterone in 1935 and diethylstilbestrol in 1938. Reports of individuals with GD/gender incongruence who were treated with hormones and gender-affirming surgery appeared in the press during the second half of the 20th century. The Harry Benjamin International Gender Dysphoria Association was founded in September 1979 and is now called the World Professional Association for Transgender Health (WPATH). WPATH published its first Standards of Care in 1979. These standards have since been regularly updated, providing guidance for treating persons with GD/gender incongruence (16).

Prior to 1975, few peer-reviewed articles were published concerning endocrine treatment of transgender persons. Since then, more than two thousand articles about various aspects of transgender care have appeared.

It is the purpose of this guideline to make detailed recommendations and suggestions, based on existing medical literature and clinical experience, that will enable treating physicians to maximize benefit and minimize risk when caring for individuals diagnosed with GD/gender incongruence.

In the future, we need more rigorous evaluations of the effectiveness and safety of endocrine and surgical protocols. Specifically, endocrine treatment protocols for GD/gender incongruence should include the careful assessment of the following: (1) the effects of prolonged delay of puberty in adolescents on bone health, gonadal function, and the brain (including effects on cognitive, emotional, social, and sexual development); (2) the effects of treatment in adults on sex hormone levels; (3) the requirement for and the effects of progestins and other agents used to suppress endogenous sex steroids during treatment; and (4) the risks and benefits of gender-affirming hormone treatment in older transgender people.

To successfully establish and enact these protocols, a commitment of mental health and endocrine investigators is required to collaborate in long-term, large-scale studies across countries that use the same diagnostic and inclusion criteria, medications, assay methods, and response assessment tools (*e.g.*, the European Network for the Investigation of Gender Incongruence) (17, 18).

Terminology and its use vary and continue to evolve. Table 1 contains the definitions of terms as they are used throughout this guideline.

Biological Determinants of Gender Identity Development

One's self-awareness as male or female changes gradually during infant life and childhood. This process of cognitive and affective learning evolves with interactions with parents, peers, and environment. A fairly accurate timetable exists outlining the steps in this process (19). Normative psychological literature, however, does not address if and when gender identity becomes crystallized and what factors contribute to the development of a gender identity that is not congruent with the gender of rearing. Results of studies from a variety of biomedical disciplines—genetic, endocrine, and neuroanatomic—support the concept that gender identity and/or gender expression (20) likely reflect a complex interplay of biological, environmental, and cultural factors (21, 22).

With respect to endocrine considerations, studies have failed to find differences in circulating levels of sex steroids between transgender and nontransgender individuals (23). However, studies in individuals with a disorder/difference of sex development (DSD) have informed our understanding of the role that hormones may play in gender identity outcome, even though most persons with GD/gender incongruence do not have a DSD. For example, although most 46,XX adult individuals with virilizing congenital adrenal hyperplasia caused by mutations in *CYP21A2* reported a female gender identity, the prevalence of GD/gender incongruence was much greater in this group than in the general population without a DSD. This supports the concept that there is a role for prenatal/postnatal androgens in gender development (24–26), although some studies indicate that prenatal androgens are more likely to affect gender behavior and sexual orientation rather than gender identity *per se* (27, 28).

Researchers have made similar observations regarding the potential role of androgens in the development of gender identity in other individuals with DSD. For example, a review of two groups of 46,XY persons, each with androgen synthesis deficiencies and female raised, reported transgender male (female-to-male) gender role changes in 56% to 63% and 39% to 64% of patients, respectively (29). Also, in 46,XY female-raised individuals with cloacal

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Table 1. Definitions of Terms Used in This Guideline

Biological sex, biological male or female: These terms refer to physical aspects of maleness and femaleness. As these may not be in line with each other (*e.g.*, a person with XY chromosomes may have female-appearing genitalia), the terms biological sex and biological male or female are imprecise and should be avoided.

Cisgender: This means not transgender. An alternative way to describe individuals who are not transgender is "non-transgender people."

Gender-affirming (hormone) treatment: See "gender reassignment"

Gender dysphoria: This is the distress and unease experienced if gender identity and designated gender are not completely congruent (see Table 2). In 2013, the American Psychiatric Association released the fifth edition of the DSM-5, which replaced "gender identity disorder" with "gender dysphoria" and changed the criteria for diagnosis.

Gender expression: This refers to external manifestations of gender, expressed through one's name, pronouns, clothing, haircut, behavior, voice, or body characteristics. Typically, transgender people seek to make their gender expression align with their gender identity, rather than their designated gender.

Gender identity/experienced gender: This refers to one's internal, deeply held sense of gender. For transgender people, their gender identity does not match their sex designated at birth. Most people have a gender identity of man or woman (or boy or girl). For some people, their gender identity does not fit neatly into one of those two choices. Unlike gender expression (see below), gender identity is not visible to others.

Gender identity disorder: This is the term used for GD/gender incongruence in previous versions of DSM (see "gender dysphoria"). The ICD-10 still uses the term for diagnosing child diagnoses, but the upcoming ICD-11 has proposed using "gender incongruence of childhood."

Gender incongruence: This is an umbrella term used when the gender identity and/or gender expression differs from what is typically associated with the designated gender. Gender incongruence is also the proposed name of the gender identity–related diagnoses in ICD-11. Not all individuals with gender incongruence have gender dysphoria or seek treatment.

Gender variance: See "gender incongruence"

Gender reassignment: This refers to the treatment procedure for those who want to adapt their bodies to the experienced gender by means of hormones and/or surgery. This is also called gender-confirming or gender-affirming treatment.

Gender-reassignment surgery (gender-confirming/gender-affirming surgery): These terms refer only to the surgical part of gender-confirming/gender-affirming treatment.

Gender role: This refers to behaviors, attitudes, and personality traits that a society (in a given culture and historical period) designates as masculine or feminine and/or that society associates with or considers typical of the social role of men or women.

Sex designated at birth: This refers to sex assigned at birth, usually based on genital anatomy.

Sex: This refers to attributes that characterize biological maleness or femaleness. The best known attributes include the sex-determining genes, the sex chromosomes, the H-Y antigen, the gonads, sex hormones, internal and external genitalia, and secondary sex characteristics.

Sexual orientation: This term describes an individual's enduring physical and emotional attraction to another person. Gender identity and sexual orientation are not the same. Irrespective of their gender identity, transgender people may be attracted to women (gynephilic), attracted to men (androphilic), bisexual, asexual, or queer.

Transgender: This is an umbrella term for people whose gender identity and/or gender expression differs from what is typically associated with their sex designated at birth. Not all transgender individuals seek treatment.

Transgender male (also: trans man, female-to-male, transgender male): This refers to individuals assigned female at birth but who identify and live as men.

Transgender woman (also: trans woman, male-to female, transgender female): This refers to individuals assigned male at birth but who identify and live as women.

Transition: This refers to the process during which transgender persons change their physical, social, and/or legal characteristics consistent with the affirmed gender identity. Prepubertal children may choose to transition socially.

Transsexual: This is an older term that originated in the medical and psychological communities to refer to individuals who have permanently transitioned through medical interventions or desired to do so.

exstrophy and penile agenesis, the occurrence of transgender male changes was significantly more prevalent than in the general population (30, 31). However, the fact that a high percentage of individuals with the same conditions did not change gender suggests that cultural factors may play a role as well.

With respect to genetics and gender identity, several studies have suggested heritability of GD/gender incongruence (32, 33). In particular, a study by Heylens *et al.* (33) demonstrated a 39.1% concordance rate for gender identity disorder (based on the DSM-IV criteria) in 23 monozygotic twin pairs but no concordance in 21 same-sex dizygotic or seven opposite-sex twin pairs. Although numerous investigators have sought to identify specific genes associated with GD/gender incongruence, such studies have been inconsistent and without strong statistical significance (34–38).

Studies focusing on brain structure suggest that the brain phenotypes of people with GD/gender incongruence differ in various ways from control males and females, but that there is not a complete sex reversal in brain structures (39).

In summary, although there is much that is still unknown with respect to gender identity and its expression, compelling studies support the concept that biologic factors, in addition to environmental factors, contribute to this fundamental aspect of human development.

Natural History of Children With GD/Gender Incongruence

With current knowledge, we cannot predict the psychosexual outcome for any specific child. Prospective follow-up studies show that childhood GD/gender incongruence does not invariably persist into adolescence and adulthood (so-called "desisters"). Combining all outcome studies to date, the GD/gender incongruence of a minority of prepubertal children appears to persist in adolescence (20, 40). In adolescence, a significant number of these desisters identify as homosexual or bisexual. It may be that children who only showed some gender nonconforming characteristics have been included in the follow-up studies, because the DSM-IV text revision criteria for a diagnosis were rather broad. However, the persistence of GD/gender incongruence into adolescence is more likely if it had been extreme in childhood (41, 42). With the newer, stricter criteria of the DSM-5 (Table 2), persistence rates may well be different in future studies.

1.0 Evaluation of Youth and Adults

Gender-affirming treatment is a multidisciplinary effort. After evaluation, education, and diagnosis, treatment may include mental health care, hormone therapy, and/or surgical therapy. Together with an MHP, hormone-prescribing clinicians should examine the psychosocial impact of the potential changes on people's lives, including mental health, friends, family, jobs, and their role in society. Transgender individuals should be encouraged to experience living in the new gender role and assess whether this improves their quality of life. Although the focus of this guideline is gender-affirming hormone therapy, collaboration with appropriate professionals responsible for each aspect of treatment maximizes a successful outcome.

Diagnostic assessment and mental health care

GD/gender incongruence may be accompanied with psychological or psychiatric problems (43–51). It is therefore necessary that clinicians who prescribe hormones and are involved in diagnosis and psychosocial assessment meet the following criteria: (1) are competent in using the DSM and/or the ICD for diagnostic purposes, (2) are able to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) are trained in diagnosing psychiatric conditions, (4) undertake or refer for appropriate treatment, (5) are able to do a psychosocial assessment of the patient's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) regularly attend relevant professional meetings.

Because of the psychological vulnerability of many individuals with GD/gender incongruence, it is important that mental health care is available before, during, and sometimes also after transitioning. For children and adolescents, an MHP who has training/experience in child and adolescent gender development (as well as child and adolescent psychopathology) should make the diagnosis, because assessing GD/gender incongruence in children and adolescents is often extremely complex.

During assessment, the clinician obtains information from the individual seeking gender-affirming treatment. In the case

Table 2. DSM-5 Criteria for Gender Dysphoria in Adolescents and Adults

A. A marked incongruence between one's experienced/expressed gender and natal gender of at least 6 mo in duration, as manifested by at least two of the following:
   1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
   2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
   3. A strong desire for the primary and/or secondary sex characteristics of the other gender
   4. A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
   5. A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)
   6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender)

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:
   1. The condition exists with a disorder of sex development.
   2. The condition is posttransitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (*e.g.*, penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

Reference: American Psychiatric Association (14).

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of adolescents, the clinician also obtains information from the parents or guardians regarding various aspects of the child's general and psychosexual development and current functioning. On the basis of this information, the clinician:

- decides whether the individual fulfills criteria for treatment (see Tables 2 and 3) for GD/gender incongruence (DSM-5) or transsexualism (DSM-5 and/or ICD-10);
- informs the individual about the possibilities and limitations of various kinds of treatment (hormonal/surgical and nonhormonal), and if medical treatment is desired, provides correct information to prevent unrealistically high expectations;
- assesses whether medical interventions may result in unfavorable psychological and social outcomes.

In cases in which severe psychopathology, circumstances, or both seriously interfere with the diagnostic work or make satisfactory treatment unlikely, clinicians should assist the adolescent in managing these other issues. Literature on postoperative regret suggests that besides poor quality of surgery, severe psychiatric comorbidity and lack of support may interfere with positive outcomes (52–56).

For adolescents, the diagnostic procedure usually includes a complete psychodiagnostic assessment (57) and an assessment of the decision-making capability of the youth. An evaluation to assess the family's ability to endure stress, give support, and deal with the complexities of the adolescent's situation should be part of the diagnostic phase (58).

Social transitioning

A change in gender expression and role (which may involve living part time or full time in another gender role that is consistent with one's gender identity) may test the person's resolve, the capacity to function in the affirmed gender, and the adequacy of social, economic, and psychological supports. It assists both the individual and the clinician in their judgments about how to proceed (16). During social transitioning, the person's feelings about the social transformation (including coping with the responses of others) is a major focus of the counseling. The optimal timing for social transitioning may differ between individuals. Sometimes people wait until they start gender-affirming hormone treatment to make social transitioning easier, but individuals increasingly start social transitioning long before they receive medically supervised, gender-affirming hormone treatment.

Criteria

Adolescents and adults seeking gender-affirming hormone treatment and surgery should satisfy certain criteria before proceeding (16). Criteria for gender-affirming hormone therapy for adults are in Table 4, and criteria for gender-affirming hormone therapy for adolescents are in Table 5. Follow-up studies in adults meeting these criteria indicate a high satisfaction rate with treatment (59). However, the quality of evidence is usually low. A few follow-up studies on adolescents who fulfilled these criteria also indicated good treatment results (60–63).

Recommendations for Those Involved in the Gender-Affirming Hormone Treatment of Individuals With GD/Gender Incongruence

1.1. We advise that only trained MHPs who meet the following criteria should diagnose GD/gender incongruence in adults: (1) competence in using the DSM and/or the ICD for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)

1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or ICD for diagnostic

Table 3. ICD-10 Criteria for Transsexualism

Transsexualism (F64.0) has three criteria:
1. The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatments.
2. The transsexual identity has been present persistently for at least 2 y.
3. The disorder is not a symptom of another mental disorder or a genetic, DSD, or chromosomal abnormality.

Table 4. Criteria for Gender-Affirming Hormone Therapy for Adults

1. Persistent, well-documented gender dysphoria/gender incongruence
2. The capacity to make a fully informed decision and to consent for treatment
3. The age of majority in a given country (if younger, follow the criteria for adolescents)
4. Mental health concerns, if present, must be reasonably well controlled

Reproduced from World Professional Association for Transgender Health (16).

purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)

Evidence

Individuals with gender identity issues may have psychological or psychiatric problems (43–48, 50, 51, 64, 65). It is therefore necessary that clinicians making the diagnosis are able to make a distinction between GD/gender incongruence and conditions that have similar features. Examples of conditions with similar features are body dysmorphic disorder, body identity integrity disorder (a condition in which individuals have a sense that their anatomical configuration as an able-bodied person is somehow wrong or inappropriate) (66), or certain forms of eunuchism (in which a person is preoccupied with or engages in castration and/or penectomy for

Table 5. Criteria for Gender-Affirming Hormone Therapy for Adolescents

Adolescents are eligible for GnRH agonist treatment if:

1. A qualified MHP has confirmed that:
- the adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed),
- gender dysphoria worsened with the onset of puberty,
- any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment,
- the adolescent has sufficient mental capacity to give informed consent to this (reversible) treatment,

2. And the adolescent:
- has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility,
- has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,

3. And a pediatric endocrinologist or other clinician experienced in pubertal assessment
- agrees with the indication for GnRH agonist treatment,
- has confirmed that puberty has started in the adolescent (Tanner stage ≥G2/B2),
- has confirmed that there are no medical contraindications to GnRH agonist treatment.

Adolescents are eligible for subsequent sex hormone treatment if:

1. A qualified MHP has confirmed:
- the persistence of gender dysphoria,
- any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start sex hormone treatment,
- the adolescent has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment,

2. And the adolescent:
- has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility),
- has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,

3. And a pediatric endocrinologist or other clinician experienced in pubertal induction:
- agrees with the indication for sex hormone treatment,
- has confirmed that there are no medical contraindications to sex hormone treatment.

Reproduced from World Professional Association for Transgender Health (16).

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reasons that are not gender identity related) (11). Clinicians should also be able to diagnose psychiatric conditions accurately and ensure that these conditions are treated appropriately, particularly when the conditions may complicate treatment, affect the outcome of gender-affirming treatment, or be affected by hormone use.

Values and preferences

The task force placed a very high value on avoiding harm from hormone treatment in individuals who have conditions other than GD/gender incongruence and who may not benefit from the physical changes associated with this treatment and placed a low value on any potential benefit these persons believe they may derive from hormone treatment. This justifies the good practice statement.

1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).

1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 |⊕⊕◯◯)

Evidence

In most children diagnosed with GD/gender incongruence, it did not persist into adolescence. The percentages differed among studies, probably dependent on which version of the DSM clinicians used, the patient's age, the recruitment criteria, and perhaps cultural factors. However, the large majority (about 85%) of prepubertal children with a childhood diagnosis did not remain GD/gender incongruent in adolescence (20). If children have completely socially transitioned, they may have great difficulty in returning to the original gender role upon entering puberty (40). Social transition is associated with the persistence of GD/gender incongruence as a child progresses into adolescence. It may be that the presence of GD/gender incongruence in prepubertal children is the earliest sign that a child is destined to be transgender as an adolescent/adult (20). However, social transition (in addition to GD/gender incongruence) has been found to contribute to the likelihood of persistence.

This recommendation, however, does not imply that children should be discouraged from showing gender-variant behaviors or should be punished for exhibiting such behaviors. In individual cases, an early complete social transition may result in a more favorable outcome, but there are currently no criteria to identify the GD/gender-incongruent children to whom this applies. At the present time, clinical experience suggests that persistence of GD/gender incongruence can only be reliably assessed after the first signs of puberty.

Values and preferences

The task force placed a high value on avoiding harm with gender-affirming hormone therapy in prepubertal children with GD/gender incongruence. This justifies the strong recommendation in the face of low-quality evidence.

1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 |⊕⊕⊕◯)

Remarks

Persons considering hormone use for gender affirmation need adequate information about this treatment in general and about fertility effects of hormone treatment in particular to make an informed and balanced decision (67, 68). Because young adolescents may not feel qualified to make decisions about fertility and may not fully understand the potential effects of hormonal interventions, consent and protocol education should include parents, the referring MHP(s), and other members of the adolescent's support group. To our knowledge, there are no formally evaluated decision aids available to assist in the discussion and decision regarding the future fertility of adolescents or adults beginning gender-affirming treatment.

Treating early pubertal youth with GnRH analogs will temporarily impair spermatogenesis and oocyte maturation. Given that an increasing number of transgender youth want to preserve fertility potential, delaying or temporarily discontinuing GnRH analogs to promote gamete maturation is an option. This option is often not preferred, because mature sperm production is associated with later stages of puberty and with the significant development of secondary sex characteristics.

For those designated male at birth with GD/gender incongruence and who are in early puberty, sperm production and the development of the reproductive tract are insufficient for the cryopreservation of sperm. However, prolonged pubertal suppression using GnRH analogs is reversible and clinicians should inform these individuals that sperm production can be initiated following prolonged gonadotropin suppression. This can be accomplished by spontaneous gonadotropin recovery after

cessation of GnRH analogs or by gonadotropin treatment and will probably be associated with physical manifestations of testosterone production, as stated above. Note that there are no data in this population concerning the time required for sufficient spermatogenesis to collect enough sperm for later fertility. In males treated for precocious puberty, spermarche was reported 0.7 to 3 years after cessation of GnRH analogs (69). In adult men with gonadotropin deficiency, sperm are noted in seminal fluid by 6 to 12 months of gonadotropin treatment. However, sperm numbers when partners of these patients conceive are far below the "normal range" (70, 71).

In girls, no studies have reported long-term, adverse effects of pubertal suppression on ovarian function after treatment cessation (72, 73). Clinicians should inform adolescents that no data are available regarding either time to spontaneous ovulation after cessation of GnRH analogs or the response to ovulation induction following prolonged gonadotropin suppression.

In males with GD/gender incongruence, when medical treatment is started in a later phase of puberty or in adulthood, spermatogenesis is sufficient for cryopreservation and storage of sperm. *In vitro* spermatogenesis is currently under investigation. Restoration of spermatogenesis after prolonged estrogen treatment has not been studied.

In females with GD/gender incongruence, the effect of prolonged treatment with exogenous testosterone on ovarian function is uncertain. There have been reports of an increased incidence of polycystic ovaries in transgender males, both prior to and as a result of androgen treatment (74–77), although these reports were not confirmed by others (78). Pregnancy has been reported in transgender males who have had prolonged androgen treatment and have discontinued testosterone but have not had genital surgery (79, 80). A reproductive endocrine gynecologist can counsel patients before gender-affirming hormone treatment or surgery regarding potential fertility options (81). Techniques for cryopreservation of oocytes, embryos, and ovarian tissue continue to improve, and oocyte maturation of immature tissue is being studied (82).

2.0 Treatment of Adolescents

During the past decade, clinicians have progressively acknowledged the suffering of young adolescents with GD/gender incongruence. In some forms of GD/gender incongruence, psychological interventions may be useful and sufficient. However, for many adolescents with GD/gender incongruence, the pubertal physical changes are unbearable. As early medical intervention may prevent psychological harm, various clinics have decided to start treating young adolescents with GD/gender incongruence with puberty-suppressing medication (a GnRH analog). As compared with starting gender-affirming treatment long after the first phases of puberty, a benefit of pubertal suppression at early puberty may be a better psychological and physical outcome.

In girls, the first physical sign of puberty is the budding of the breasts followed by an increase in breast and fat tissue. Breast development is also associated with the pubertal growth spurt, and menarche occurs ~2 years later. In boys, the first physical change is testicular growth. A testicular volume ≥4 mL is seen as consistent with the initiation of physical puberty. At the beginning of puberty, estradiol and testosterone levels are still low and are best measured in the early morning with an ultrasensitive assay. From a testicular volume of 10 mL, daytime testosterone levels increase, leading to virilization (83). Note that pubic hair and/or axillary hair/odor may not reflect the onset of gonadarche; instead, it may reflect adrenarche alone.

2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment (Table 5), and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 ⊕⊕◯◯)

2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty (Tanner stages G2/B2). (2 ⊕⊕◯◯)

Evidence

Pubertal suppression can expand the diagnostic phase by a long period, giving the subject more time to explore options and to live in the experienced gender before making a decision to proceed with gender-affirming sex hormone treatments and/or surgery, some of which is irreversible (84, 85). Pubertal suppression is fully reversible, enabling full pubertal development in the natal gender, after cessation of treatment, if appropriate. The experience of full endogenous puberty is an undesirable condition for the GD/gender-incongruent individual and may seriously interfere with healthy psychological functioning and well-being. Treating GD/gender-incongruent adolescents entering puberty with GnRH analogs has been shown to improve psychological functioning in several domains (86).

Another reason to start blocking pubertal hormones early in puberty is that the physical outcome is improved compared with initiating physical transition after puberty has been completed (60, 62). Looking like a man or woman when living as the opposite sex creates difficult

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barriers with enormous life-long disadvantages. We therefore advise starting suppression in early puberty to prevent the irreversible development of undesirable secondary sex characteristics. However, adolescents with GD/gender incongruence should experience the first changes of their endogenous spontaneous puberty, because their emotional reaction to these first physical changes has diagnostic value in establishing the persistence of GD/gender incongruence (85). Thus, Tanner stage 2 is the optimal time to start pubertal suppression. However, pubertal suppression treatment in early puberty will limit the growth of the penis and scrotum, which will have a potential effect on future surgical treatments (87).

Clinicians can also use pubertal suppression in adolescents in later pubertal stages to stop menses in transgender males and prevent facial hair growth in transgender females. However, in contrast to the effects in early pubertal adolescents, physical sex characteristics (such as more advanced breast development in transgender boys and lowering of the voice and outgrowth of the jaw and brow in transgender girls) are not reversible.

Values and preferences

These recommendations place a high value on avoiding an unsatisfactory physical outcome when secondary sex characteristics have become manifest and irreversible, a higher value on psychological well-being, and a lower value on avoiding potential harm from early pubertal suppression.

Remarks

Table 6 lists the Tanner stages of breast and male genital development. Careful documentation of hallmarks of pubertal development will ensure precise timing when initiating pubertal suppression once puberty has started. Clinicians can use pubertal LH and sex steroid levels to confirm that puberty has progressed sufficiently before starting pubertal suppression (88). Reference ranges for sex steroids by Tanner stage may vary depending on the assay used. Ultrasensitive sex steroid and gonadotropin assays will help clinicians document early pubertal changes.

Irreversible and, for GD/gender-incongruent adolescents, undesirable sex characteristics in female puberty are breasts, female body habitus, and, in some cases, relative short stature. In male puberty, they are a prominent Adam's apple; low voice; male bone configuration, such as a large jaw, big feet and hands, and tall stature; and male hair pattern on the face and extremities.

2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 |⊕⊕◯◯)

Evidence

Clinicians can suppress pubertal development and gonadal function most effectively via gonadotropin suppression using GnRH analogs. GnRH analogs are long-acting agonists that suppress gonadotropins by GnRH receptor desensitization after an initial increase of gonadotropins during ~10 days after the first and (to a lesser degree) the second injection (89). Antagonists immediately suppress pituitary gonadotropin secretion (90, 91). Long-acting GnRH analogs are the currently preferred treatment option. Clinicians may consider long-acting GnRH antagonists when evidence on their safety and efficacy in adolescents becomes available.

During GnRH analog treatment, slight development of secondary sex characteristics may regress, and in a later phase of pubertal development, it will stop. In girls, breast tissue will become atrophic, and menses will stop. In boys, virilization will stop, and testicular volume may decrease (92).

An advantage of using GnRH analogs is the reversibility of the intervention. If, after extensive exploration of his/her transition wish, the individual no longer desires transition, they can discontinue pubertal suppression. In subjects with

Table 6. Tanner Stages of Breast Development and Male External Genitalia

The description of Tanner stages for breast development:
1. Prepubertal
2. Breast and papilla elevated as small mound; areolar diameter increased
3. Breast and areola enlarged, no contour separation
4. Areola and papilla form secondary mound
5. Mature; nipple projects, areola part of general breast contour

For penis and testes:
1. Prepubertal, testicular volume <4 mL
2. Slight enlargement of penis; enlarged scrotum, pink, texture altered, testes 4–6 mL
3. Penis longer, testes larger (8–12 mL)
4. Penis and glans larger, including increase in breadth; testes larger (12–15 mL), scrotum dark
5. Penis adult size; testicular volume > 15 ml

Adapted from Lawrence (56).

precocious puberty, spontaneous pubertal development has been shown to resume after patients discontinue taking GnRH analogs (93).

Recommendations 2.1 to 2.3 are supported by a prospective follow-up study from The Netherlands. This report assessed mental health outcomes in 55 transgender adolescents/young adults (22 transgender females and 33 transgender males) at three time points: (1) before the start of GnRH agonist (average age of 14.8 years at start of treatment), (2) at initiation of gender-affirming hormones (average age of 16.7 years at start of treatment), and (3) 1 year after "gender-reassignment surgery" (average age of 20.7 years) (63). Despite a decrease in depression and an improvement in general mental health functioning, GD/gender incongruence persisted through pubertal suppression, as previously reported (86). However, following sex hormone treatment and gender-reassignment surgery, GD/gender incongruence was resolved and psychological functioning steadily improved (63). Furthermore, well-being was similar to or better than that reported by age-matched young adults from the general population, and none of the study participants regretted treatment. This study represents the first long-term follow-up of individuals managed according to currently existing clinical practice guidelines for transgender youth, and it underscores the benefit of the multidisciplinary approach pioneered in The Netherlands; however, further studies are needed.

Side effects

The primary risks of pubertal suppression in GD/gender-incongruent adolescents may include adverse effects on bone mineralization (which can theoretically be reversed with sex hormone treatment), compromised fertility if the person subsequently is treated with sex hormones, and unknown effects on brain development. Few data are available on the effect of GnRH analogs on BMD in adolescents with GD/gender incongruence. Initial data in GD/gender-incongruent subjects demonstrated no change of absolute areal BMD during 2 years of GnRH analog therapy but a decrease in BMD *z* scores (85). A recent study also suggested suboptimal bone mineral accrual during GnRH analog treatment. The study reported a decrease in areal BMD *z* scores and of bone mineral apparent density *z* scores (which takes the size of the bone into account) in 19 transgender males treated with GnRH analogs from a mean age of 15.0 years (standard deviation = 2.0 years) for a median duration of 1.5 years (0.3 to 5.2 years) and in 15 transgender females treated from 14.9 (±1.9) years for 1.3 years (0.5 to 3.8 years), although not all changes were statistically significant (94). There was incomplete catch-up at age 22 years after sex hormone treatment from age 16.6 (±1.4) years for a median duration of 5.8 years (3.0 to 8.0 years) in transgender females and from age 16.4 (±2.3) years for 5.4 years (2.8 to 7.8 years) in transgender males. Little is known about more prolonged use of GnRH analogs. Researchers reported normal BMD *z* scores at age 35 years in one individual who used GnRH analogs from age 13.7 years until age 18.6 years before initiating sex hormone treatment (65).

Additional data are available from individuals with late puberty or GnRH analog treatment of other indications. Some studies reported that men with constitutionally delayed puberty have decreased BMD in adulthood (95). However, other studies reported that these men have normal BMD (96, 97). Treating adults with GnRH analogs results in a decrease of BMD (98). In children with central precocious puberty, treatment with GnRH analogs has been found to result in a decrease of BMD during treatment by some (99) but not others (100). Studies have reported normal BMD after discontinuing therapy (69, 72, 73, 101, 102). In adolescents treated with growth hormone who are small for gestational age and have normal pubertal timing, 2-year GnRH analog treatments did not adversely affect BMD (103). Calcium supplementation may be beneficial in optimizing bone health in GnRH analog–treated individuals (104). There are no studies of vitamin D supplementation in this context, but clinicians should offer supplements to vitamin D–deficient adolescents. Physical activity, especially during growth, is important for bone mass in healthy individuals (103) and is therefore likely to be beneficial for bone health in GnRH analog–treated subjects.

GnRH analogs did not induce a change in body mass index standard deviation score in GD/gender-incongruent adolescents (94) but caused an increase in fat mass and decrease in lean body mass percentage (92). Studies in girls treated for precocious puberty also reported a stable body mass index standard deviation score during treatment (72) and body mass index and body composition comparable to controls after treatment (73).

Arterial hypertension has been reported as an adverse effect in a few girls treated with GnRH analogs for precocious/early puberty (105, 106). Blood pressure monitoring before and during treatment is recommended.

Individuals may also experience hot flashes, fatigue, and mood alterations as a consequence of pubertal suppression. There is no consensus on treatment of these side effects in this context.

It is recommended that any use of pubertal blockers (and subsequent use of sex hormones, as detailed below) include a discussion about implications for fertility (see recommendation 1.3). Transgender adolescents may

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want to preserve fertility, which may be otherwise compromised if puberty is suppressed at an early stage and the individual completes phenotypic transition with the use of sex hormones.

Limited data are available regarding the effects of GnRH analogs on brain development. A single cross-sectional study demonstrated no compromise of executive function (107), but animal data suggest there may be an effect of GnRH analogs on cognitive function (108).

Values and preferences

Our recommendation of GnRH analogs places a higher value on the superior efficacy, safety, and reversibility of the pubertal hormone suppression achieved (as compared with the alternatives) and a relatively lower value on limiting the cost of therapy. Of the available alternatives, depot and oral progestin preparations are effective. Experience with this treatment dates back prior to the emergence of GnRH analogs for treating precocious puberty in papers from the 1960s and early 1970s (109–112). These compounds are usually safe, but some side effects have been reported (113–115). Only two recent studies involved transgender youth (116, 117). One of these studies described the use of oral lynestrenol monotherapy followed by the addition of testosterone treatment in transgender boys who were at Tanner stage B4 or further at the start of treatment (117). They found lynestrenol safe, but gonadotropins were not fully suppressed. The study reported metrorrhagia in approximately half of the individuals, mainly in the first 6 months. Acne, headache, hot flashes, and fatigue were other frequent side effects. Another progestin that has been studied in the United States is medroxyprogesterone. This agent is not as effective as GnRH analogs in lowering endogenous sex hormones either and may be associated with other side effects (116). Progestin preparations may be an acceptable treatment for persons without access to GnRH analogs or with a needle phobia. If GnRH analog treatment is not available (insurance denial, prohibitive cost, or other reasons), postpubertal, transgender female adolescents may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see adult section).

Remarks

Measurements of gonadotropin and sex steroid levels give precise information about gonadal axis suppression, although there is insufficient evidence for any specific short-term monitoring scheme in children treated with GnRH analogs (88). If the gonadal axis is not completely suppressed—as evidenced by (for example) menses, erections, or progressive hair growth—the interval of GnRH analog treatment can be shortened or the dose increased. During treatment, adolescents should be monitored for negative effects of delaying puberty, including a halted growth spurt and impaired bone mineral accretion. Table 7 illustrates a suggested clinical protocol.

Anthropometric measurements and X-rays of the left hand to monitor bone age are informative for evaluating growth. To assess BMD, clinicians can perform dual-energy X-ray absorptiometry scans.

2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule (see Table 8) after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years (Table 5). (1 |⊕⊕◯◯)

2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 |⊕◯◯◯)

2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment (Table 9). (2 |⊕⊕◯◯)

Table 7. Baseline and Follow-Up Protocol During Suppression of Puberty

Every 3–6 mo
Anthropometry: height, weight, sitting height, blood pressure, Tanner stages
Every 6–12 mo
Laboratory: LH, FSH, E2/T, 25OH vitamin D
Every 1–2 y
Bone density using DXA
Bone age on X-ray of the left hand (if clinically indicated)

Adapted from Hembree *et al.* (118).

Abbreviations: DXA, dual-energy X-ray absorptiometry; E2, estradiol; FSH, follicle stimulating hormone; LH, luteinizing hormone; T, testosterone;

Table 8. Protocol Induction of Puberty

Induction of female puberty with oral 17β-estradiol, increasing the dose every 6 mo:
- 5 μg/kg/d
- 10 μg/kg/d
- 15 μg/kg/d
- 20 μg/kg/d
- Adult dose = 2–6 mg/d
- *In postpubertal transgender female adolescents, the dose of 17β-estradiol can be increased more rapidly:*
  - 1 mg/d for 6 mo
  - 2 mg/d

Induction of female puberty with transdermal 17β-estradiol, increasing the dose every 6 mo (new patch is placed every 3.5 d):
- 6.25–12.5 μg/24 h (cut 25-μg patch into quarters, then halves)
- 25 μg/24 h
- 37.5 μg/24 h
- Adult dose = 50–200 μg/24 h
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological estradiol levels (see Table 15).*

Induction of male puberty with testosterone esters increasing the dose every 6 mo (IM or SC):
- 25 mg/m^2/2 wk (or alternatively, half this dose weekly, or double the dose every 4 wk)
- 50 mg/m^2/2 wk
- 75 mg/m^2/2 wk
- 100 mg/m^2/2 wk
- Adult dose = 100–200 mg every 2 wk
- *In postpubertal transgender male adolescents the dose of testosterone esters can be increased more rapidly:*
  - 75 mg/2 wk for 6 mo
  - 125 mg/2 wk
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological testosterone levels (see Table 14).*

Adapted from Hembree *et al.* (118).

Abbreviations: IM, intramuscularly; SC, subcutaneously.

Evidence

Adolescents develop competence in decision making at their own pace. Ideally, the supervising medical professionals should individually assess this competence, although no objective tools to make such an assessment are currently available.

Many adolescents have achieved a reasonable level of competence by age 15 to 16 years (119), and in many countries 16-year-olds are legally competent with regard to medical decision making (120). However, others believe that although some capacities are generally achieved before age 16 years, other abilities (such as good risk assessment) do not develop until well after 18 years (121). They suggest that health care procedures should be divided along a matrix of relative risk, so that younger adolescents can be allowed to decide about low-risk procedures, such as most diagnostic tests and common therapies, but not about high-risk procedures, such as most surgical procedures (121).

Currently available data from transgender adolescents support treatment with sex hormones starting at age 16 years (63, 122). However, some patients may incur potential risks by waiting until age 16 years. These include the potential risk to bone health if puberty is suppressed

Table 9. Baseline and Follow-up Protocol During Induction of Puberty

Every 3–6 mo
- •Anthropometry: height, weight, sitting height, blood pressure, Tanner stages

Every 6–12 mo
- •In transgender males: hemoglobin/hematocrit, lipids, testosterone, 25OH vitamin D
- •In transgender females: prolactin, estradiol, 25OH vitamin D

Every 1–2 y
- •BMD using DXA
- •Bone age on X-ray of the left hand (if clinically indicated)

BMD should be monitored into adulthood (until the age of 25–30 y or until peak bone mass has been reached).
For recommendations on monitoring once pubertal induction has been completed, see Tables 14 and 15.

Adapted from Hembree *et al.* (118).

Abbreviation: DXA, dual-energy X-ray absorptiometry.

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for 6 to 7 years before initiating sex hormones (*e.g.*, if someone reached Tanner stage 2 at age 9-10 years old). Additionally, there may be concerns about inappropriate height and potential harm to mental health (emotional and social isolation) if initiation of secondary sex characteristics must wait until the person has reached 16 years of age. However, only minimal data supporting earlier use of gender-affirming hormones in transgender adolescents currently exist (63). Clearly, long-term studies are needed to determine the optimal age of sex hormone treatment in GD/gender-incongruent adolescents.

The MHP who has followed the adolescent during GnRH analog treatment plays an essential role in assessing whether the adolescent is eligible to start sex hormone therapy and capable of consenting to this treatment (Table 5). Support of the family/environment is essential. Prior to the start of sex hormones, clinicians should discuss the implications for fertility (see recommendation 1.5). Throughout pubertal induction, an MHP and a pediatric endocrinologist (or other clinician competent in the evaluation and induction of pubertal development) should monitor the adolescent. In addition to monitoring therapy, it is also important to pay attention to general adolescent health issues, including healthy life style choices, such as not smoking, contraception, and appropriate vaccinations (*e.g.*, human papillomavirus).

For the induction of puberty, clinicians can use a similar dose scheme for hypogonadal adolescents with GD/gender incongruence as they use in other individuals with hypogonadism, carefully monitoring for desired and undesired effects (Table 8). In transgender female adolescents, transdermal 17β-estradiol may be an alternative for oral 17β-estradiol. It is increasingly used for pubertal induction in hypogonadal females. However, the absence of low-dose estrogen patches may be a problem. As a result, individuals may need to cut patches to size themselves to achieve appropriate dosing (123). In transgender male adolescents, clinicians can give testosterone injections intramuscularly or subcutaneously (124, 125).

When puberty is initiated with a gradually increasing schedule of sex steroid doses, the initial levels will not be high enough to suppress endogenous sex steroid secretion. Gonadotropin secretion and endogenous production of testosterone may resume and interfere with the effectiveness of estrogen treatment, in transgender female adolescents (126, 127). Therefore, continuation of GnRH analog treatment is advised until gonadectomy. Given that GD/gender-incongruent adolescents may opt not to have gonadectomy, long-term studies are necessary to examine the potential risks of prolonged GnRH analog treatment. Alternatively, in transgender male adolescents, GnRH analog treatment can be discontinued once an adult dose of testosterone has been reached and the individual is well virilized. If uterine bleeding occurs, a progestin can be added. However, the combined use of a GnRH analog (for ovarian suppression) and testosterone may enable phenotypic transition with a lower dose of testosterone in comparison with testosterone alone. If there is a wish or need to discontinue GnRH analog treatment in transgender female adolescents, they may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see section 3.0 "Hormonal Therapy for Transgender Adults").

Values and preferences

The recommendation to initiate pubertal induction only when the individual has sufficient mental capacity (roughly age 16 years) to give informed consent for this partly irreversible treatment places a higher value on the ability of the adolescent to fully understand and oversee the partially irreversible consequences of sex hormone treatment and to give informed consent. It places a lower value on the possible negative effects of delayed puberty. We may not currently have the means to weigh adequately the potential benefits of waiting until around age 16 years to initiate sex hormones vs the potential risks/harm to BMD and the sense of social isolation from having the timing of puberty be so out of sync with peers (128).

Remarks

Before starting sex hormone treatment, effects on fertility and options for fertility preservation should be discussed. Adult height may be a concern in transgender adolescents. In a transgender female adolescent, clinicians may consider higher doses of estrogen or a more rapid tempo of dose escalation during pubertal induction. There are no established treatments yet to augment adult height in a transgender male adolescent with open epiphyses during pubertal induction. It is not uncommon for transgender adolescents to present for clinical services after having completed or nearly completed puberty. In such cases, induction of puberty with sex hormones can be done more rapidly (see Table 8). Additionally, an adult dose of testosterone in transgender male adolescents may suffice to suppress the gonadal axis without the need to use a separate agent. At the appropriate time, the multidisciplinary team should adequately prepare the adolescent for transition to adult care.

3.0 Hormonal Therapy for Transgender Adults

The two major goals of hormonal therapy are (1) to reduce endogenous sex hormone levels, and thus reduce

the secondary sex characteristics of the individual's designated gender, and (2) to replace endogenous sex hormone levels consistent with the individual's gender identity by using the principles of hormone replacement treatment of hypogonadal patients. The timing of these two goals and the age at which to begin treatment with the sex hormones of the chosen gender is codetermined in collaboration with both the person pursuing transition and the health care providers. The treatment team should include a medical provider knowledgeable in transgender hormone therapy, an MHP knowledgeable in GD/gender incongruence and the mental health concerns of transition, and a primary care provider able to provide care appropriate for transgender individuals. The physical changes induced by this sex hormone transition are usually accompanied by an improvement in mental well-being (129, 130).

3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and the criteria for the endocrine phase of gender transition before beginning treatment. (1 |⊕⊕⊕◯)

3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment (Table 10). (1 |⊕⊕⊕◯)

3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 |⊕⊕◯◯)

Evidence

It is the responsibility of the treating clinician to confirm that the person fulfills criteria for treatment. The treating clinician should become familiar with the terms and criteria presented in Tables 1–5 and take a thorough history from the patient in collaboration with the other members of the treatment team. The treating clinician must ensure that the desire for transition is appropriate; the consequences, risks, and benefits of treatment are well understood; and the desire for transition persists. They also need to discuss fertility preservation options (see recommendation 1.3) (67, 68).

Transgender males

Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males (Appendix A) (113, 114, 131–134). Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism (135). Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range (this is dependent on the specific assay, but is typically 320 to 1000 ng/dL) (Table 11) (136). Sustained supraphysiologic levels of testosterone increase the risk of adverse reactions (see section 4.0 "Adverse Outcome Prevention and Long-Term Care") and should be avoided.

Similar to androgen therapy in hypogonadal men, testosterone treatment in transgender males results in increased muscle mass and decreased fat mass, increased facial hair and acne, male pattern baldness in those genetically predisposed, and increased sexual desire (137).

Table 10. Medical Risks Associated With Sex Hormone Therapy

Transgender female: estrogen
Very high risk of adverse outcomes:
•Thromboembolic disease
Moderate risk of adverse outcomes:
•Macroprolactinoma
•Breast cancer
•Coronary artery disease
•Cerebrovascular disease
•Cholelithiasis
•Hypertriglyceridemia
Transgender male: testosterone
Very high risk of adverse outcomes:
•Erythrocytosis (hematocrit > 50%)
Moderate risk of adverse outcomes:
•Severe liver dysfunction (transaminases > threefold upper limit of normal)
•Coronary artery disease
•Cerebrovascular disease
•Hypertension
•Breast or uterine cancer

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Table 11. Hormone Regimens in Transgender Persons

Transgender females[a]	
Estrogen	
Oral	
Estradiol	2.0–6.0 mg/d
Transdermal	
Estradiol transdermal patch (New patch placed every 3–5 d)	0.025–0.2 mg/d
Parenteral	
Estradiol valerate or cypionate	5–30 mg IM every 2 wk 2–10 mg IM every week
Anti-androgens	
Spironolactone	100–300 mg/d
Cyproterone acetate[b]	25–50 mg/d
GnRH agonist	3.75 mg SQ (SC) monthly 11.25 mg SQ (SC) 3-monthly
Transgender males	
Testosterone	
Parenteral testosterone	
Testosterone enanthate or cypionate	100–200 mg SQ (IM) every 2 wk or SQ (SC) 50% per week
Testosterone undecanoate[c]	1000 mg every 12 wk
Transdermal testosterone	
Testosterone gel 1.6%[d]	50–100 mg/d
Testosterone transdermal patch	2.5–7.5 mg/d

Abbreviations: IM, intramuscularly; SQ, sequentially; SC, subcutaneously.

[a]Estrogens used with or without antiandrogens or GnRH agonist.

[b]Not available in the United States.

[c]One thousand milligrams initially followed by an injection at 6 wk then at 12-wk intervals.

[d]Avoid cutaneous transfer to other individuals.

In transgender males, testosterone will result in clitoromegaly, temporary or permanent decreased fertility, deepening of the voice, cessation of menses (usually), and a significant increase in body hair, particularly on the face, chest, and abdomen. Cessation of menses may occur within a few months with testosterone treatment alone, although high doses of testosterone may be required. If uterine bleeding continues, clinicians may consider the addition of a progestational agent or endometrial ablation (138). Clinicians may also administer GnRH analogs or depot medroxyprogesterone to stop menses prior to testosterone treatment.

Transgender females

The hormone regimen for transgender females is more complex than the transgender male regimen (Appendix B). Treatment with physiologic doses of estrogen alone is insufficient to suppress testosterone levels into the normal range for females (139). Most published clinical studies report the need for adjunctive therapy to achieve testosterone levels in the female range (21, 113, 114, 132–134, 139, 140).

Multiple adjunctive medications are available, such as progestins with antiandrogen activity and GnRH agonists (141). Spironolactone works by directly blocking androgens during their interaction with the androgen receptor (114, 133, 142). It may also have estrogenic activity (143). Cyproterone acetate, a progestational compound with antiandrogenic properties (113, 132, 144), is widely used in Europe. 5α-Reductase inhibitors do not reduce testosterone levels and have adverse effects (145).

Dittrich *et al.* (141) reported that monthly doses of the GnRH agonist goserelin acetate in combination with estrogen were effective in reducing testosterone levels with a low incidence of adverse reactions in 60 transgender females. Leuprolide and transdermal estrogen were as effective as cyproterone and transdermal estrogen in a comparative retrospective study (146).

Patients can take estrogen as oral conjugated estrogens, oral 17β-estradiol, or transdermal 17β-estradiol. Among estrogen options, the increased risk of thromboembolic events associated with estrogens in general seems most concerning with ethinyl estradiol specifically (134, 140, 141), which is why we specifically suggest that it not be used in any transgender treatment plan. Data distinguishing among other estrogen options are less well established although there is some thought that oral routes of administration are more thrombogenic due to the "first pass effect" than are transdermal and parenteral routes, and that the risk of thromboembolic events is dose-dependent. Injectable estrogen and sublingual

estrogen may benefit from avoiding the first pass effect, but they can result in more rapid peaks with greater overall periodicity and thus are more difficult to monitor (147, 148). However, there are no data demonstrating that increased periodicity is harmful otherwise.

Clinicians can use serum estradiol levels to monitor oral, transdermal, and intramuscular estradiol. Blood tests cannot monitor conjugated estrogens or synthetic estrogen use. Clinicians should measure serum estradiol and serum testosterone and maintain them at the level for premenopausal females (100 to 200 pg/mL and <50 ng/dL, respectively). The transdermal preparations and injectable estradiol cypionate or valerate preparations may confer an advantage in older transgender females who may be at higher risk for thromboembolic disease (149).

Values

Our recommendation to maintain levels of gender-affirming hormones in the normal adult range places a high value on the avoidance of the long-term complications of pharmacologic doses. Those patients receiving endocrine treatment who have relative contraindications to hormones should have an in-depth discussion with their physician to balance the risks and benefits of therapy.

Remarks

Clinicians should inform all endocrine-treated individuals of all risks and benefits of gender-affirming hormones prior to initiating therapy. Clinicians should strongly encourage tobacco use cessation in transgender females to avoid increased risk of VTE and cardiovascular complications. We strongly discourage the unsupervised use of hormone therapy (150).

Not all individuals with GD/gender incongruence seek treatment as described (*e.g.*, male-to-eunuchs and individuals seeking partial transition). Tailoring current protocols to the individual may be done within the context of accepted safety guidelines using a multidisciplinary approach including mental health. No evidence-based protocols are available for these groups (151). We need prospective studies to better understand treatment options for these persons.

3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 |⊕○○○)

Evidence

Transgender males

Physical changes that are expected to occur during the first 1 to 6 months of testosterone therapy include cessation of menses, increased sexual desire, increased facial and body hair, increased oiliness of skin, increased muscle, and redistribution of fat mass. Changes that occur within the first year of testosterone therapy include deepening of the voice (152, 153), clitoromegaly, and male pattern hair loss (in some cases) (114, 144, 154, 155) (Table 12).

Transgender females

Physical changes that may occur in transgender females in the first 3 to 12 months of estrogen and antiandrogen therapy include decreased sexual desire, decreased spontaneous erections, decreased facial and body hair (usually mild), decreased oiliness of skin, increased breast tissue growth, and redistribution of fat mass (114, 139, 149, 154, 155, 161) (Table 13). Breast development is generally maximal at 2 years after initiating hormones (114, 139, 149, 155). Over a long period of time, the prostate gland and testicles will undergo atrophy.

Although the time course of breast development in transgender females has been studied (150), precise information about other changes induced by sex hormones is lacking (141). There is a great deal of variability among individuals, as evidenced during pubertal development. We all know that a major concern for transgender females is breast development. If we work with estrogens, the result will be often not what the transgender female expects.

Alternatively, there are transgender females who report an anecdotal improved breast development, mood, or sexual desire with the use of progestogens. However, there have been no well-designed studies of the role of progestogens in feminizing hormone regimens, so the question is still open.

Our knowledge concerning the natural history and effects of different cross-sex hormone therapies on breast

Table 12. Masculinizing Effects in Transgender Males

Effect	Onset	Maximum
Skin oiliness/acne	1–6 mo	1–2 y
Facial/body hair growth	6–12 mo	4–5 y
Scalp hair loss	6–12 mo	—[a]
Increased muscle mass/strength	6–12 mo	2–5 y
Fat redistribution	1–6 mo	2–5 y
Cessation of menses	1–6 mo	—[b]
Clitoral enlargement	1–6 mo	1–2 y
Vaginal atrophy	1–6 mo	1–2 y
Deepening of voice	6–12 mo	1–2 y

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157), Wierckx *et al.* (158).

[a] Prevention and treatment as recommended for biological men.

[b] Menorrhagia requires diagnosis and treatment by a gynecologist.

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Table 13. Feminizing Effects in Transgender Females

Effect	Onset	Maximum
Redistribution of body fat	3–6 mo	2–3 y
Decrease in muscle mass and strength	3–6 mo	1–2 y
Softening of skin/decreased oiliness	3–6 mo	Unknown
Decreased sexual desire	1–3 mo	3–6 mo
Decreased spontaneous erections	1–3 mo	3–6 mo
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 mo	2–3 y
Decreased testicular volume	3–6 mo	2–3 y
Decreased sperm production	Unknown	>3 y
Decreased terminal hair growth	6–12 mo	>3 y[a]
Scalp hair	Variable	—[b]
Voice changes	None	—[c]

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157).

[a]Complete removal of male sexual hair requires electrolysis or laser treatment or both.

[b]Familial scalp hair loss may occur if estrogens are stopped.

[c]Treatment by speech pathologists for voice training is most effective.

development in transgender females is extremely sparse and based on the low quality of evidence. Current evidence does not indicate that progestogens enhance breast development in transgender females, nor does evidence prove the absence of such an effect. This prevents us from drawing any firm conclusion at this moment and demonstrates the need for further research to clarify these important clinical questions (162).

Values and preferences

Transgender persons have very high expectations regarding the physical changes of hormone treatment and are aware that body changes can be enhanced by surgical procedures (*e.g.*, breast, face, and body habitus). Clear expectations for the extent and timing of sex hormone–induced changes may prevent the potential harm and expense of unnecessary procedures.

4.0 Adverse Outcome Prevention and Long-Term Care

Hormone therapy for transgender males and females confers many of the same risks associated with sex hormone replacement therapy in nontransgender persons. The risks arise from and are worsened by inadvertent or intentional use of supraphysiologic doses of sex hormones, as well as use of inadequate doses of sex hormones to maintain normal physiology (131, 139).

4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every 3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 |⊕⊕◯◯)

Evidence

Pretreatment screening and appropriate regular medical monitoring are recommended for both transgender males and females during the endocrine transition and periodically thereafter (26, 155). Clinicians should monitor weight and blood pressure, conduct physical exams, and assess routine health questions, such as tobacco use, symptoms of depression, and risk of adverse events such as deep vein thrombosis/pulmonary embolism and other adverse effects of sex steroids.

Transgender males

Table 14 contains a standard monitoring plan for transgender males on testosterone therapy (154, 159). Key issues include maintaining testosterone levels in the physiologic normal male range and avoiding adverse events resulting from excess testosterone therapy, particularly erythrocytosis, sleep apnea, hypertension, excessive weight gain, salt retention, lipid changes, and excessive or cystic acne (135).

Because oral 17-alkylated testosterone is not recommended, serious hepatic toxicity is not anticipated with parenteral or transdermal testosterone use (163, 164). Past concerns regarding liver toxicity with testosterone have been alleviated with subsequent reports that indicate the risk of serious liver disease is minimal (144, 165, 166).

Transgender females

Table 15 contains a standard monitoring plan for transgender females on estrogens, gonadotropin suppression, or antiandrogens (160). Key issues include avoiding supraphysiologic doses or blood levels of estrogen that may lead to increased risk for thromboembolic disease, liver dysfunction, and hypertension. Clinicians should monitor serum estradiol levels using laboratories participating in external quality control, as measurements of estradiol in blood can be very challenging (167).

VTE may be a serious complication. A study reported a 20-fold increase in venous thromboembolic disease in a large cohort of Dutch transgender subjects (161). This increase may have been associated with the use of the synthetic estrogen, ethinyl estradiol (149). The incidence decreased when clinicians stopped administering ethinyl estradiol (161). Thus, the use of synthetic estrogens and conjugated estrogens is undesirable because of the inability to regulate doses by measuring serum levels and the risk of thromboembolic disease. In a German gender clinic, deep vein thrombosis occurred in 1 of 60 of transgender females treated with a GnRH analog and oral

Table 14. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Male

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
2. Measure serum testosterone every 3 mo until levels are in the normal physiologic male range:[a]
   a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is 400–700 ng/dL to 400 ng/dL. Alternatively, measure peak and trough levels to ensure levels remain in the normal male range.
   b. For parenteral testosterone undecanoate, testosterone should be measured just before the following injection. If the level is <400 ng/dL, adjust dosing interval.
   c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 h after application).
3. Measure hematocrit or hemoglobin at baseline and every 3 mo for the first year and then one to two times a year. Monitor weight, blood pressure, and lipids at regular intervals.
4. Screening for osteoporosis should be conducted in those who stop testosterone treatment, are not compliant with hormone therapy, or who develop risks for bone loss.
5. If cervical tissue is present, monitoring as recommended by the American College of Obstetricians and Gynecologists.
6. Ovariectomy can be considered after completion of hormone transition.
7. Conduct sub- and periareolar annual breast examinations if mastectomy performed. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

[a] Adapted from Lapauw *et al.* (154) and Ott *et al.* (159).

estradiol (141). The patient who developed a deep vein thrombosis was found to have a homozygous C677 T mutation in the methylenetetrahydrofolate reductase gene. In an Austrian gender clinic, administering gender-affirming hormones to 162 transgender females and 89 transgender males was not associated with VTE, despite an 8.0% and 5.6% incidence of thrombophilia (159). A more recent multinational study reported only 10 cases of VTE from a cohort of 1073 subjects (168). Thrombophilia screening of transgender persons initiating hormone treatment should be restricted to those with a personal or family history of VTE (159). Monitoring D-dimer levels during treatment is not recommended (169).

4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 l⊕⊕◯◯)

Evidence

Estrogen therapy can increase the growth of pituitary lactrotroph cells. There have been several reports of prolactinomas occurring after long-term, high-dose estrogen therapy (170–173). Up to 20% of transgender females treated with estrogens may have elevations in prolactin levels associated with enlargement of the pituitary gland (156). In most cases, the serum prolactin levels will return to the normal range with a reduction or discontinuation of the estrogen therapy or discontinuation of cyproterone acetate (157, 174, 175).

The onset and time course of hyperprolactinemia during estrogen treatment are not known. Clinicians should measure prolactin levels at baseline and then at least annually during the transition period and every 2 years thereafter. Given that only a few case studies reported prolactinomas, and prolactinomas were not reported in large cohorts of estrogen-treated persons, the risk is likely to be very low. Because the major presenting findings of microprolactinomas (hypogonadism and sometimes gynecomastia) are not apparent in transgender females, clinicians may perform radiologic examinations of the pituitary in those patients whose prolactin levels persistently increase despite stable or reduced estrogen levels. Some transgender individuals receive psychotropic medications that can increase prolactin levels (174).

Table 15. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Female

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of feminization and for development of adverse reactions.
2. Measure serum testosterone and estradiol every 3 mo.
   a. Serum testosterone levels should be <50 ng/dL.
   b. Serum estradiol should not exceed the peak physiologic range: 100–200 pg/mL.
3. For individuals on spironolactone, serum electrolytes, particularly potassium, should be monitored every 3 mo in the first year and annually thereafter.
4. Routine cancer screening is recommended, as in nontransgender individuals (all tissues present).
5. Consider BMD testing at baseline (160). In individuals at low risk, screening for osteoporosis should be conducted at age 60 years or in those who are not compliant with hormone therapy.

This table presents strong recommendations and does not include lower level recommendations.

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4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 ⊕⊕◯◯)

Evidence

Transgender males

Administering testosterone to transgender males results in a more atherogenic lipid profile with lowered high-density lipoprotein cholesterol and higher triglyceride and low-density lipoprotein cholesterol values (176–179). Studies of the effect of testosterone on insulin sensitivity have mixed results (178, 180). A randomized, open-label uncontrolled safety study of transgender males treated with testosterone undecanoate demonstrated no insulin resistance after 1 year (181, 182). Numerous studies have demonstrated the effects of sex hormone treatment on the cardiovascular system (160, 179, 183, 184). Long-term studies from The Netherlands found no increased risk for cardiovascular mortality (161). Likewise, a meta-analysis of 19 randomized trials in nontransgender males on testosterone replacement showed no increased incidence of cardiovascular events (185). A systematic review of the literature found that data were insufficient (due to very low–quality evidence) to allow a meaningful assessment of patient-important outcomes, such as death, stroke, myocardial infarction, or VTE in transgender males (176). Future research is needed to ascertain the potential harm of hormonal therapies (176). Clinicians should manage cardiovascular risk factors as they emerge according to established guidelines (186).

Transgender females

A prospective study of transgender females found favorable changes in lipid parameters with increased high-density lipoprotein and decreased low-density lipoprotein concentrations (178). However, increased weight, blood pressure, and markers of insulin resistance attenuated these favorable lipid changes. In a meta-analysis, only serum triglycerides were higher at ≥24 months without changes in other parameters (187). The largest cohort of transgender females (mean age 41 years, followed for a mean of 10 years) showed no increase in cardiovascular mortality despite a 32% rate of tobacco use (161).

Thus, there is limited evidence to determine whether estrogen is protective or detrimental on lipid and glucose metabolism in transgender females (176). With aging, there is usually an increase of body weight. Therefore, as with nontransgender individuals, clinicians should monitor and manage glucose and lipid metabolism and blood pressure regularly according to established guidelines (186).

4.4. We recommend that clinicians obtain BMD measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 ⊕⊕◯◯)

Evidence

Transgender males

Baseline bone mineral measurements in transgender males are generally in the expected range for their pretreatment gender (188). However, adequate dosing of testosterone is important to maintain bone mass in transgender males (189, 190). In one study (190), serum LH levels were inversely related to BMD, suggesting that low levels of sex hormones were associated with bone loss. Thus, LH levels in the normal range may serve as an indicator of the adequacy of sex steroid administration to preserve bone mass. The protective effect of testosterone may be mediated by peripheral conversion to estradiol, both systemically and locally in the bone.

Transgender females

A baseline study of BMD reported T scores less than −2.5 in 16% of transgender females (191). In aging males, studies suggest that serum estradiol more positively correlates with BMD than does testosterone (192, 193) and is more important for peak bone mass (194). Estrogen preserves BMD in transgender females who continue on estrogen and antiandrogen therapies (188, 190, 191, 195, 196).

Fracture data in transgender males and females are not available. Transgender persons who have undergone gonadectomy may choose not to continue consistent sex steroid treatment after hormonal and surgical sex reassignment, thereby becoming at risk for bone loss. There have been no studies to determine whether clinicians should use the sex assigned at birth or affirmed gender for assessing osteoporosis (*e.g.*, when using the FRAX tool). Although some researchers use the sex assigned at birth (with the assumption that bone mass has usually peaked for transgender people who initiate hormones in early adulthood), this should be assessed on a case-by-case basis until there are more data available. This assumption will be further complicated by the increasing prevalence of transgender people who undergo hormonal transition at a pubertal age or soon after puberty. Sex for comparison within risk assessment tools may be based on the age at which hormones were initiated and the length of exposure to hormones. In some cases, it may be

reasonable to assess risk using both the male and female calculators and using an intermediate value. Because all subjects underwent normal pubertal development, with known effects on bone size, reference values for birth sex were used for all participants (154).

4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for those designated female at birth. (2 ⊕⊕◯◯)

4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 ⊕◯◯◯)

Evidence

Studies have reported a few cases of breast cancer in transgender females (197–200). A Dutch study of 1800 transgender females followed for a mean of 15 years (range of 1 30 years) found one case of breast cancer. The Women's Health Initiative study reported that females taking conjugated equine estrogen without progesterone for 7 years did not have an increased risk of breast cancer as compared with females taking placebo (137).

In transgender males, a large retrospective study conducted at the U.S. Veterans Affairs medical health system identified seven breast cancers (194). The authors reported that this was not above the expected rate of breast cancers in cisgender females in this cohort. Furthermore, they did report one breast cancer that developed in a transgender male patient after mastectomy, supporting the fact that breast cancer can occur even after mastectomy. Indeed, there have been case reports of breast cancer developing in subareolar tissue in transgender males, which occurred after mastectomy (201, 202).

Women with primary hypogonadism (Turner syndrome) treated with estrogen replacement exhibited a significantly decreased incidence of breast cancer as compared with national standardized incidence ratios (203, 204). These studies suggest that estrogen therapy does not increase the risk of breast cancer in the short term (<20 to 30 years). We need long-term studies to determine the actual risk, as well as the role of screening mammograms. Regular examinations and gynecologic advice should determine monitoring for breast cancer.

Prostate cancer is very rare before the age of 40, especially with androgen deprivation therapy (205). Childhood or pubertal castration results in regression of the prostate and adult castration reverses benign prostate hypertrophy (206). Although van Kesteren *et al.* (207) reported that estrogen therapy does not induce hypertrophy or premalignant changes in the prostates of transgender females, studies have reported cases of benign prostatic hyperplasia in transgender females treated with estrogens for 20 to 25 years (208, 209). Studies have also reported a few cases of prostate carcinoma in transgender females (210–214).

Transgender females may feel uncomfortable scheduling regular prostate examinations. Gynecologists are not trained to screen for prostate cancer or to monitor prostate growth. Thus, it may be reasonable for transgender females who transitioned after age 20 years to have annual screening digital rectal examinations after age 50 years and prostate-specific antigen tests consistent with U.S. Preventive Services Task Force Guidelines (215).

4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

Evidence

Although aromatization of testosterone to estradiol in transgender males has been suggested as a risk factor for endometrial cancer (216), no cases have been reported. When transgender males undergo hysterectomy, the uterus is small and there is endometrial atrophy (217, 218). Studies have reported cases of ovarian cancer (219, 220). Although there is limited evidence for increased risk of reproductive tract cancers in transgender males, health care providers should determine the medical necessity of a laparoscopic total hysterectomy as part of a gender-affirming surgery to prevent reproductive tract cancer (221).

Values

Given the discomfort that transgender males experience accessing gynecologic care, our recommendation for the medical necessity of total hysterectomy and oophorectomy places a high value on eliminating the risks of female reproductive tract disease and cancer and a lower value on avoiding the risks of these surgical procedures (related to the surgery and to the potential undesirable health consequences of oophorectomy) and their associated costs.

Remarks

The sexual orientation and type of sexual practices will determine the need and types of gynecologic care required following transition. Additionally, in certain countries, the approval required to change the sex in a birth certificate for transgender males may be dependent on having a complete hysterectomy. Clinicians should help patients research nonmedical administrative criteria and

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provide counseling. If individuals decide not to undergo hysterectomy, screening for cervical cancer is the same as all other females.

5.0 Surgery for Sex Reassignment and Gender Confirmation

For many transgender adults, genital gender-affirming surgery may be the necessary step toward achieving their ultimate goal of living successfully in their desired gender role. The type of surgery falls into two main categories: (1) those that directly affect fertility and (2) those that do not. Those that change fertility (previously called sex reassignment surgery) include genital surgery to remove the penis and gonads in the male and removal of the uterus and gonads in the female. The surgeries that effect fertility are often governed by the legal system of the state or country in which they are performed. Other gender-conforming surgeries that do not directly affect fertility are not so tightly governed.

Gender-affirming surgical techniques have improved markedly during the past 10 years. Reconstructive genital surgery that preserves neurologic sensation is now the standard. The satisfaction rate with surgical reassignment of sex is now very high (187). Additionally, the mental health of the individual seems to be improved by participating in a treatment program that defines a pathway of gender-affirming treatment that includes hormones and surgery (130, 144) (Table 16).

Surgery that affects fertility is irreversible. The World Professional Association for Transgender Health Standards of Care (222) emphasizes that the "threshold of 18 should not be seen as an indication in itself for active intervention." If the social transition has not been satisfactory, if the person is not satisfied with or is ambivalent about the effects of sex hormone treatment, or if the person is ambivalent about surgery then the individual should not be referred for surgery (223, 224).

Gender-affirming genital surgeries for transgender females that affect fertility include gonadectomy, penectomy, and creation of a neovagina (225, 226). Surgeons often invert the skin of the penis to form the wall of the vagina, and several literatures reviews have reported on outcomes (227). Sometimes there is inadequate tissue to form a full neovagina, so clinicians have revisited using intestine and found it to be successful (87, 228, 229). Some newer vaginoplasty techniques may involve autologuous oral epithelial cells (230, 231).

The scrotum becomes the labia majora. Surgeons use reconstructive surgery to fashion the clitoris and its hood, preserving the neurovascular bundle at the tip of the penis as the neurosensory supply to the clitoris. Some surgeons are also creating a sensate pedicled-spot adding a G spot to the neovagina to increase sensation (232). Most recently, plastic surgeons have developed techniques to fashion labia minora. To further complete the feminization, uterine transplants have been proposed and even attempted (233).

Neovaginal prolapse, rectovaginal fistula, delayed healing, vaginal stenosis, and other complications do sometimes occur (234, 235). Clinicians should strongly remind the transgender person to use their dilators to maintain the depth and width of the vagina throughout the postoperative period. Genital sexual responsivity and other aspects of sexual function are usually preserved following genital gender-affirming surgery (236, 237).

Ancillary surgeries for more feminine or masculine appearance are not within the scope of this guideline. Voice therapy by a speech language pathologist is available to transform speech patterns to the affirmed gender (148). Spontaneous voice deepening occurs during testosterone treatment of transgender males (152, 238). No studies have compared the effectiveness of speech therapy, laryngeal surgery, or combined treatment.

Breast surgery is a good example of gender-confirming surgery that does not affect fertility. In all females, breast size exhibits a very broad spectrum. For transgender females to make the best informed decision, clinicians should delay breast augmentation surgery until the patient has completed at least 2 years of estrogen therapy, because the breasts continue to grow during that time (141, 155).

Another major procedure is the removal of facial and masculine-appearing body hair using either electrolysis or

Table 16. Criteria for Gender-Affirming Surgery, Which Affects Fertility

1. Persistent, well-documented gender dysphoria
2. Legal age of majority in the given country
3. Having continuously and responsibly used gender-affirming hormones for 12 mo (if there is no medical contraindication to receiving such therapy)
4. Successful continuous full-time living in the new gender role for 12 mo
5. If significant medical or mental health concerns are present, they must be well controlled
6. Demonstrable knowledge of all practical aspects of surgery (*e.g.*, cost, required lengths of hospitalizations, likely complications, postsurgical rehabilitation)

laser treatments. Other feminizing surgeries, such as that to feminize the face, are now becoming more popular (239–241).

In transgender males, clinicians usually delay gender-affirming genital surgeries until after a few years of androgen therapy. Those surgeries that affect fertility in this group include oophorectomy, vaginectomy, and complete hysterectomy. Surgeons can safely perform them vaginally with laparoscopy. These are sometimes done in conjunction with the creation of a neopenis. The cosmetic appearance of a neopenis is now very good, but the surgery is multistage and very expensive (242, 243). Radial forearm flap seems to be the most satisfactory procedure (228, 244). Other flaps also exist (245). Surgeons can make neopenile erections possible by reinervation of the flap and subsequent contraction of the muscle, leading to stiffening of the neopenis (246, 247), but results are inconsistent (248). Surgeons can also stiffen the penis by imbedding some mechanical device (*e.g.*, a rod or some inflatable apparatus) (249, 250). Because of these limitations, the creation of a neopenis has often been less than satisfactory. Recently, penis transplants are being proposed (233).

In fact, most transgender males do not have any external genital surgery because of the lack of access, high cost, and significant potential complications. Some choose a metaoidioplasty that brings forward the clitoris, thereby allowing them to void in a standing position without wetting themselves (251, 252). Surgeons can create the scrotum from the labia majora with good cosmetic effect and can implant testicular prostheses (253).

The most important masculinizing surgery for the transgender male is mastectomy, and it does not affect fertility. Breast size only partially regresses with androgen therapy (155). In adults, discussions about mastectomy usually take place after androgen therapy has started. Because some transgender male adolescents present after significant breast development has occurred, they may also consider mastectomy 2 years after they begin androgen therapy and before age 18 years. Clinicians should individualize treatment based on the physical and mental health status of the individual. There are now newer approaches to mastectomy with better outcomes (254, 255). These often involve chest contouring (256). Mastectomy is often necessary for living comfortably in the new gender (256).

5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically necessary and would benefit the patient's overall health and/or well-being. (1 |⊕⊕◯◯)

5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)

5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)

5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 |⊕◯◯◯)

5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 |⊕⊕◯◯).

5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 |⊕◯◯◯)

Evidence

Owing to the lack of controlled studies, incomplete follow-up, and lack of valid assessment measures, evaluating various surgical approaches and techniques is difficult. However, one systematic review including a large numbers of studies reported satisfactory cosmetic and functional results for vaginoplasty/neovagina construction (257). For transgender males, the outcomes are less certain. However, the problems are now better understood (258). Several postoperative studies report significant long-term psychological and psychiatric pathology (259–261). One study showed satisfaction with breasts, genitals, and femininity increased significantly and showed the importance of surgical treatment as a key therapeutic option for transgender females (262). Another analysis demonstrated that, despite the young average age at death following surgery and the relatively larger number of individuals with somatic morbidity, the study does not allow for determination of

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causal relationships between, for example, specific types of hormonal or surgical treatment received and somatic morbidity and mortality (263). Reversal surgery in regretful male-to-female transsexuals after sexual reassignment surgery represents a complex, multistage procedure with satisfactory outcomes. Further insight into the characteristics of persons who regret their decision postoperatively would facilitate better future selection of applicants eligible for sexual reassignment surgery. We need more studies with appropriate controls that examine long-term quality of life, psychosocial outcomes, and psychiatric outcomes to determine the long-term benefits of surgical treatment.

When a transgender individual decides to have gender-affirming surgery, both the hormone prescribing clinician and the MHP must certify that the patient satisfies criteria for gender-affirming surgery (Table 16).

There is some concern that estrogen therapy may cause an increased risk for venous thrombosis during or following surgery (176). For this reason, the surgeon and the hormone-prescribing clinician should collaborate in making a decision about the use of hormones before and following surgery. One study suggests that preoperative factors (such as compliance) are less important for patient satisfaction than are the physical postoperative results (56). However, other studies and clinical experience dictate that individuals who do not follow medical instructions and do not work with their physicians toward a common goal do not achieve treatment goals (264) and experience higher rates of postoperative infections and other complications (265, 266). It is also important that the person requesting surgery feels comfortable with the anatomical changes that have occurred during hormone therapy. Dissatisfaction with social and physical outcomes during the hormone transition may be a contraindication to surgery (223).

An endocrinologist or experienced medical provider should monitor transgender individuals after surgery. Those who undergo gonadectomy will require hormone replacement therapy, surveillance, or both to prevent adverse effects of chronic hormone deficiency.

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ABSTRACT

Background: Transgender healthcare is a rapidly evolving interdisciplinary field. In the last decade, there has been an unprecedented increase in the number and visibility of transgender and gender diverse (TGD) people seeking support and gender-affirming medical treatment in parallel with a significant rise in the scientific literature in this area. The World Professional Association for Transgender Health (WPATH) is an international, multidisciplinary, professional association whose mission is to promote evidence-based care, education, research, public policy, and respect in transgender health. One of the main functions of WPATH is to promote the highest standards of health care for TGD people through the Standards of Care (SOC). The SOC was initially developed in 1979 and the last version (SOC-7) was published in 2012. In view of the increasing scientific evidence, WPATH commissioned a new version of the Standards of Care, the SOC-8.

Aim: The overall goal of SOC-8 is to provide health care professionals (HCPs) with clinical guidance to assist TGD people in accessing safe and effective pathways to achieving lasting personal comfort with their gendered selves with the aim of optimizing their overall physical health, psychological well-being, and self-fulfillment.

Methods: The SOC-8 is based on the best available science and expert professional consensus in transgender health. International professionals and stakeholders were selected to serve on the SOC-8 committee. Recommendation statements were developed based on data derived from independent systematic literature reviews, where available, background reviews and expert opinions. Grading of recommendations was based on the available evidence supporting interventions, a discussion of risks and harms, as well as the feasibility and acceptability within different contexts and country settings.

Results: A total of 18 chapters were developed as part of the SOC-8. They contain recommendations for health care professionals who provide care and treatment for TGD people. Each of the recommendations is followed by explanatory text with relevant references. General areas related to transgender health are covered in the chapters Terminology, Global Applicability, Population Estimates, and Education. The chapters developed for the diverse population of TGD people include Assessment of Adults, Adolescents, Children, Nonbinary, Eunuchs, and Intersex Individuals, and people living in Institutional Environments. Finally, the chapters related to gender-affirming treatment are Hormone Therapy, Surgery and Postoperative Care, Voice and Communication, Primary Care, Reproductive Health, Sexual Health, and Mental Health.

Conclusions: The SOC-8 guidelines are intended to be flexible to meet the diverse health care needs of TGD people globally. While adaptable, they offer standards for promoting optimal health care and guidance for the treatment of people experiencing gender incongruence. As in all previous versions of the SOC, the criteria set forth in this document for gender-affirming medical interventions are clinical guidelines; individual health care professionals and programs may modify these in consultation with the TGD person.

KEYWORDS

adolescents; assessment; children; communication; education; endocrinology; eunuch; gender diverse; health care professional; institutional settings; intersex; mental health; nonbinary; population; postoperative care; primary care; reproductive health; sexual health; SOC8; Standards of Care; surgery; terminology; transgender; voice

Table of contents

INTRODUCTION

Purpose and use of the Standards of Care

The overall goal of the World Professional Association for Transgender Health's (WPATH) Standards of Care—Eighth Edition (SOC-8) is to provide clinical guidance to health care professionals to assist transgender and gender diverse (TGD) people in accessing safe and effective pathways to achieving lasting personal comfort with their gendered selves with the aim of optimizing their overall physical health, psychological well-being, and self-fulfillment. This assistance may include but is not limited to hormonal and surgical treatments, voice and communication therapy, primary care, hair removal, reproductive and sexual health, and mental health care. Healthcare systems should provide medically necessary gender-affirming health care for TGD people: See Chapter 2—Global Applicability, Statement 2.1.

WPATH is an international, multidisciplinary, professional association whose mission is to promote evidence-based care, education, research, public policy, and respect in transgender health. Founded in 1979, the organization currently has over 3,000 health care professionals, social scientists, and legal professionals, all of whom are engaged in clinical practice, research, education and advocacy that affects the lives of TGD people. WPATH envisions a world wherein people of all gender identities and gender expressions have access to evidence-based health care, social services, justice, and equality.

One of the main functions of WPATH is to promote the highest standards of health care for individuals through the Standards of Care (SOC) for the health of TGD people. The SOC-8 is based on the best available science and expert professional consensus. The SOC was initially developed in 1979, and the last version was published in 2012.

Most of the research and experience in this field comes from a North American and Western European perspective; thus, adaptations of the SOC-8 to other parts of the world are necessary. Suggestions for approaches to cultural relativity and cultural competence are included in this version of the SOC.

WPATH recognizes that health is not only dependent upon high-quality clinical care but also relies on social and political climates that ensure social tolerance, equality, and the full rights of citizenship. Health is promoted through public policies and legal reforms that advance tolerance and equity for gender diversity and that eliminate prejudice, discrimination, and stigma. WPATH is committed to advocacy for these policy and legal changes. Thus, health care professionals who provide care to TGD people are called upon to advocate for improved access to safe and licensed gender-affirming care while respecting the autonomy of individuals.

While this is primarily a document for health care professionals, individuals, their families, and social institutions may also use the SOC-8 to understand how it can assist with promoting optimal health for members of this diverse population.

The SOC-8 has 18 chapters containing recommendations for health care professionals working with TGD people. Each of the recommendations is followed by explanatory text with relevant references. The recommendations for the initiation of gender-affirming medical and/or surgical treatments (GAMSTs) for adults and adolescents are contained in their respective chapters (see Assessment for Adults and Adolescent chapters). A summary of the recommendations and criteria for GAMST can be found in Appendix D.

Populations included in the SOC-8

In this document, we use the phrase transgender and gender diverse (TGD) to be as broad and comprehensive as possible in describing members of the many varied communities that exist globally of people with gender identities or expressions that differ from the gender socially attributed to the sex assigned to them at birth. This includes people who have culturally specific and/or language-specific experiences, identities or expressions, which may or may not be based on or encompassed by Western conceptualizations of gender or the language used to describe it.

WPATH SOC-8 expands who is included under the TGD umbrella, and the settings in which these guidelines should be applied to promote equity and human rights.

Globally, TGD people encompass a diverse array of gender identities and expressions and have differing needs for gender-affirming care across their lifespan that is related to individual goals and characteristics, available health care resources, and sociocultural and political contexts. When standards of care are absent for certain groups this vacuum can result in a multiplicity of therapeutic approaches, including those that may be counterproductive or harmful. The SOC-8 includes recommendations to promote health and well-being for gender diverse groups that have often been neglected and/or marginalized, including nonbinary people, eunuch, and intersex individuals.

The SOC-8 continues to outline the appropriate care of TGD youth, which includes, when indicated, the use of puberty suppression and, when indicated, the use of gender-affirming hormones.

Worldwide, TGD people commonly experience transphobia, stigmatization, ignorance, and refusal of care when seeking health care services, which contributes to significant health disparities. TGD people often report having to teach their medical providers how to care for them due to the latter's insufficient knowledge and training. Intersectional forms of discrimination, social marginalization, and hate crimes against TGD people lead to minority stress. Minority stress is associated with mental health disparities exemplified by increased rates of depression, suicidality, and non-suicidal self-injuries than rates in cisgender populations. Professionals from every discipline should consider the marked vulnerability of many TGD people. WPATH urges health care authorities, policymakers, and medical societies to discourage and combat transphobia among health care professionals and ensure every effort is made to refer TGD people to professionals with experience and willingness to provide gender-affirming care.

Flexibility in the SOC

The SOC-8 guidelines are intended to be flexible to meet the diverse health care needs of TGD people globally. While adaptable, they offer standards for promoting optimal health care and for guiding treatment of people experiencing gender incongruence. As in all previous versions of the SOC, the criteria put forth in this document for gender-affirming interventions are clinical guidelines; individual health care professionals and programs may modify them in consultation with the TGD person. Clinical departures from the SOC may come about because of a patient's unique anatomic, social, or psychological situation; an experienced health care professional's evolving method of handling a common situation; a research protocol; lack of resources in various parts of the world; or the need for specific harm-reduction strategies. These departures should be recognized as such, explained to the patient, and documented for quality patient care and legal protection. This documentation is also valuable for the accumulation of new data, which can be retrospectively examined to allow for health care—and the SOC—to evolve.

The SOC-8 supports the role of informed decision-making and the value of harm reduction approaches. In addition, this version of the SOC recognizes and validates various expressions of gender that may not necessitate psychological, hormonal, or surgical treatments. Health care professionals can use the SOC to help patients consider the full range of health services open to them in accordance with their clinical needs for gender expression.

Diversity versus Diagnosis

The expression of gender characteristics, including identities, that are not stereotypically associated with one's sex assigned at birth is a common and a culturally diverse human phenomenon that should not be seen as inherently negative or pathological. Unfortunately, gender nonconformity and diversity in gender identity and expression is stigmatized in many societies around the world. Such stigma can lead to prejudice and discrimination, resulting in "minority stress." Minority stress is unique (additive to general stressors experienced by all people), socially based, and chronic, and may make TGD individuals more vulnerable to developing mental health concerns such as anxiety and depression. In addition to prejudice and discrimination in society at large, stigma can contribute to abuse and

neglect in one's interpersonal relationships, which in turn can lead to psychological distress. However, these symptoms are socially induced and are not inherent to being TGD.

While Gender Dysphoria (GD) is still considered a mental health condition in the Diagnostic and Statistical Manual of Mental Disorders, (DSM-5-TR) of the American Psychiatric Association. Gender incongruence is no longer seen as pathological or a mental disorder in the world health community. Gender Incongruence is recognized as a condition in the International Classification of Diseases and Related Health Problems, 11th Version of the World Health Organization (ICD-11). Because of historical and current stigma, TGD people can experience distress or dysphoria that may be addressed with various gender-affirming treatment options. While nomenclature is subject to change and new terminology and classifications may be adopted by various health organizations or administrative bodies, the medical necessity of treatment and care is clearly recognized for the many people who experience dissonance between their sex assigned at birth and their gender identity.

Not all societies, countries, or health care systems require a diagnosis for treatment. However, in some countries these diagnoses may facilitate access to medically necessary health care and can guide further research into effective treatments.

Health care services

The goal of gender-affirming care is to partner with TGD people to holistically address their social, mental, and medical health needs and well-being while respectfully affirming their gender identity. Gender-affirming care supports TGD people across the lifespan—from the very first signs of gender incongruence in childhood through adulthood and into older age—as well as people with concerns and uncertainty about their gender identity, either prior to or after transition.

Transgender health care is greater than the sum of its parts, involving holistic inter- and multidisciplinary care between endocrinology, surgery, voice and communication, primary care, reproductive health, sexual health and mental health disciplines to support gender-affirming interventions as well as preventive care and chronic disease management. Gender-affirming interventions include puberty suppression, hormone therapy, and gender-affirming surgeries among others. It should be emphasized there is no 'one-size-fits-all' approach and TGD people may need to undergo all, some, or none of these interventions to support their gender affirmation. These guidelines encourage the use of a patient-centered care model for initiation of gender- affirming interventions and update many previous requirements to reduce barriers to care.

Ideally, communication and coordination of care should occur between providers to optimize outcomes and the timing of gender-affirming interventions centered on the patient's needs and desires and to minimize harm. In well-resourced settings, multidisciplinary consultation and care coordination is often routine, but many regions worldwide lack facilities dedicated to transgender care. For these regions, if possible, it is strongly recommended that individual care providers create a network to facilitate transgender health care that is not available locally.

Worldwide, TGD people are sometime forced by family members or religious communities to undergo conversion therapy. WPATH strongly recommends against any use of reparative or conversion therapy (see statements 6.5 and 18.10).

Health care settings

The SOC-8 are guidelines rooted in the fundamental rights of TGD people that apply to all settings in which health care is provided regardless of an individual's social or medical circumstances. This includes a recommendation to apply the standards of care for TGD people who are incarcerated or living in other institutional settings.

Due to a lack of knowledgeable providers, untimely access, cost barriers and/or previous stigmatizing health care experiences, many TGD people take non-prescribed hormone therapy. This poses health risks associated with the use of unmonitored therapy in potentially supratherapeutic doses and the potential exposure to blood-borne illnesses if needles are shared for administration. However, for many individuals, it is the only means of acquiring medically necessary

gender-affirming treatment that is otherwise inaccessible. Non-prescribed hormone use should be approached with a harm-reduction lens to ensure individuals are connected with providers who can prescribe safe and monitored hormone therapy.

In some countries, the rights of TGD are increasingly being recognized, and gender clinics are being established that can serve as templates for care. In other countries, however, such facilities are lacking and care may be more fragmented and under-resourced. Nonetheless, different models of care are being pioneered, including efforts to decentralize gender-affirming care within primary care settings and establish telehealth services to reduce barriers and improve access. Regardless of the method of care delivery, the principles of gender-affirming care as outlined in the SOC-8 should be adapted to align with local sociocultural, political, and medical contexts.

Methodology

This version of the Standards of Care (SOC-8) is based upon a more rigorous and methodological evidence-based approach than previous versions. This evidence is not only based on the published literature (direct as well as background evidence) but also on consensus-based expert opinion. Evidence-based guidelines include recommendations intended to optimize patient care that are informed by a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility.

While evidence-based research provides the basis for sound clinical practice guidelines and recommendations, it must be balanced by the realities and feasibility of providing care in diverse settings. The process for development of the SOC-8 incorporated the recommendations on clinical practice guideline development set forth by the National Academies of Medicine and the World Health Organization, which addressed transparency, conflict-of-interest policy, committee composition, and group process.

The SOC-8 guidelines committee was multidisciplinary and consisted of subject matter experts, health care professionals, researchers, and stakeholders with diverse perspectives and geographic representation. A guideline methodologist assisted with the planning and development of questions and systematic reviews with additional input provided by an international advisory committee and during the public comment period. All committee members completed conflict of interest declarations. Recommendations in the SOC-8 are based on available evidence supporting interventions, a discussion of risks and harms, as well as feasibility and acceptability within different contexts and country settings. Consensus on the final recommendations was attained using the Delphi process that included all members of the guidelines committee and required that recommendation statements were approved by at least 75% of members. A detailed overview of the SOC-8 Methodology is included in Appendix A.

SOC-8 Chapters Summary

The SOC-8 represents a significant advancement from previous versions. Changes in this version are based upon a fundamentally different methodology, significant cultural shifts, advances in clinical knowledge, and appreciation of the many health care issues that can arise for TGD people beyond hormone therapy and surgery.

These updated guidelines continue the process started with the SOC-7 in 2011 to broaden in scope and move from a narrow focus on psychological requirements for "diagnosing transgenderism" and medical treatments for alleviation of gender dysphoria to gender-affirming care for the whole person. WPATH SOC-8 expands guidelines specifying who is included under the TGD umbrella, what should and should not be offered with gender-affirming care, and the settings in which these guidelines should be applied to promote equity and human rights.

The SOC-8 has several new chapters such as the Assessment of Adults, Education, Eunuchs, and a Nonbinary chapter. In addition, the chapter for children and adolescents of the SOC-7 has been divided into two different chapters. Overall, the SOC-8 is considerably longer than previous versions and provides a more in-depth introduction and recommendations for health care professionals. A summary of every chapter of the SOC-8 can be found below:

Chapter 1—Terminology

This new chapter lays the framework for language used in the SOC-8 and offers consensually agreed upon recommendations for the use of terminology. The chapter provides (1) terms and definitions, and (2) best practices for utilizing them. This document is accompanied by a glossary (see Appendix B) of common terms and language to provide a framework for use and interpretation of the SOC-8.

Chapter 2—Global Applicability

This chapter references key literature related to development and delivery of health care services, broader advocacy care for TGD people from beyond Western Europe and North America and provides recommendations for adapting and translating the SOC-8 to varied contexts.

Chapter 3—Population Estimates

This chapter updates the population estimates of TGD people in society. Based on the current evidence, this proportion may range from a fraction of a percent to several percentage points depending on the inclusion criteria, age group, and geographic location.

Chapter 4—Education

This new chapter provides a general review of the literature related to education in TGD health care. It offers recommendations at governmental, nongovernmental, institutional and provider levels to increase access to competent, compassionate health care. The intent is to lay the groundwork in the education area and invite a much broader and deeper discussion among educators and health care professionals.

Chapter 5—Assessment of Adults

This new chapter provides guidance on the assessment of TGD adults who are requesting gender-affirming medical and surgical treatments (GAMSTs). It describes and updates the assessment process as part of a patient-centered approach and the criteria that health care professionals may follow in order to recommend GAMSTs to TGD adults.

Chapter 6—Adolescents

This new chapter is dedicated to TGD adolescents, is distinct from the child chapter, and has been created for this 8th edition of the Standards of Care given (1) the exponential growth in adolescent referral rates; (2) the increase in studies available specific to adolescent gender diversity-related care; and (3) the unique developmental and gender-affirming care issues of this age group. This chapter provides recommendations regarding the assessment process of adolescents requiring GAMSTs as well as recommendations when working with TGD youth and their families.

Chapter 7—Children

This new chapter pertains to prepubescent gender diverse children and focuses on developmentally appropriate psychosocial practices and therapeutic approaches.

Chapter 8—Nonbinary

This new chapter in the SOC-8 consists of a broad description of the term nonbinary and its usage from a biopsychosocial, cultural, and intersectional perspective. The need for access to gender-affirming care, specific gender-affirming medical interventions, as well as an appropriate level of support is discussed.

Chapter 9—Eunuchs

This new chapter describes the unique needs of eunuchs, and how the SOC can be applied to this population.

Chapter 10—Intersex

This chapter focuses on the clinical care of intersex individuals. It addresses the evolving terminology, prevalence, and diverse presentations of such individuals and provides recommendations for providing psychosocial and medical care with their evidence-based explanations.

Chapter 11—Institutional Environments

This chapter has been expanded to include both carceral and non-carceral settings and has been built upon the last 3 versions of the SOC. This chapter describes how the SOC-8 can be applied to individuals living in these settings.

Chapter 12—Hormone Therapy

This chapter describes the initiation of gender-affirming hormone therapy, the recommended regimens, screening for health concerns before and during hormone therapy, and specific considerations regarding hormone therapy prior to surgery. It includes an expanded discussion about the safety of gonadotropin releasing hormone (GnRH) agonists in youth, various hormone regimens, monitoring to include the development of potential therapy-related health concerns, and guidance on how hormone providers should collaborate with surgeons.

Chapter 13—Surgery and Postoperative Care

This chapter describes a spectrum of gender-affirming surgical procedures for the diverse and heterogeneous community of individuals who identify as TGD. It provides a discussion about the optimal surgical training in GAS procedures, post-surgical aftercare and follow-up, access to surgery by adults and adolescents, and individually customized surgeries.

Chapter 14—Voice and Communication

This chapter describes professional voice and communication support and interventions that are inclusive of and attentive to all aspects of diversity and no longer limited only to voice feminization and masculinization. Recommendations are now framed as affirming the roles and responsibilities of professionals involved in voice and communication support.

Chapter 15—Primary Care

This chapter discusses the importance of primary care for TGD individuals, including topics of cardiovascular and metabolic health, cancer screening, and primary care systems.

Chapter 16—Reproductive Health

This chapter provides recent data on fertility perspectives and parenthood goals in gender diverse youth and adults, advances in fertility preservation methods (including tissue cryopreservation), guidance regarding preconception and pregnancy care, prenatal counseling, and chest feeding. Contraceptive methods and considerations for TGD individuals are also reviewed.

Chapter 17—Sexual Health

This new chapter acknowledges the profound impact of sexual health on physical and psychological well-being for TGD people. The chapter advocates for sexual functioning, pleasure, and satisfaction to be included in TGD-related care.

Chapter 18—Mental Health

This chapter discusses principles of care for managing mental health conditions in TGD adults and the nexus of mental health care and transition care. Psychotherapy may be beneficial but should not be a requirement for gender-affirming treatment, and conversion treatment should not be offered.

CHAPTER 1 Terminology

This chapter will lay the framework for language used in the SOC-8. It offers recommendations for use of terminology. It provides (1) terms and definitions, and (2) best practices for utilizing them. This document is accompanied by a glossary of common terms and language to provide a framework for use and interpretation of the SOC-8. See Appendix B for glossary.

Terminology

In this document, we use the phrase transgender and gender diverse (TGD) to be as broad and comprehensive as possible in describing members of the many varied communities globally of people with gender identities or expressions that differ from the gender socially attributed to the sex assigned to them at birth. This includes people who have culturally specific and/or language-specific experiences, identities or expressions, and/or that are not based on or encompassed by Western conceptualizations of gender, or the language used to describe it. TGD is used for convenience as a shorthand for transgender and gender diverse.

The decision to use transgender and gender diverse resulted from an active process and was not without controversy. Discussions centered on avoiding over-emphasis on the term transgender, integrating nonbinary gender identities and experiences, recognizing global variations in understandings of gender, avoiding the term gender nonconforming, and recognizing the changing nature of language because what is current now may not be so in coming years. Thus, the term transgender and gender diverse was chosen with the intent to be most inclusive and to highlight the many diverse gender identities, expressions, experiences, and health care needs of TGD people. A Delphi process was used wherein SOC-8 chapter authors were anonymously and iteratively surveyed over several rounds to obtain consensus on terms. The SOC-8 presents standards of care that strive to be applicable to TGD people globally, no matter how a person self-identifies or expresses their gender.

Context

The language selected in this chapter may not be (nor ever could be) comprehensive of every culture and geographic region/locale. Differences and debates over appropriate terms and specific terminologies are common, and no single term can be used without controversy. The goal of this chapter is to be as inclusive as possible and offer a shared vocabulary that is respectful and reflective of varied experiences of TGD people while remaining accessible to health practitioners and providers, and the public, for the purposes of this document. Ultimately, access to transition-related health care should be based on providing adequate information and obtaining informed consent from the individual, and not on what words TGD people, or their service providers, use to describe their identities. Using language and terminology that is respectful and culturally responsive is a basic foundation in the provision of affirming care, as is reducing the stigma and harm experienced by many TGD people seeking health care. It is vital for service providers to discuss with service users what language is most comfortable for them and to use that language whenever possible.

This chapter explains why current terms are being used in preference to others. Rather than use specific terms for medical, legal, and advocacy groups, the aim is to foster a shared language and understanding in the field of TGD health, and the many related fields (e.g., epidemiology, law), in order to optimize the health of transgender and gender diverse people.

Sex, gender, gender identity, and gender expression are used in the English language as descriptors that can apply to all people—those who are TGD, and those who are not. There are complex reasons why very specific language may be the *most* respectful, *most* inclusive, or *most* accepted by global TGD communities, including the presence or absence of words to describe these concepts in languages other than English; the structural relationship between sex and gender; legal landscapes at the local, national, and international levels; and the consequences of historical and present-day stigma that TGD people face.

Statements of Recommendations

1.1- We recommend health care professionals use culturally relevant language (including terms to describe transgender and gender diverse people) when applying the Standards of Care in different global settings.
1.2- We recommend health care professionals use language in health care settings that uphold the principles of safety, dignity, and respect.
1.3- We recommend health care professionals discuss with transgender and gender diverse people what language or terminology they prefer.

Because at present, the field of TGD health is heavily dominated by the English language, there are two specific problems that constantly arise in setting the context for terminology. The first problem is that words exist in English that do not exist in other languages (e.g., "sex" and "gender" are only represented by one word in Urdu and many other languages). The second problem is that there are words that exist outside of English that do not have a direct translation into English (e.g., *travesti*, *fa'afafine*, *hijra*, *selrata*, *muxe*, *kathoey*, *transpinoy*, *waria*, *machi*). Practically, this means the heavy influence of English in this field impacts both what terms are widely used and which people or identities are most represented or validated by those terms. The words used also shape the narratives that contribute to beliefs and perceptions. While in past versions of the Standards of Care, World Professional Association for Transgender Health (WPATH) has used only transgender as a broadly defined umbrella term, version 8 broadens this language to use TGD as the umbrella term throughout the document (see Chapter 2—Global Applicability).

Furthermore, the ever-evolving nature of language is impacted by external factors and the social, structural, and personal pressures and violence enacted on TGD people and their bodies. Many of the terms and phrases used historically have been marred by how, when, and why they were used in discussing TGD people, and have thus fallen out of use or are hotly contested among TGD people, with some individuals preferring terms others find offensive. Some wish that these Standards of Care could provide a coherent set of universally accepted terms to describe TGD people, identities, and related health services. Such a list, however, does not and cannot exist without exclusion of some people and without reinforcing structural oppressions, with regards to race, national origin, Indigenous status, socioeconomic status, religion, language(s) spoken, and ethnicity, among other intersectionalities. It is very likely that at least some of the terminology used in SOC-8 will be outdated by the time version 9 is developed. Some people will be frustrated by this reality, but it is hoped it will be seen instead as an opportunity for individuals and communities to develop and refine their own lexicons and for people to develop a still more nuanced understanding of the lives and needs of TGD people, including TGD people's resilience and resistance to oppression.

Finally, law and the work of legal professionals are within the remit of these Standards of Care. As such, language used most widely in international law is included here to help with the development of the functional definitions of these terms and encourage their usage in legal contexts in lieu of more antiquated and/or offensive terms. The currently most thorough document in international human rights law uses the term "gender diverse."[1]

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 1.1

We recommend health care professionals use culturally relevant language (including terms to describe transgender and gender diverse people) when applying the Standards of Care in different global settings.

Culturally relevant language is used to describe TGD people in different global settings. For example, the concepts of sex, gender, and gender diversity differ across contexts, as does the language used to describe them. Thus, the language used when caring

for TGD people in Thailand is not going to be the same as that used for TGD care in Nigeria. When applying the Standards of Care globally, we recommend health care professionals (HCPs) utilize local language and terms to deliver care in their specific cultural and/or geographical locale.

Gender affirmation refers to the process of recognizing or affirming TGD people in their gender identity—whether socially, medically, legally, behaviorally, or some combination of these (Reisner, Poteat et al., 2016). Health care that is gender-affirming or trans-competent utilizes culturally specific language in caring for TGD people. Gender-affirming care is not synonymous with transition-related care. Provision of transition-related care, such as medical gender affirmation via hormones or surgery, does not alone ensure provision of gender-affirming care, nor does it indicate the quality or safety of the health care provided.

Consultation and partnerships with TGD communities can help to ensure relevancy and inclusivity of the language used in providing health care locally in a particular context and setting.

Statement 1.2

We recommend health care professionals use language in health care settings that upholds the principles of safety, dignity, and respect.

Safety, dignity, and respect are basic human rights (International Commission of Jurists, 2007). We recommend HCPs utilize language and terminology that uphold these human rights when providing care for TGD people. Many TGD people have experienced stigma, discrimination, and mistreatment in health care settings, resulting in suboptimal care and poor health outcomes (Reisner, Poteat et al., 2016; Safer et al., 2016; Winter, Settle et al., 2016). Such experiences include misgendering, being refused care or denied services when sick or injured and having to educate HCPs to be able to receive adequate care (James et al., 2016). Consequently, many TGD people feel unsafe accessing health care. They may avoid health care systems and seek other means of getting health-related needs met, such as taking hormones without a medical prescription or monitoring and relying on peers for medical advice. Furthermore, previous negative experiences in health care settings are associated with future avoidance of care among TGD people.

Many TGD people have been treated unjustly, with prejudice, and without dignity or respect by HCPs, and lack of trust is often a barrier to care. Using language grounded in the principles of safety, dignity, and respect in health care settings is paramount to ensure the health, well-being, and rights of TGD people globally. Language is a significant component of gender-affirming care, but language alone does not resolve or mitigate the systematic abuse and sometimes violence TGD people face globally in care settings. Language is but one important step toward patient/client-centered and equitable health care among TGD people. Other concrete actions HCPs can take include obtaining informed consent and refraining from making assumptions about a person's needs based on their gender or TGD status.

Statement 1.3

We recommend health care professionals discuss with transgender and gender diverse people what language or terminology they prefer.

In providing health care to TGD people, we recommend HCPs discuss with their patients what language or terminology they prefer be used when referring to them. This discussion includes asking TGD people how they would like to be addressed in terms of name and pronouns, how they self-identify their gender, and about the language that should be used to describe their body parts. Utilizing affirming language or terminology is a key component of TGD-affirming care (Lightfoot et al., 2021; Vermeir et al., 2018). Furthermore, these discussions and communications can serve to build rapport and reduce the mistrust many TGD people feel toward HCPs and experience within health care systems. Discussions and usage of language or terminology can also facilitate engagement and retention in care that is not specifically TGD-related, such as uptake of routine preventive screenings and any necessary medical follow-up of findings. In electronic health records, organ/anatomical inventories can be standardly used to inform appropriate clinical care, rather than relying solely on assigned sex at birth and/or gender identity designations.

HCPs and health care settings can implement standardized procedures to facilitate these conversations such as: using intake forms that include chosen pronouns and name, inviting

all staff (regardless of gender, i.e., cisgender, TGD) to use pronouns in introductions, having pronouns accompany names on a document for all patients, and not using gendered honorifics (e.g., Ms., Mr.). Policies for HCPs and health care settings can be put in place to ensure a TGD person's privacy and right to confidentiality, including when they disclose being a TGD person, and if/how to appropriately document. For example, a clinic policy may be to record this information as private and confidential between HCPs and patients/clients, and that it should only be disclosed on a "need to know" basis.

Note

1. A/73/152, Report of the Independent Expert on protection against violence and discrimination based on sexual orientation and gender identity

CHAPTER 2 Global Applicability

People who defy cultural boundaries of sex and gender have existed in cultures worldwide since ancient times, sometimes acknowledged in local language terms (Feinberg, 1996). In contrast to the more recent pathologization of gender diversity as an illness, some cultures traditionally celebrated and welcomed this diversity (e.g., Nanda, 2014; Peletz, 2009). Today, the English language umbrella term transgender and gender diverse (TGD) describes a huge variety of gender identities and expressions, and therefore a population with diverse health care experiences and needs. Together, TGD people represent important aspects of human diversity the World Professional Association for Transgender Health (WPATH) asserts should be valued and celebrated. TGD people continue to make vital contributions to the societies in which they live, although often these are unrecognized.

Disturbingly, many TGD people in the modern world experience stigma, prejudice, discrimination, harassment, abuse and violence, resulting in social, economic and legal marginalization, poor mental and physical health, and even death—a process that has been characterized as a stigma-sickness slope (Winter, Diamond et al., 2016). Experiences such as these (and the anticipation or fear of encountering such experiences) leads to what Meyer has described as minority stress (Meyer, 2003; see also Bockting et al., 2013 writing specifically about TGD people), and are associated with poor physical (e.g. Rich et al, 2020) and psychological (e.g., Bränström et al., 2022; Scandurra et al., 2017; Shipherd et al., 2019, Tan et al., 2021) health outcomes.

Violence against TGD people is a particular problem. Seen from a global perspective, it is widespread, diverse in nature (emotional, sexual and physical, e.g., see Mujugira et al., 2021), and involves a range of perpetrators (including State actors). Statistics on murder, the form of violence most extreme in its consequences, are alarming. Worldwide, there were over 4,000 documented killings between January 2008 and September 2021; a statistic widely regarded as flawed by under-reporting (TGEU, 2020).

Since the publication of the Standards of Care Version 7 (SOC-7), there have been dramatic changes in perspectives on TGD people and their health care. Mainstream global medicine no longer classifies TGD identities as a mental disorder. In the Diagnostic and Statistical Manual Version 5 (DSM-5) from the American Psychiatric Association (APA, 2013), the diagnosis of *Gender Dysphoria* focuses on any distress and discomfort that accompanies being TGD, rather than on the gender identity itself. A text revision (DSM-5-TR) was published in 2022. In the International Classification of Diseases, Version 11 (ICD-11), the diagnostic manual of the World Health Organization (WHO, 2019b), the *Gender Incongruence* diagnosis is placed in a chapter on sexual health and focuses on the person's experienced identity and any need for gender-affirming treatment that might stem from that identity. Such developments, involving a depathologization (or more precisely a de-psychopathologization) of transgender identities, are fundamentally important on a number of grounds. In the field of health care, they may have helped support a care model that emphasizes patients' active participation in decision-making about their own health care, supported by primary health care professionals (HCPs) (Baleige et al., 2021). It is reasonable to suppose these developments may also promote more socially inclusive policies such as legislative reform regarding gender recognition that facilitates a rights-based approach, without imposing requirements for diagnosis, hormone therapy and/or surgery. TGD people who have changed gender markers on key documents enjoy better mental health (e.g., Bauer et al., 2015; Scheim et al., 2020). A more rights-based approach in this area may contribute greatly to the overall health and well-being of TGD people (Arístegui et al., 2017).

Previous editions of the SOC have revealed much of the recorded clinical experience and knowledge in this area is derived from North American and Western European sources. They have focused on gender-affirming health care in high income countries that enjoy relatively well-resourced health care systems (including those with trained mental health providers, endocrinologists, surgeons and other specialists) and where services are often funded publicly or (at least for some patients) through private insurance.

For many countries, health care provision for TGD people is aspirational; with resourcing in this area limited or non-existent, and services often unavailable, inappropriate, difficult to access and/or unaffordable. Few if any HCPs (primary or specialist) may exist. Funding for gender-affirming health care may be absent, with patients often bearing the full costs of whatever health care they access. Health care providers often lack clinical and/or cultural competence in this area. Training for work with these patients may be limited (e.g., Martins et al., 2020). For all these reasons and because of mainstream "Western" medicine's historical view of TGD people as mentally disordered (a perspective that has only recently changed), TGD people have commonly found themselves disempowered as health care consumers.

Health care providers have found the relevant literature is largely North American and European, which present particular challenges for persons working in health care systems that are especially poorly resourced. Recent initiatives that often involve TGD stakeholders as partners are changing this situation somewhat by providing a body of knowledge about good practice in other regions, including how to provide effective, culturally-competent TGD health care in low- and middle-income countries outside the global north.

Within the field, a wide range of valuable health care resources have been developed in recent years. Dahlen et al (2021) review twelve international clinical practice guidelines; over half those reviewed originate from professional bodies based in North America (e.g., Hembree et al., 2017) or Europe (e.g., T'Sjoen et al., 2020). Three are from WHO (the most recent being WHO, 2016). Nowadays, there are numerous other resources, not on Dahlen et al.'s list, that explicitly draw on expertise from regions outside North America and Europe. Examples can be found in Asia and the Pacific (APTN, 2022; Health Policy Project et al., 2015), the Caribbean (PAHO, 2014), Thailand, Australia (Telfer et al., 2020), Aotearoa New Zealand (Oliphant et al., 2018), and South Africa (Tomson et al., 2021) (see also TRANSIT (UNDP et al., 2016)). These resources have commonly been created through the initiatives of or in partnership with TGD communities locally or internationally. This partnership approach, focused on meeting local needs in culturally safe and competent ways, can also have broad international relevance. Some of these publications may be of particular value to those planning, organizing and delivering services in low-income, low-resource countries. There are likely to be other resources published in languages other than English of which we are unaware.

Globally, TGD identities may be associated with differing conceptual frameworks of sex, gender, and sexuality and exist in widely diverse cultural (and sometimes spiritual) contexts and histories. Considering the complex relationships between social and cultural factors, the law, and the demand for and provisions of gender-affirming health care, the SOC-8 should be interpreted through a lens that is appropriate for and within the context of each HCP's individual practice while maintaining alignment to the core principles that underscore it (APTN and UNDP, 2012; Health Policy Project et al., 2015; PAHO, 2014).

It is within this context and by drawing broadly on the experiences of TGD people and health care providers internationally that we consider the global applicability of SOC-8 within this chapter. We set out key considerations for HCPs and conclude by recommending core principles and practices fundamental to contemporary health care for TGD people, regardless of where they live or whether there are resources available to those who seek to provide such health care.

Statement 2.1

We recommend health care systems should provide medically necessary gender-affirming health care for transgender and gender diverse people.

Medical necessity is a term common to health care coverage and insurance policies globally. A common definition of medical necessity as used by insurers or insurance companies is "Health care services that a physician and/or health care professional, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are: (a) in accordance with generally accepted standards of medical practice; (b) clinically

Statements of Recommendations

2.1- We recommend health care systems should provide medically necessary gender-affirming health care for transgender and gender diverse people.
2.2- We recommend health care professionals and other users of the Standards of Care, Version 8 (SOC-8) apply the recommendations in ways that meet the needs of local transgender and gender diverse communities, by providing culturally sensitive care that recognizes the realities of the countries they are practicing in.
2.3- We recommend health care providers understand the impact of social attitudes, laws, economic circumstances, and health systems on the lived experiences of transgender and gender diverse people worldwide.
2.4- We recommend translations of the SOC focus on cross-cultural, conceptual, and literal equivalence to ensure alignment with the core principles that underpin the SOC-8.
2.5- We recommend health care professionals and policymakers always apply the SOC-8 core principles to their work with transgender and gender diverse people to ensure respect for human rights and access to appropriate and competent health care, including:

General principles
- Be empowering and inclusive. Work to reduce stigma and facilitate access to appropriate health care for all who seek it;
- Respect diversity. Respect all clients and all gender identities. Do not pathologize differences in gender identity or expression;
- Respect universal human rights including the right to bodily and mental integrity, autonomy and self-determination; freedom from discrimination, and the right to the highest attainable standard of health.

Principles around developing and implementing appropriate services and accessible health care
- Involve transgender and gender diverse people in the development and implementation of services;
- Become aware of social, cultural, economic, and legal factors that might impact the health (and health care needs) of transgender and gender diverse people, as well as the willingness and the capacity of the person to access services;
- Provide health care (or refer to knowledgeable colleagues) that affirms gender identities and expressions, including health care that reduces the distress associated with gender dysphoria (if this is present);
- Reject approaches that have the goal or effect of conversion and avoid providing any direct or indirect support for such approaches or services.

Principles around delivering competent services
- Become knowledgeable (get training, where possible) about the health care needs of transgender and gender diverse people, including the benefits and risks of gender-affirming care;
- Match the treatment approach to the specific needs of clients, particularly their goals for gender identity and expression;
- Focus on promoting health and well-being rather than solely the reduction of gender dysphoria, which may or may not be present;
- Commit to harm reduction approaches where appropriate;
- Enable the full and ongoing informed participation of transgender and gender diverse people in decisions about their health and well-being;
- Improve experiences of health services including those related to administrative systems and continuity of care.

Principles around working towards improved health through wider community approaches
- Put people in touch with communities and peer support networks;
- Support and advocate for clients within their families and communities (schools, workplaces, and other settings) where appropriate.

appropriate, in terms of type, frequency, extent, site and duration, and considered effective for the patient's illness, injury, or disease; and (c) not primarily for the convenience of the patient, physician, or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease." The treating HCP asserts and documents that a proposed treatment is medically necessary for treatment of the condition (American Medical Association, 2016).

Generally, "accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, designated Medical Specialty Societies and/or legitimate Medical Colleges' recommendations, and the views of physicians and/or HCPs practicing in relevant clinical areas.

Medical necessity is central to payment, subsidy, and/or reimbursement for health care in parts of the world. The treating HCP may assert and document that a given treatment is medically necessary for the prevention or treatment of the condition. If health policies and practices challenge the medical necessity of a treatment, there may be an opportunity to appeal to a governmental agency or other entity for an independent medical review.

It should be recognized gender diversity is common to all human beings and is not pathological. However, gender incongruence that causes clinically significant distress and impairment often requires medically necessary clinical

interventions. In many countries, medically necessary gender-affirming care is documented by the treating health professional as treatment for Gender Incongruence (HA60 in ICD-11; WHO, 2019b) and/or as treatment for Gender Dysphoria (F64.0 in DSM-5-TR; APA, 2022).

There is strong evidence demonstrating the benefits in quality of life and well-being of gender-affirming treatments, including endocrine and surgical procedures, properly indicated and performed as outlined by the Standards of Care (Version 8), in TGD people in need of these treatments (e.g., Ainsworth & Spiegel, 2010; Aires et al., 2020; Aldridge et al., 2020; Almazan & Keuroghlian, 2021; Al-Tamimi et al., 2019; Balakrishnan et al., 2020; Baker et al., 2021; Buncamper et al., 2016; Cardoso da Silva et al., 2016; Eftekhar Ardebili, 2020; Javier et al., 2022; Lindqvist et al., 2017; Mullins et al., 2021; Nobili et al., 2018; Owen-Smith et al., 2018; Özkan et al., 2018; T'Sjoen et al., 2019; van de Grift, Elaut et al., 2018; White Hughto & Reisner, Poteat et al., 2016; Wierckx, van Caenegem et al., 2014; Yang, Zhao et al., 2016). Gender-affirming interventions may also include hair removal/transplant procedures, voice therapy/surgery, counseling, and other medical procedures required to effectively affirm an individual's gender identity and reduce gender incongruence and dysphoria. Additionally, legal name and sex or gender change on identity documents can also be beneficial and, in some jurisdictions, are contingent on medical documentation that patients may call on practitioners to produce.

Gender-affirming interventions are based on decades of clinical experience and research; therefore, they are not considered experimental, cosmetic, or for the mere convenience of a patient. They are safe and effective at reducing gender incongruence and gender dysphoria (e.g., Aires et al., 2020; Aldridge et al., 2020; Al-Tamimi et al., 2019; Balakrishnan et al., 2020; Baker et al., 2021; Bertrand et al., 2017; Buncamper et al., 2016; Claes et al., 2018; Eftekhar Ardebili, 2020; Esmonde et al., 2019; Javier et al., 2022; Lindqvist et al., 2017; Lo Russo et al., 2017; Marinkovic & Newfield, 2017; Mullins et al., 2021; Nobili et al., 2018; Olson-Kennedy, Rosenthal et al., 2018; Özkan et al., 2018; Poudrier et al., 2019; T'Sjoen et al., 2019; van de Grift, Elaut et al., 2018; White Hughto & Reisner, Poteat et al., 2016; Wierckx, van Caenegem et al., 2014; Wolter et al., 2015; Wolter et al., 2018).

Consequently, WPATH urges health care systems to provide these medically necessary treatments and eliminate any exclusions from their policy documents and medical guidelines that preclude coverage for any medically necessary procedures or treatments for the health and well-being of TGD individuals. In other words, governments should ensure health care services for TGD people are established, extended or enhanced (as appropriate) as elements in any Universal Health Care, public health, government-subsidized systems, or government-regulated private systems that may exist. Health care systems should ensure ongoing health care, both routine and specialized, is readily accessible and affordable to all citizens on an equitable basis.

Medically necessary gender-affirming interventions are discussed in SOC-8. These include but are not limited to hysterectomy +/- bilateral salpingo-oophorectomy; bilateral mastectomy, chest reconstruction or feminizing mammoplasty, nipple resizing or placement of breast prostheses; genital reconstruction, for example, phalloplasty and metoidioplasty, scrotoplasty, and penile and testicular prostheses, penectomy, orchiectomy, vaginoplasty, and vulvoplasty; hair removal from the face, body, and genital areas for gender affirmation or as part of a preoperative preparation process; gender-affirming facial surgery and body contouring; voice therapy and/or surgery; as well as puberty blocking medication and gender-affirming hormones; counseling or psychotherapeutic treatment as appropriate for the patient and based on a review of the patient's individual circumstances and needs.

Statement 2.2

We recommend health care professionals and other users of the Standards of Care, Version 8 (SOC-8) apply the recommendations in ways that meet the needs of local transgender and gender diverse communities, by providing culturally sensitive care that recognizes the realities of the countries they are practicing in.

TGD people identify in many different ways worldwide, and those identities exist within a cultural context. In English speaking countries, TGD people variously identify as *transsexual,*

trans, gender nonconforming, gender queer or diverse, nonbinary, or indeed *transgender and/or gender diverse,* as well as by other identities; including (for many identifying inside the gender binary) *male* or *female.* (e.g., James et al., 2016; Strauss et al., 2017; Veale et al., 2019).

Elsewhere, identities include but are not limited to *travesti* (across much of Latin America), *hijra* (across much of South Asia), *khwaja sira* (in Pakistan), *achout* (in Myanmar), *maknyah, paknyah* (in Malaysia), *waria* (Indonesia) *kathoey, phuying kham phet, sao praphet song* (Thailand), *bakla, transpinay, transpinoy* (Philippines), *fa'afafine* (Samoa), *mahu* (French Polynesia, Hawai'i), *leiti* (Tonga), *fakafifine* (Niue), *pinapinaaine* (Tuvalu and Kiribati), *vakasalewalewa* (Fiji), *palopa* (Papua Niugini), *brotherboys* and *sistergirls* (Aboriginal and Torres Strait Islander people in Australia), and *akava'ine* (Cook Islands) (e.g., APTN and UNDP, 2012; Health Policy Project et al., 2015; Kerry, 2014). There are also a large number of *two spirit* identities across North America (e.g., *nadleehi* in Navajo (Diné) culture) (Sheppard & Mayo, 2013). The identities to which each of these terms refer are often culturally complex and may exist in a spiritual or religious context. Depending on the cultures and the identities concerned, some may be regarded as so-called "third genders" lying beyond the gender binary (e.g., Graham, 2010; Nanda, 2014; Peletz, 2009). Some TGD identities are less firmly established than others. In many places worldwide, the visibility of transgender men and nonbinary trans masculine identities is relatively recent, with few or no applicable traditional terms in local languages (Health Policy Project et al., 2015). Regardless of where or with whom HCPs work (including those working with ethnic minority persons, migrants and refugees), they need to be aware of the cultural context in which people have grown up and live as well as the consequences for health care.

Worldwide the availability, accessibility, acceptability and quality of health care vary greatly, with resulting inequities within and across countries (OECD, 2019). In some countries, formal health care systems exist alongside established traditional and folk health care systems, with indigenous models of health underpinning the importance of holistic health care (WHO, 2019a). HCPs should be aware of the traditions and realities within which health care is available and provide support that is sensitive to the local needs and identities of TGD people and provide them with culturally competent and safe care.

Statement 2.3

We recommend health care providers understand the impact of social attitudes, laws, economic circumstances, and health systems on the lived experiences of transgender and gender diverse people worldwide.

TGD people's lived experiences vary greatly, depending on a range of factors, including social, cultural (including spiritual), legal, economic and geographic. When TGD people live in environments that affirm their gender and/or cultural identities, then these experiences can be very positive. Families are particularly important in this regard (e.g., Pariseau et al., 2019; Yadegarfard et al., 2014; Zhou et al., 2021). However, when viewed from a global perspective, the circumstances in which TGD people live are often challenging. They are commonly denied widely accepted rights in international human rights law. These include rights to education, health and protection from medical abuses, work and an adequate standard of living, housing, freedom of movement and expression, privacy, security, life, family, freedom from arbitrary deprivation of liberty, fair trial, treatment with humanity while in detention, and freedom from torture, inhuman or degrading treatment or punishment (International Commission of Jurists, 2007, 2017).

It is widely accepted that denial of rights can impact sexual and gender minority health and well-being (e.g., OHCHR et al., 2016; WHO, 2015). We therefore reaffirm here the importance of the rights listed above for TGD people and note WPATH's previous rights advocacy, including through numerous policy documents (e.g., WPATH, 2016, 2017, 2019). HCPs can play an important role in rights advocacy, including the right to quality gender-affirming health care that is appropriate, affordable, and accessible.

Across the world, a large number of studies detail the challenges TGD people face in their lives, and the impact on their health and well-being (e.g., Aurat Foundation, 2016;

Bhattacharya & Ghosh, 2020; Chumakov et al., 2021; Coleman et al., 2018; Heylens, Elaut et al., 2014; Human Rights Watch, 2014; James et al, 2016; Lee, Operario et al., 2020; Luz et al., 2022; McNeil et al., 2012, 2013; Motmans et al., 2017; Muller et al., 2019; Scandurra et al., 2017; Strauss et al., 2019; Suen et al., 2017; Valashany & Janghorbani, 2019; Veale et al., 2019; Wu et al., 2017). The research shows TGD people often experience stigma and prejudice as well as discrimination and harassment, abuse and violence, or they live in anticipation and fear of such actions. Social values and attitudes hostile to TGD people, often communicated to young people in school curricula (e.g., Olivier & Thurasukam, 2018), are also expressed in family rejection (e.g., Yadegarfard et al., 2014), and perpetuated in laws, policies and practices that limit freedom to express one's gender identity and sexuality and hinder access to housing, public spaces, education, employment and services (including health care). The end result is TGD people are commonly deprived of a wide range of opportunities available to their cisgender counterparts and are pushed to the margins of society, without family supports. To make matters worse, across much of the world TGD people's access to legal gender recognition is restricted or non-existent (e.g., ILGA World, 2020a; TGEU, 2021; UNDP and APTN, 2017). In some countries, such barriers nowadays draw on support from "gender-critical theorists" (as critiqued by e.g., Madrigal-Borloz, 2021; Zanghellini, 2020).

Gender identity change efforts (gender reparative or gender conversion programs aimed at making the person cisgender) are widespread, cause harm to TGD people (e.g., APTN, 2020a, 2020b, 2020c, 2021; Bishop, 2019; GIRES et al., 2020; Turban, Beckwith et al., 2020), and (like efforts targeting sexual orientation) are considered unethical (e.g., APS, 2021; Trispiotis and Purshouse, 2021; Various, 2019, 2021). These efforts may be viewed as a form of violence. The UN independent expert on protection against violence and discrimination based on sexual orientation and gender identity has called for a global ban on such practices (Madrigal-Borloz, 2020). An increasing number of jurisdictions are outlawing such work (ILGA World, 2020b).

Inequities arise from a range of factors, including economic considerations and values underpinning the provision of health care systems, particularly with regard to the emphasis placed on public-, private- and self-funding of health care. Lack of access to appropriate and affordable health care can lead to a greater reliance on informal knowledge systems. This includes information about self-administration of hormones, which, in many cases, is undertaken without necessary medical monitoring or supervision (e.g., Do et al., 2018; Liu et al., 2020; Rashid et al., 2022; Reisner et al., 2021; Winter & Doussantousse, 2009).

In some parts of the world, large numbers of transgender women employ silicone as a means of modifying their bodies, drawing on the services of silicone "pumpers" and/or attending pumping "parties", often within their communities. The immediate results of silicone pumping contrast with significant downstream health risks (e.g., Aguayo-Romero et al., 2015; Bertin et al., 2019; Regmi et al., 2021), particularly where industrial silicone or other injectable substances have been used and where surgical removal may be difficult.

Finally, sexual health outcomes for TGD people are poor. HIV prevalence for transgender women reporting to clinical organizations in metropolitan areas is approximately 19% worldwide, which is 49 times higher than the background prevalence rate in the general population (Baral et al., 2013). Sexual health outcomes for transgender men are also problematic (e.g., Mujugira et al., 2021).

Statement 2.4

We recommend translations of the SOC focus on cross-cultural, conceptual and literal equivalence to ensure alignment with the core principles that underpin the SOC-8.

Much of the research literature on TGD people is produced in high-income and English-speaking countries. global northern perspectives about TGD people (including those related to health care needs and provision) dominate this literature. A May 2021 Scopus database search undertaken by the current authors shows 99% of the literature on transgender health care comes out of Europe, North America, Australia, or New Zealand. Overall, 96% of the literature is in the English language. TGD people of the Global

South have received relatively little attention in the English language literature, and the work of those HCPs who interact with them has often gone unrecognized and unpublished or has not been translated into English. Applying resources produced in the global north risks overlooking the relevance and nuance of local knowledge, cultural frameworks and practices, and missed opportunities to learn from the work of others.

When translating the principles set out in the SOC, we recommend following best practice guidelines for language translation to ensure high quality written resources are produced that are culturally and linguistically appropriate to the local situation. It is important translators have knowledge about TGD identities and cultures to check that literal translations are culturally competent and safe for local TGD people. It is also important translation should follow established processes for quality assurance (Centers for Medicare & Medicaid Services, 2010; Sprager & Martinez, 2015)

Statement 2.5

We recommend health care professionals and policymakers always apply the SOC-8 core principles to their work with transgender and gender diverse people to ensure respect for human rights and access to appropriate and competent health care, including:

General principles

- Be empowering and inclusive. Work to reduce stigma and facilitate access to appropriate health care, for all who seek it;
- Respect diversity. Respect all clients and all gender identities. Do not pathologize differences in gender identity or expression;
- Respect universal human rights, including the right to bodily and mental integrity, autonomy, and self-determination; freedom from discrimination and the right to the highest attainable standard of health.

Principles around developing and implementing appropriate services and accessible health care

- Involve TGD people in the development and implementation of services;
- Become aware of social, cultural, economic, and legal factors that might impact the health (and health care needs) of transgender and gender diverse people, as well as the willingness and capacity of the person to access services;
- Provide health care (or refer to knowledgeable colleagues) that affirms gender identities and expressions, including health care that reduces the distress associated with gender dysphoria (if this is present);
- Reject approaches that have the goal or effect of conversion, and avoid providing any direct or indirect support for such approaches or services

Principles around delivering competent services

- Become knowledgeable (get training, where possible) about the health care needs of transgender and gender diverse people, including the benefits and risks of gender-affirming care;
- Match the treatment approach to the specific needs of clients, particularly their goals for gender identity and expression;
- Focus on promoting health and well-being rather than solely the reduction of gender dysphoria, which may or may not be present;
- Commit to harm reduction approaches where appropriate;
- Enable the full and ongoing informed participation of transgender and gender diverse people in decisions about their health and well-being;
- Improve experiences of health services, including those associated with administrative systems and continuity of care.

Principles around working towards improved health through wider community approaches

- Put people in touch with communities and peer support networks;
- Support and advocate for clients within their families and communities (schools, workplaces, and other settings) where appropriate.

We have already cited research detailing the broad range of challenges TGD people may face; social economic and legal obstacles, as well those related to health care access. While overall health care services are diverse across the world (in terms of availability, accessibility, and quality), those services available to TGD people are often inadequate. Numerous reports from diverse regions worldwide show, while TGD people may report positive health care experiences, many others do not (e.g., Callander et al., 2019; Costa, da Rosa Filho et al., 2018; Do et al., 2018; Gourab et al., 2019; Health Policy Project et al., 2015; Liu et al., 2020; Motmans et al., 2017; Muller et al., 2019; PAHO, 2014; Reisner et al., 2021; Strauss et al., 2017; TGEU, 2017). Mainstream health care options often do not meet their needs for general, sexual, or gender-affirming health care. Standard patient management procedures at clinics and hospitals often fail to recognize the gender identities of their TGD patients (including where outside of the binary their patients identify). Patients may be housed in wards that are gender inappropriate for them, putting them at risk of sexual harassment. TGD patients often encounter unsupportive or hostile attitudes from HCPs and ancillary staff and may even be refused service. Of great concern, HCPs in some parts of the world are involved in gender identity change efforts of the sort described earlier in this chapter.

Throughout the world, there are many other barriers to the provision of gender-affirming health care. Health care professionals may often be unwilling to provide the services TGD people seek. In some countries, there may be laws or regulations inhibiting or preventing them from doing so. When general practitioners and other health care providers do not have access to clear guidelines in their own language, they may be deterred from providing services. Even in situations where health care is available, patients may find it is difficult to access because of distance, gatekeeping practices, supply and demand issues that result in long wait lists or cost increases. Indeed, gender-affirming procedures may not be incorporated into a universal health care provision or be covered by private insurance, even though similar procedures may be covered for cisgender patients.

For all these reasons, many TGD people avoid formal health care services whenever they can. Their own communities commonly fill the void, acting as important resources for their members. They provide social and emotional support, often in an otherwise hostile environment. In addition, they often act as reservoirs of shared information about available options for health care, including parallel and informal health care options outside of (and more accessible and affordable than) mainstream medicine. As we saw earlier in this chapter, this often includes sharing of information about silicone and other injectable substances for bodily transformation and about hormones that are self-administered without necessary medical monitoring or supervision. WHO notes TGD individuals who self-administer gender-affirming hormones would benefit from access to evidence-based information, quality products, and sterile injection equipment (WHO, 2021). Access to such information can form part of a broader harm reduction approach (e.g., Idrus & Hyman, 2014).

Putting the important core principles outlined above into practice can improve health care experiences and promote respect for TGD people in all local contexts. This can occur regardless of the realities of a health care system (including the cultural, social, legal, economic context in which health care is provided), the level of provision available, or the TGD people seeking such services.

CHAPTER 3 Population Estimates

In the previous edition of its Standards of Care, Version 7, World Professional Association for Transgender Health (WPATH) identified only a small number of articles attempting to estimate the size of the transgender and gender diverse (TGD) population and characterized the state-of-the-science as "a starting point" requiring further systematic study (Coleman et al., 2012). Since then, the literature on this topic has expanded considerably as evidenced by a number of recent reviews that have sought to synthesize the available evidence (Arcelus et al., 2015; Collin et al., 2016; Goodman et al., 2019; Meier & Labuski, 2013; Zhang et al., 2020).

In reviewing epidemiologic data pertaining to the TGD population, it may be best to avoid the terms "incidence" and "prevalence." Avoiding these and similar terms may preclude inappropriate pathologizing of TGD people (Adams et al., 2017; Bouman et al., 2017). Moreover, the term "incidence" may not be applicable in this situation because it assumes TGD status has an easily identifiable time of onset, a prerequisite for calculating incidence estimates (Celentano & Szklo, 2019). For all the above reasons, we recommend using the terms "number" and "proportion" to signify the absolute and the relative size of the TGD population.

Perhaps the most important consideration in reviewing this literature is the variable definition applied to the TGD population (Collin et al., 2016; Meier & Labuski, 2013). In clinic-based studies, the data on TGD people are typically limited to individuals who received transgender-related diagnoses or counseling or those who requested or underwent gender-affirming therapy, whereas survey-based research typically relies on a broader, more inclusive definition based on self-reported gender identities.

Another methodological consideration in assessing the size and distribution of the TGD population is the need to understand what constitutes the sampling frame. As noted in recent reviews (Goodman et al., 2019; Zhang et al., 2020), many of the published studies, especially those conducted more than a decade ago, first assessed the number of patients seen at a particular clinical center and then divided that number by an approximated population size. This was unlikely to produce an accurate estimate because the numerator in the calculations is not necessarily included in the denominator, and the true size of the denominator often remains unknown.

With these considerations in mind, it is advisable to focus specifically on recent (published within the last decade) peer-reviewed studies that utilized sound methodology in identifying TGD people within a well-defined sampling frame. For all of the above reasons, the present chapter is focused on studies that met the following inclusion criteria 1) appeared in press in 2009 or later; 2) used a clear definition of TGD status; 3) calculated proportions of TGD people based on a well-defined population denominator; and 4) were peer-reviewed. These types of studies can provide more accurate contemporary estimates.

The available studies can be assigned into three groups 1) those that reported proportions of TGD people among individuals enrolled in large health care systems; 2) those that presented results from population surveys of predominantly adult participants; and 3) those that were based on surveys of youth conducted in schools. Of these three categories, the most informative and methodologically sound studies are summarized below. Additional details about these and other similar studies can be found in recent literature reviews (Goodman et al., 2019; Zhang et al., 2020).

Among studies that estimated the size of the TGD population enrolled in large health care systems, all were conducted in the US, and all relied on information obtained from electronic health records. Four of those health system-based studies relied exclusively on diagnostic codes to ascertain the TGD population; two studies (Blosnich et al., 2013; Kauth et al., 2014) used data from the Veterans Health Affairs system, which provides care to over 9 million people, and two studies (Dragon et al., 2017; Ewald et al., 2019) used claims data from Medicare, the federal health insurance program that primarily covers people 65 years of age or older. The proportions of TGD people reported in these diagnostic code-based studies ranged from approximately 0.02% to 0.03%. Another more recent publication also used Medicare data along with commercial insurance claims to identify TGD people and applied expanded inclusion criteria to supplement

diagnostic codes with information on procedures and hormone therapy (Jasuja et al., 2020). Using this methodology, the proportion of TGD people among all persons enrolled in the participating health plans was 0.03%. The sixth health systems-based study (Quinn et al., 2017) was conducted at Kaiser Permanente plans in the states of Georgia and California; these plans provide care to approximately 8 million members enrolled through employers, government programs, or individually. The TGD population in the Kaiser Permanente study was ascertained across all age groups using both diagnostic codes and free-text clinical notes. The proportions of TGD people identified at Kaiser Permanente were higher than the corresponding proportions reported in the Veterans Health Affairs and Medicare studies with the most recent estimates ranging from 0.04 to 0.08%.

In contrast to results from the health system-based studies, findings from surveys that relied on self-reported TGD status produced much higher estimates. Two US studies took advantage of the Behavioral Risk Factor Surveillance Study (BRFSS), which is an annual telephone survey conducted in all 50 states and US territories (Conron et al., 2012; Crissman et al., 2017). The first study used data from the 2007–2009 BRFSS cycles in the state of Massachusetts, and the second study used the 2014 BRFSS data from 19 states and the territory of Guam. Both studies reported that approximately 0.5% of adult participants (at least 18 years of age) responded *"Yes"* to the question *"Do you consider yourself to be transgender?"*

An internet-based survey administered to a sample of the Dutch population 15–70 years of age (Kuyper & Wijsen, 2014) asked participants to score the following two questions using a 5-point Likert scale: *"Could you indicate to which degree you psychologically experience yourself as a man?"* and *"Could you indicate to which degree you psychologically experience yourself as a woman?"* The respondents were considered "gender ambivalent" if they gave the same score to both statements and "gender incongruent" when they reported a lower score for their sex assigned at birth than for their gender identity. The proportions of participants reporting incongruent and ambivalent gender identity were 1.1% and 4.6%, respectively, for persons who were assigned male at birth (AMAB), and 0.8% and 3.2%, respectively, for persons assigned female at birth (AFAB).

A similarly designed study estimated the proportion of TGD residents in the Flanders region of Belgium using a sample drawn from the country's National Register (Van Caenegem, Wierckx et al., 2015). Participants were asked to score the following statements: *"I feel like a woman"* and *"I feel like a man"* on a 5-point Likert scale. Using the same definitions applied in the Dutch study (Kuyper & Wijsen, 2014), the proportion of gender incongruent individuals was 0.7% for AMAB people and 0.6% for AFAB people. The corresponding estimates for gender ambivalence among AMAB and AFAB people were 2.2% and 1.9%, respectively.

A more recent population-based study evaluated the proportion of TGD people among approximately 50,000 adult residents of Stockholm County, Sweden (Åhs et al., 2018). The numerator was determined by asking participants the following question: *"I would like hormones or surgery to be more like someone of a different sex."* Two additional items were designed to identify individuals experiencing gender incongruence: *"I feel like someone of a different sex"* and *"I would like to live as or be treated as someone of a different sex."* The need for either hormone therapy or gender-affirming surgery was reported by 0.5% of participants. Individuals who expressed feeling like someone of a different sex and those who wanted to live as or be treated as a person of another sex constituted 2.3% and 2.8% of the total sample, respectively.

Population-based data outside of North America and Western Europe are less common. One recent study offers valuable data from a large representative survey of 6,000 adults in Brazil (Spizzirri et al., 2021). Gender identity of participants was assessed based on the following three questions 1) *"Which of the following options best describes how you currently feel?"* (Options: I feel I am a man, I feel I am a woman, and I feel I am neither a man nor a woman); 2) *"What is the sex on your birth certificate?"* (Options: male, female, and undetermined); and 3) *"Which of*

these situations do you most closely relate to?" (Options: I was born male, but I have felt female since childhood; I was born female, but I have felt male since childhood; I was born male, and I feel comfortable with my body; I was born female, and I feel comfortable with my body). Based on the responses to these three questions, the authors determined 1.9% of the survey respondents were TGD (0.7% defined as transgender, and 1.2% defined as nonbinary).

The literature on the population proportions of TGD youth (persons under 19 years of age) includes several survey studies conducted in schools. A 2012 national cross-sectional survey in New Zealand collected information on TGD identity among high school students (Clark et al., 2014). Among over 8,000 survey participants, 1.2% self-identified as TGD and 2.5% reported they were not sure. Another study of schoolchildren was based on a 2016 survey of 9th and 11th grade students (ages 14–18 years) in the US state of Minnesota (Eisenberg et al., 2017). Of the nearly 81,000 survey respondents, 2.7% reported being TGD. A more recent study (Johns et al., 2019) presented results of the Youth Risk Behavior Survey (YRBS), which is conducted biennially among local, state, and nationally representative samples of US high school students in grades 9–12 (approximate age range 13–19 years). The 2017 YRBS cycle was carried out in 10 states and 9 large urban areas and included the following sequence: "*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*?" Among nearly 120,000 participants across the 19 sites, 1.8% responded "*Yes, I am transgender,*" and 1.6% responded "*I am not sure if I am transgender.*"

Another recently published school-based study in the US presented results of a 2015 survey conducted in Florida and California with the aim of identifying gender diverse children and adolescents in a sample of just over 6,000 students in grades 9–12 (Lowry et al., 2018). "High gender-nonconforming" was used to define AMAB children who reported being very/mostly/somewhat feminine or AFAB children who reported being very/mostly/somewhat masculine. Based on these definitions, the proportions of TGD participants were reported to be 13% among AMAB students, 4% among AFAB students, and 8.4% overall.

Only one study examined the proportion of self-identified TGD children in a younger age group. Shields et al. analyzed the data from a 2011 survey of 2,700 students in grades 6–8 (age range 11–13 years) across 22 San Francisco public middle schools (Shields et al., 2013). Thirty-three children self-identified as TGD based on the question *"What is your gender?"* where the possible responses were *"female, male, or transgender."* The resulting proportion of transgender survey respondents was 1.3%. However, this definition would exclude TGD persons self-identifying as nonbinary and those who do not explicitly identify as transgender.

Taken together, these data indicate among health system-based studies that relied on diagnostic codes or other evidence documented in the medical records (Blosnich et al., 2013; Dragon et al., 2017; Ewald et al., 2019; Kauth et al., 2014; Quinn et al., 2017), the proportions of TGD people reported in recent years (2011–2016) ranged from 0.02% to 0.08%. By contrast, when the TGD status was ascertained based on self-report, the corresponding proportions were orders of magnitude higher and reasonably consistent, if the studies used similar definitions. When the surveys specifically inquired about "transgender" identity, the estimates ranged from 0.3% to 0.5% among adults and from 1.2% to 2.7% in children and adolescents. When the definition was expanded to include broader manifestations of gender diversity, such as gender incongruence or gender ambivalence, the corresponding proportions were higher: 0.5% to 4.5% among adults and 2.5% to 8.4% among children and adolescents.

As reviewed elsewhere (Goodman et al., 2019), another noteworthy observation is the continuous increase in both the size and the composition of the TGD population with upward trends in the proportion of TGD people observed in health care systems, through population-based surveys, as well as in the data on legal gender recognition. The higher estimates observed in more recent literature support some of the previous publications indicating the size of TGD population was

Summary of reported proportions of TGD people in the general population

Health systems-based studies: 0.02–0.1%
Survey-based studies of adults: 0.3–0.5% (transgender), 0.3–4.5% (all TGD)
Survey-based studies of children and adolescents: 1.2–2.7% (transgender), 2.5–8.4% (all TGD)

likely underestimated in earlier studies (Olyslager & Conway, 2008).

The temporal trends in AMAB to AFAB ratio have also been reported in studies analyzing referrals to clinics as well as data from integrated health systems; this ratio has changed from predominantly AMAB in previous decades to predominantly AFAB in recent years, especially among TGD youth (Aitken et al., 2015; de Graaf, Carmichael et al., 2018; de Graaf, Giovanardi et al. 2018; Steensma et al., 2018; Zhang et al., 2021). The trend towards a greater proportion of TGD people in younger age groups and the age-related differences in the AMAB to AFAB ratio likely represent the "cohort effect," which reflects sociopolitical advances, changes in referral patterns, increased access to health care and to medical information, less pronounced cultural stigma, and other changes that have a differential impact across generations (Ashley 2019d; Pang et al., 2020; Zhang et al., 2020).

Despite recent improvements in the quality of published studies, an important limitation of the existing literature is the relative paucity of peer-reviewed publications from regions outside of Western Europe or North America. Some of the relevant information on global estimates can be obtained from reports supported by the governments or non-governmental organizations (Fisher et al., 2019; Kasianczuk & Trofymenko, 2020), but these reports may be difficult to systematically identify and evaluate until they appear in peer-reviewed literature. Other barriers to evaluating the global distribution of the TGD populations include inadequate access to demographic data and over-representation of English-language journals in the world literature.

These limitations notwithstanding, the available highest-quality data clearly indicate TGD people represent a sizable and growing proportion of the general population. Based on the credible evidence available to date, this proportion may range from a fraction of a percent to several percentage points depending on the inclusion criteria, age group, and geographic location. Accurate estimates of the proportion, distribution, and composition of the TGD population as well as a projection of resources required to adequately support the health needs of TGD people should rely on systematically collected high-quality data, which are now increasingly available. Continuous and routine collection of these data is needed to decrease variability and minimize over- and under-estimation of the reported results. For example, far more accurate and precise estimates should become available when population censuses begin systematically collecting and reporting data on sex assigned at birth and gender identity, including asexual and nonbinary categories, using the now well-validated two-step method. The first such census-based estimate was released by the national statistical office of Canada. Based on the 2021 census data, 100,815 of 30.5 million Canadians self-identified as transgender or nonbinary; this accounted for 0.33% of the population 15 years of age or older (Statistics Canada, 2022). Consistent with the published literature, the proportions of transgender and nonbinary people were much higher for Generation Z (born between 1997 and 2006, 0.79%) and millennials (born between 1981 and 1996, 0.51%) than for Generation X (born between 1966 and 1980, 0.19%), baby boomers (born between 1946 and 1965, 0.15%), and the Interwar and Greatest Generations (born in 1945 or earlier, 0.12%). While these results represent the highest quality data available to date, it is not clear how the population proportions reported in Canada may compare with those in other countries. The variability in the definitions of what constitutes the TGD population and the differences in data collection methods can be reduced further by improving international collaborations.

CHAPTER 4 Education

This chapter will provide a general review of the literature related to education in transgender and gender diverse (TGD) health care. Recommendations are offered at governmental, nongovernmental, institutional, and provider levels with the goal of increasing access to competent, compassionate health care. In turn, this increased access should improve health outcomes in TGD populations. As this is a novel chapter in the World Professional Association for Transgender Health (WPATH) Standards of Care, the intent is to lay the groundwork for the education area and invite a broader and deeper discussion among educators and health professionals.

Health professionals involved in transgender care encompass a broad range of disciplines. Health professional education varies considerably by country or region in terms of structure, licensure, and policy. Published literature on education in TGD health care is predominantly from North America, Europe, Australia and New Zealand. This chapter does not provide a review of the education literature for each discipline, the needs specific to each discipline (which can be found in the relevant chapters), or the needs specific to each country/region's health education system. Greater understanding and research are needed on the intersection of health education systems, licensure, and transgender health across the world.

On a global level, TGD health education is imperative if national and international health disparities are to be addressed. Cultural competency related to TGD communities continues to be lacking. The World Bank Group (2018) reports widespread discrimination, harassment, violence, and abuse affecting TGD people. They also report TGD people face the highest rates of violence and discrimination (World Bank Group, 2018). Although many higher income countries have national antidiscrimination laws with gender identity as a protected characteristic, discrimination in the workplace, in education, and in health care remains problematic (World Bank Group, 2018).

Across disciplines, curricula at all levels—undergraduate, graduate, residency, or continuing education—historically have ignored TGD cultural or clinical education. The Joint Commission (US) has recommended health care organizations "provide educational programs and forums that support the unique needs of the LGBT community" and "offer educational opportunities that address LGBT health issues" (The Joint Commission, 2011). However, this is not enforced.

On an individual level, several questions need answers. What type of education interventions can most effectively address transphobia and lead to long-standing changes in attitudes? What interventions translate into increasing the number of care providers in this area as well as the number of TGD people receiving care? Does clinical exposure increase the confidence of providers over time? What educational interventions lead to improved health outcomes in the TGD population and, if so, when and how did these interventions accomplish this? Although health professions have begun to incorporate TGD health into education using a variety of modalities and at varying levels of training, efforts differ by health profession and are neither systemic nor systematic in nature (e.g., Brennan et al., 2012; Chinn, 2013; Eliason et al., 2010; Lim et al., 2015; Obedin-Maliver et al., 2011; Rondahl, 2009).

Attaining cultural humility with the full appreciation of the intersectionality of humanity is an ultimate educational goal. That said, this initial call for education is focused on building the foundation in cultural awareness and cultural competency that is currently weak or non-existent in much of the world.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statements of Recommendations

4.1- We recommend all personnel working in governmental, nongovernmental, and private agencies receive cultural-awareness training focused on treating transgender and gender diverse individuals with dignity and respect.
4.2- We recommend all members of the health care workforce receive cultural-awareness training focused on treating transgender and gender diverse individuals with dignity during orientation and as part of annual or continuing education.
4.3- We recommend institutions involved in the training of health professionals develop competencies and learning objectives for transgender and gender diverse health within each of the competency areas for their specialty.

Recommendation 4.1

We recommend all personnel working in governmental, nongovernmental, and private agencies receive cultural-knowledge training focused on treating transgender and gender diverse individuals with dignity and respect.

Article 1 of the United Nations Universal Declaration of Human Rights states, "All human beings are born free and equal in dignity and rights" (United Nations, 1948). Only recently has this fundamental statement included the recognition that TGD rights are human rights (UNOCHR, 2018). Globally, training at all levels about TGD communities continues to be lacking. As recently as 2002, only 3% of Fortune 500 companies had antidiscrimination protection for TGD employees, and none offered insurance coverage for gender-affirming health care (Human Rights Campaign Foundation, 2017). By 2022, 91% of Fortune 500 companies included gender identity in US non-discrimination policies, and 66% offered TGD-inclusive insurance coverage. However, only 72% provide any form of lesbian, gay, bisexual, transgender and queer/questioning (LGBTQ) cultural knowledge training for their workforce (Human Rights Campaign Foundation, 2022). This lack of understanding fosters discrimination across the board. Taken together, these inconsistencies negatively affect the health of individuals and communities and exacerbate the health disparities and inequities they face. In Britain, only 28% of TGD workers felt the senior leadership were committed to TGD equality; only 21% of TGD employees would consider reporting transphobic harassment in the workplace (Stonewall, 2018). For those who are openly TGD, 34% were excluded by their co-workers, 35% were abused by customers, 24% were denied promotion due to their gender identity, and 11% were fired (Stonewall, 2018). In southeastern Europe, the World Bank stated there is widespread discrimination, harassment, violence, and abuse, and TGD people in that region faced the highest rates of violence and discrimination (World Bank Group, 2018). Often the discrimination went unreported with 60% of individuals not filing a report because of a lack of faith the complaint would be addressed, a fear of further discrimination or ridicule, and a reluctance to be outed (World Bank Group, 2018). Although many countries in the region have national antidiscrimination laws with gender identity as a protected characteristic, discrimination in the workplace, in education, and in health care remains problematic (World Bank Group, 2018). It is the responsibility of the governmental, nongovernmental, and private agencies in these countries with anti-discrimination laws to ensure the rights of the TGD population. They are, therefore, obligated to find ways in which discrimination and stigma can be decreased. One of these is through education. Local cultures that foster anti-TGD attitudes are often a barrier to this needed education. Although cultural competency trainings have led to equivocal results, Shepherd (2019) recommends that providing cultural knowledge training that prioritizes local cultural issues and focuses on the values of openness, non-judgment, and responsiveness may lead to the desired results. Implementing cultural knowledge training requires a leadership willing to prioritize the training and to dedicate the time, money, and human capital to delivering initial and ongoing training.

Recommendation 4.2

We recommend all members of the health care workforce receive cultural-knowledge training focused on treating transgender and gender diverse individuals with dignity during orientation and as part of annual or continuing education.

Across disciplines, curricula at all levels—undergraduate, graduate, residency, or continuing

education—historically have ignored TGD cultural or clinical education. Factors contributing to this lack of inclusion include lack of faculty knowledge, experience, comfort with the subject matter, faculty bias, limited space within the existing curriculum, and lack of guidance on how to integrate the topics (McDowell & Bower, 2016). Research into the lack of and the need for such education does not specifically address TGD health concerns. Rather, the existing literature subsumes TGD health education within the broader discussion of the lack of LGBTQ-focused cultural and clinical-competency training. As an example, nursing baccalaureate programs included only an average of 2.12 hours of instruction on LGBTQ health (Lim et al., 2015). A fair assumption is that the amount of time devoted to TGD-specific health issues constituted only a fraction of this time.

Within the broader context of LGBTQ competency, the lack of TGD cultural- and clinical-competency training is a long-known shortfall of health care education (Aldridge et al., 2021). In the US, the Department of Health and Human Services' *Healthy People 2020,* (United States Department of Health and Human Services (2013, April 10)), the National Academy of Medicine (The Institute of Medicine, 2011), and the Joint Commission (The Joint Commission, 2011) all recognized lack of education negatively impacts the ability of LGBTQ people, including TGD individuals, to obtain appropriate, medically necessary care. The UK's House of Commons Women and Equalities Committee found lack of education contributed to TGD health disparities in the National Health Service (House of Commons Women and Equalities Committee, 2015, December 8). The lack of TGD health care education has been identified in the US (Obedin-Maliver et al., 2011), UK (Tollemache et al., 2021), South Africa (de Vries et al., 2020; Taylor et al., 2018; Wilson et al., 2014), Canada (Bauer et al., 2014), Australia (Riggs & Bartholomaeus, 2016), Sweden, Spain, Serbia, Poland (Burgwal et al., 2021), and Pakistan (Martins et al., 2020) among other countries.

In addition to developing curriculum, Shepherd (2022) states both clinical and organizational components are necessary to improve clinical encounters and consumer satisfaction. On an organizational level, it must be feasible as well as locally and practically oriented (Shepherd, 2022). On an individual level, in addition to knowledge training, health care professionals are better served employing generic traits that focus on the values of openness, non-judgment, and responsiveness (Shepherd, 2018).

Recommendation 4.3.

We recommend institutions involved in the training of health professionals develop competencies and learning objectives for transgender and gender diverse health within each of the competency areas for their specialty.

Each health profession has its own educational institutions, administrative, and licensing bodies, which vary by country and specialization within the profession. No major health professional organizations, educational institutions, or licensing bodies appear to require training in TGD health. While these organizations increasingly recommend including LGBTQ intersex health, rarely do they specify competencies, skills, or learning objectives for working with TGD people within their specialty. Published material on health professional education in TGD health is focused primarily on nursing, medicine, and mental health and is predominantly from North America, Europe, Australia, and New Zealand. An increased understanding of transgender health and medical/health professional education systems and requirements globally is essential.

Despite the increasing visibility of TGD people, access to knowledgeable and culturally- competent health professionals remain an overwhelming need around the world (James et al., 2016; Lerner et al., 2020; Müller, 2017). Lack of knowledgeable providers is a major barrier to gender-affirming care for transgender persons (Puckett et al., 2018; Safer et al., 2016) and contributes to large health disparities (Giffort & Underman, 2016; Reisman et al., 2019). The lack of adequate professional education in TGD health is a global problem (Do & Nguyen, 2020; Martins et al., 2020; Parameshwaran et al., 2017) that occurs at all levels of training (Dubin et al., 2018) and traverses health disciplines (Glick et al., 2020; Gunjawate et al., 2020; Johnson & Federman,

2014) and medical specialties (Fung et al., 2020; Korpaisarn and Safer, 2018).

Challenges remain as studies to date have small sample sizes, involve one-time training, include multiple disciplines at multiple career levels, focus on short-term outcomes, and often cover all LGBTQI topics rather than TGD-specific ones that are usually acquired post-licensure and are not the focus of most currently studied educational interventions (Dubin et al., 2018).

To successfully implement the recommendations, institutions may need to consider developing 1) systemic and systematic approaches to developing and implementing competencies for each health discipline across the professional lifespan; 2) standardized assessments for learners, with input from the TGD community; and 3) allotment of curricular resources, including trained faculty, as well as time in accordance with clear, consensual learning objectives (Dubin et al., 2018; Pratt-Chapman, 2020). In addition, evaluations of these interventions should not only focus on outcomes but also strive to understand how, when, and why these outcomes are occurring (Allen et al., 2021).

CHAPTER 5 Assessment of Adults

This chapter provides guidance for the assessment of transgender and gender diverse (TGD) adults who are requesting medically necessary gender-affirming medical and/or surgical treatments (GAMSTs) to better align their body with their gender identity (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1).

TGD adults are people at or above the age of majority in their country, who have some form of gender diversity. The developmental elements of the adolescent chapter, including the importance of parental/caregiver involvement, may be relevant for the care of young adults too, even if they are above the age of majority.

This chapter includes all forms of gender identities and transitions including, but not limited to, male, female, gender diverse, nonbinary, agender, and eunuch. The population of TGD adults is heterogeneous and will vary according to their clinical need, biological, psychological, and social situations, as well as their access to health care. As such, any assessment for GAMSTs will need to be adapted to the scientific, clinical, and community knowledge base of the presenting gender identity as well as local circumstances. This chapter recognizes individuals may experience different local levels of clinical or regulatory oversight when the state or others are providing health care.

An individual's gender identity is an internal identification and experience. The role of the assessor is to assess for the presence of gender incongruence and identify any co-existing mental health concerns, to offer information about GAMSTs, to support the TGD person in considering the effects/risks of GAMSTs, and to assess if the TGD person has the capacity to understand the treatment being offered and if the treatment is likely to be of benefit. The assessor can also assist a TGD person to consider choices that could improve their GAMST outcomes. The GAMST assessment approach described in this chapter recognizes the lived experience and self-knowledge of the TGD person and the clinical knowledge of the assessing health care professional (HCP). Consequently, with this approach, the decision to move forward with GAMSTs is shared between the TGD person and the assessing HCP, with both playing a key part in collaborative decision-making.

Some systems use a model of care for TGD adults seeking GAMSTs that prioritizes the TGD adult as the decision maker with the HCP acting as an advisor, barring serious contraindications. These models are used when considering hormone therapy rather than surgery and are often called "informed consent" models (Deutsch, 2011, 2016a). Many such models utilize an abbreviated assessment that focuses primarily on the ability of a TGD person to grant informed consent and to utilize information about GAMSTs to inform their medical decision-making. There is significant variability in such models across jurisdictions, systems, and HCPs (Deutsch, 2011; Morenz et al., 2020). Informed consent models have been used for some time for hormone prescription in many local settings.

This chapter is intended to offer flexible global guidance that must be adapted to local circumstances. HCPs will need to determine which assessment approaches best meet the needs in their local settings. The evaluation of these approaches is best undertaken in collaboration with TGD people.

Since TGD people represent a diverse array of gender identities and expressions and have differing needs for GAMSTs, no single assessment process will fit every person or every situation. Some TGD people may need a comparatively brief assessment process for GAMSTs. For TGD adults with a complex presentation or for those who are requesting less common treatments or treatments with limited research evidence, more comprehensive assessments with different members of a multidisciplinary team will be required. Assessments may be in person or through telehealth. While psychometric assessment tools have been used in some instances, they are not a required part of the assessment for GAMSTs. Counseling or psychotherapy can be helpful when requested by a TGD person. However, counseling or psychotherapy specifically focused on their TGD identity is not a requirement for the assessment or initiation of GAMSTs. Genital exams are not a prerequisite for initiation of GAMTs and should be performed only when clinically indicated.

GAMSTs can be delivered in diverse settings. Settings will depend on available health care systems within each country and may include nationalized/public health care, private sector settings, community health care settings, and charitable institutions. Local and regional circumstances may therefore influence the availability of health care. Regardless of the setting, health care offered to TGD people should be of the highest possible quality. World Professional Organization for Transgender Health (WPATH) advocates for assessment and treatment to be readily available. Access to assessment and treatment for TGD people seeking GAMSTs is critical given the clear medical necessity of these interventions and the profound benefits they offer to TGD people (Aldridge et al., 2020; Byne et al., 2012). The guidance in this chapter will need to be adapted according to local, as well as individual, clinical, and social circumstances.

The statements below are based on significant background literature, including literature demonstrating the strong positive impact of access to GAMSTs; available empirical evidence; a favorable risk-benefit ratio; and consensus of professional best practice. The empirical evidence base for the

Statements of Recommendations

5.1- We recommend health care professionals assessing transgender and gender diverse adults for physical treatments:
5.1.a- Are licensed by their statutory body and hold, at a minimum, a master's degree or equivalent training in a clinical field relevant to this role and granted by a nationally accredited statutory institution.
5.1.b- For countries requiring a diagnosis for access to care, the health care professional should be competent using the latest edition of the World Health Organization's International Classification of Diseases (ICD) for diagnosis. In countries that have not implemented the latest ICD, other taxonomies may be used; efforts should be undertaken to utilize the latest ICD as soon as practicable.
5.1.c- Are able to identify co-existing mental health or other psychosocial concerns and distinguish these from gender dysphoria, incongruence, and diversity.
5.1.d- Are able to assess capacity to consent for treatment.
5.1.e- Have experience or be qualified to assess clinical aspects of gender dysphoria, incongruence, and diversity.
5.1.f- Undergo continuing education in health care relating to gender dysphoria, incongruence, and diversity.
5.2- We suggest health care professionals assessing transgender and gender diverse adults seeking gender-affirming treatment liaise with professionals from different disciplines within the field of transgender health for consultation and referral, if required.

The following recommendations are made regarding the requirements for gender-affirming medical and surgical treatment (all should be met):
5.3- We recommend health care professionals assessing transgender and gender diverse adults for gender-affirming medical and surgical treatment:
5.3.a- Only recommend gender-affirming medical treatment requested by a TGD person when the experience of gender incongruence is marked and sustained.
5.3.b- Ensure fulfillment of diagnostic criteria prior to initiating gender-affirming treatments in regions where a diagnosis is necessary to access health care.
5.3.c- Identify and exclude other possible causes of apparent gender incongruence prior to the initiation of gender-affirming treatments.
5.3.d- Ensure that any mental health conditions that could negatively impact the outcome of gender-affirming medical treatments are assessed, with risks and benefits discussed, before a decision is made regarding treatment.
5.3.e- Ensure any physical health conditions that could negatively impact the outcome of gender-affirming medical treatments are assessed, with risks and benefits discussed, before a decision is made regarding treatment.
5.3.f- Assess the capacity to consent for the specific physical treatment prior to the initiation of this treatment.
5.3.g- Assess the capacity of the gender diverse and transgender adult to understand the effect of gender-affirming treatment on reproduction and explore reproductive options with the individual prior to the initiation of gender-affirming treatment.
5.4- We suggest, as part of the assessment for gender-affirming hormonal or surgical treatment, professionals who have competencies in the assessment of transgender and gender diverse people wishing gender-related medical treatment consider the role of social transition together with the individual.
5.5- We recommend transgender and gender diverse adults who fulfill the criteria for gender-affirming medical and surgical treatment require a single opinion for the initiation of this treatment from a professional who has competencies in the assessment of transgender and gender diverse people wishing gender-related medical and surgical treatment.
5.6- We suggest health care professionals assessing transgender and gender diverse people seeking gonadectomy consider a minimum of 6 months of hormone therapy as appropriate to the TGD person's gender goals before the TGD person undergoes irreversible surgical intervention (unless hormones are not clinically indicated for the individual).
5.7- We recommend health care professionals assessing adults who wish to detransition and seek gender-related hormone intervention, surgical intervention, or both, utilize a comprehensive multidisciplinary assessment that will include additional viewpoints from experienced health care professional in transgender health and that considers, together with the individual, the role of social transition as part of the assessment process.

assessment of TGD adults is limited. It primarily includes an assessment approach that uses specific criteria that are examined by an HCP in close cooperation with a TGD adult and does not include randomized controlled trials or long-term longitudinal research (Olsen-Kennedy et al., 2016). This is understandable given the complexity and ethical considerations of allocating patients in need of care to different assessment groups and the lack of funding for research and other resources to assess long-term outcomes of assessment approaches.

The creation of this guidance has been a complex undertaking. The criteria in this chapter have been significantly revised from SOC-7 to reduce requirements and unnecessary barriers to care. It is hoped that future research will explore the effectiveness of this model as well as evolving assessment models for hormone therapy and for surgery that will allow continued improvements to be made.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 5.1.

We recommend health care professional assessing transgender and gender diverse adults for gender-affirming treatments:

Statement 5.1.a

Are licensed by their statutory body and hold, at a minimum, a master's degree or equivalent training in a clinical field relevant to this role and granted by a nationally accredited statutory institution.

TGD people, as with all other people seeking health care, should have the highest quality of care accessible that is commensurate with the quality of care provided to all people utilizing health services (The Yogyakarta Principles, 2017). As this will vary around the globe, the nature of the professional completing an assessment for GAMSTs will vary according to the nature of health care in the local setting as well as the regulatory requirements set by licensing and registration boards. It is important the health care provided includes an assessment conducted by a competent, statutorily regulated HCP who has the competence to identify gender incongruence and conditions that can be mistaken for gender incongruence and who can support the TGD person throughout the assessment process (RCGP, 2019). Assessors must be able to refer to HCPs licensed to provide GAMSTs.

HCPs should have at a minimum a masters-level qualification in a clinical field related to transgender health or equivalent further clinical training and be statutorily regulated; examples include a mental health professional (MHP), general medical practitioner, nurse, or other qualified HCP. In some settings, statutorily regulated HCPs with lower levels of qualification may practice under the clinical supervision of a qualified HCP who takes ultimate clinical responsibility for the quality and accuracy of the completed GAMST assessment. For additional information see Chapter 4—Education.

Accessing a competent, statutorily regulated, HCP with expertise in GAMST assessment can sometimes be difficult. Consequently, ensuring continuity of care and minimizing gaps in accessible care or significantly delayed care (e.g., a long waiting list) may require that a statutorily regulated HCP without expertise provide care and support the assessment of a TGD person for GAMSTs. Avoiding unnecessary delays in care is critically important. However, TGD people should be supported to access care with an experienced HCP as soon as possible (RCGP, 2019).

Established practice requires the competence to identify and diagnose gender incongruence (Hembree et al., 2017; Reed et al., 2016; T'Sjoen et al., 2020) and the ability to identify differentials or conditions that may be mistaken as gender incongruence (Byne et al., 2018; Dhejne et al., 2016; Hembree et al., 2017). Established practice also strongly emphasizes the need for ongoing continuing education in the assessment and provision of care of TGD people (American Psychological Association, 2015; T'Sjoen et al., 2020). For more information see Chapter 4—Education.

Statement 5.1.b

For countries requiring a diagnosis for access to care, the health care professional should be competent using the latest edition of the World Health

Organization's International Classification of Diseases (ICD) for diagnosis. In countries that have not implemented the latest ICD, other taxonomies may be used; efforts should be undertaken to utilize the latest ICD as soon as practicable.

In some countries, a diagnosis of gender incongruence may be necessary to access GAMSTs (as described below). HCPs assessing TGD people in those countries should be competent to diagnose gender incongruence using the most current classification system necessary for TGD people to access GAMSTs. The ICD-11 (WHO, 2019a) is a classification system that focuses on the TGD person's experienced identity and any need for GAMSTs and does not consider a TGD identity to be a mental illness.

Statement 5.1.c

Are able to identify co-existing mental health or other psychosocial concerns and distinguish these from gender dysphoria, incongruence, and diversity.

Gender diversity is a natural variation in people and is not inherently pathological (American Psychological Association, 2015). However, assessment is best provided by an HCP who possesses some expertise in mental health in order to identify conditions that can be mistaken for gender incongruence. Such conditions are rare and, when present, are often psychological in nature (Byne et al., 2012; Byne et al., 2018; Hembree et al., 2017).

The need to include an HCP with some expertise in mental health does not require the inclusion of a psychologist, psychiatrist, or social worker in each assessment. Instead, a general medical practitioner, nurse, or other qualified HCP could also fulfill this requirement if they have sufficient expertise to identify gender incongruence, recognize mental health concerns, distinguish between these concerns and gender dysphoria, incongruence, and diversity, assist a TGD person in care planning and preparation for GAMSTs, and refer to a mental health professional (MHP), if needed. As discussed in greater depth in the mental health chapter, MHPs have an important role to play in the care of TGD people. For example, the prejudice and discrimination experienced by some TGD people (Robles et al., 2016) can lead to depression, anxiety, or worsening of other mental health conditions. In such cases, an MHP can diagnose, clarify, and treat mental health conditions. MHPs and HCPs with expertise in mental health are well-placed to assess for GAMSTs, as well as to support TGD people who require or request mental health input or support during their transition. For additional information see Chapter 18—Mental Health.

Statement 5.1.d

Are able to assess capacity to consent for treatment.

An assessment for GAMSTs must include an examination of the TGD person's ability to consent to the proposed treatment. Consent requires the cognitive capacity to understand the risks and benefits of a treatment and the potential negative and positive outcomes. It also requires the ability to retain that information for the purposes of making the decision (using aids as necessary) as well as the cognitive ability to use that understanding to make an informed decision (American Medical Association, 2021; Applebaum, 2007).

Some TGD individuals will have the capacity to grant consent immediately during the assessment. Some TGD individuals may need a longer process to be able to consent through ongoing discussion and the practice of medical decision-making skills. The presence of psychiatric illness or mental health symptoms do not pose a barrier to GAMSTs unless the psychiatric illness or mental health symptoms affect the TGD person's capacity to consent to the specific treatment being requested or affect their ability to receive treatment. This is especially important because GAMSTs have been found to reduce mental health symptomatology for TGD people (Aldridge et al., 2020).

Health care systems can consider GAMSTs for individuals who may not be able to directly consent if an appropriate legal guardian or regulator-approved independent decision maker with the power to determine health care treatment grants consent and confirms the proposed treatment is in alignment with the TGD individual's needs and wishes.

Statement 5.1.e

Have experience or be qualified to assess clinical aspects of gender dysphoria, incongruence, and diversity. For supporting text, see Statement 5.1.f.

Statement 5.1.f

Undergo continuing education in health care relating to gender dysphoria, incongruence, and diversity.

As in any other area of clinical practice, it is vital HCPs who are providing assessment for the initiation of GAMSTs are knowledgeable and experienced in the health care of TGD people. If this is not possible in the local context, the HCP providing the assessment should work closely with an HCP who is knowledgeable and experienced. As part of their clinical practice, HCPs should commit to ongoing training in TGD health care, become a member of relevant professional bodies, attend relevant professional meetings, workshops or seminars, consult with an HCP with relevant experience, and/or engage with the TGD community. This is particularly important in TGD health care as it is a relatively new field, and the knowledge and terminology are constantly changing (American Psychological Association, 2015; Thorne, Yip et al., 2019). Consequently, keeping up to date in the areas of TGD health is vital for anyone involved in an assessment for GAMSTs.

Statement 5.2

We suggest health care professionals assessing transgender and gender diverse adults seeking gender-affirming treatment liaise with professionals from different disciplines within the field of transgender health for consultation and referral, if required.

If required and if possible, assessment for GAMST should be conducted by a multidisciplinary team (Costa, Rosa-e-Silva et al., 2018; Hembree et al., 2017; Karasic & Fraser, 2018; T'Sjoen et al., 2020) with team members who have timely and adequate contact with one another. This could include an MHP, an endocrinologist, a primary care provider, a surgeon, a voice and communication specialist, TGD peer navigator, and others. In some cases, a multidisciplinary team may not be required; however, should a multidisciplinary team be needed, it is critical HCPs be able to access colleagues from different disciplines in a timely manner to complete the GAMST assessment and best support the needs of the TGD person. It is also critical TGD people be supported with follow-up appointments with any HCP who was involved during the assessment for GAMSTs, prior to, during, and after the initiation of gender-affirming treatments.

The following recommendations are made regarding the requirements for gender-affirming medical and surgical treatment (all should be met):

Statement 5.3

We recommend health care professionals assessing transgender and gender diverse adults for gender-affirming medical and surgical treatment:

Statement 5.3.a

Only recommend gender-affirming medical treatment requested by a TGD person when the experience of gender incongruence is marked and sustained.

To access GAMSTs, a TGD person's gender incongruence must be marked and sustained. This can include a need for GAMSTs and a desire to be accepted as a person of the experienced gender. Consequently, a consideration of the nature, length and consistency of gender incongruence is important. This can include such factors as a change of name and identity documents, telling others about one's gender, health care documentation, or changes in gender expression. However, marked and sustained gender incongruence can exist in the absence of disclosure to others by the TGD person (Brumbaugh-Johnson & Hull, 2019; Saeed et al., 2018; Sequeira et al., 2020). An abrupt or superficial change in gender identity or lack of persistence is insufficient to initiate gender- affirming treatments, and further assessment is recommended. In such circumstances, ongoing assessment is helpful to ensure the consistency and persistence of gender incongruence before GAMSTs are initiated.

While marked and sustained gender incongruence should be present, it is not necessary for TGD people to experience severe levels of distress regarding their gender identity to access gender- affirming treatments. In fact, access to gender-affirming treatment can act as a prophylactic measure to prevent distress (Becker et al., 2018; Giovanardi et al., 2021; Nieder et al., 2021; Nobili et al., 2018; Robles et al., 2016). A TGD adult can have sustained gender incongruence without significant distress and still benefit from GAMSTs.

Established clinical practice examines the persistence of gender incongruence when considering the initiation of GAMSTs (Chen & Loshak, 2020). In a review of 200 clinical notes, Jones, Brewin et al. (2017) identified the importance of the "stability of gender identity" when planning care. Providing GAMSTs to TGD people with persistent gender incongruence has been associated with low rates of patient regret and high rates of patient satisfaction (Becker et al., 2018; El-Hadi et al., 2018; Staples et al., 2020; Wiepjes et al., 2018). However, while the ICD 11 (WHO, 2019a) requires the presence of marked and persistent gender incongruence for a diagnosis of gender incongruence to be made, there is little specific evidence concerning the length of persistence required for treatment in adults. HCPs involved in an assessment of a TGD person for GAMSTs are encouraged to give due consideration to the life stage, history, and current circumstances of the adult being assessed.

Statement 5.3.b

Ensure fulfillment of diagnostic criteria prior to initiating gender-affirming treatments in regions where a diagnosis is necessary to access health care.

A diagnosis of gender incongruence may be necessary in some regions to access transition-related care. When a diagnosis is necessary to access GAMSTs, the assessment for GAMSTs will involve determining and assigning a diagnosis. In these instances, HCPs should have competence using the latest International Classification of Diseases and Related Health Problems (ICD) (WHO, 2019a). In regions where a diagnosis is necessary to access health care, a diagnosis of HA60 *Gender Incongruence of Adolescence or Adulthood* should be determined prior to gender-affirming interventions. Gender-affirming interventions secondary to a diagnosis of *HA6Z Gender Incongruence, Unspecified* may be considered in the context of a more comprehensive assessment by the multidisciplinary team.

There is evidence the use of rigid assessment tools for "transition readiness" may reduce access to care and are not always in the best interest of the TGD person (MacKinnon et al., 2020). Therefore, in situations where the assignment of a diagnosis is mandatory to access care, the process should be approached with trust and transparency between the HCP and the TGD individual requesting GAMST, with the needs of the TGD individual in mind. Indeed, high quality relationships between TGD people and their HCPs are associated with lower emotional distress and better outcomes (Kattari et al., 2016). Because many TGD people fear HCPs will erroneously conflate transgender identity with mental illness (Ellis et al., 2015), a diagnostic assessment should be undertaken with sensitivity to facilitate the best relationship between the provider and the TGD individual.

Statement 5.3.c

Identify and exclude other possible causes of apparent gender incongruence prior to the initiation of gender-affirming treatments.

In rare cases, TGD individuals might have a condition that may be mistaken for gender incongruence or may have another reason for seeking treatment aside from the alleviation of gender incongruence. In these cases, and when there is ambiguity regarding the diagnosis of gender incongruence, a more detailed and comprehensive assessment is important. For example, further assessment might be required to determine if gender incongruence persists outside of an acute psychotic episode. If gender incongruence persists after an acute psychotic episode resolves, GAMSTs may be considered as long as the TGD person has the capacity to consent to and undergo the specific treatment. If gender incongruence does not persist and only occurs during such an episode, treatment should not be considered. It is important such circumstances be identified and excluded prior to the initiation of GAMSTs (Byne et al., 2012, 2018; Hembree et al., 2017). It is important to understand, however, TGD people may present with gender incongruence and with a mental health condition, autistic spectrum disorder, or other neurodiversity (Glidden et al., 2016). Indeed, some mental health conditions, such as anxiety (Bouman et al., 2017), depression (Heylens, Elaut et al., 2014; Witcomb et al., 2018), and self-harm (Arcelus et al., 2016; Claes et al., 2015) are more prevalent in TGD people who have not accessed GAMSTs. Recent longitudinal studies suggest mental health symptoms experienced by TGD people tend to improve following GAMSTs (Aldridge et al., 2020; Heylens, Verroken et al., 2014;

White Hughto & Reisner, 2016). There is no evidence to suggest a benefit of withholding GAMSTs from TGD people who have gender incongruence simply on the basis that they have a mental health or neurodevelopmental condition. For more information see Chapter 18—Mental Health.

Statement 5.3.d

Ensure any mental health conditions that could negatively impact the outcome of gender-affirming medical treatments are assessed, with risks and benefits discussed, before a decision is made regarding treatment.

Like their cisgender counterparts, TGD people may have mental health problems. Treatment for mental health problems can and should occur in conjunction with GAMSTs when medical transition is needed. It is vital gender-affirming care is not impeded unless, in some extremely rare cases, there is robust evidence that doing so is necessary to prevent significant decompensation with a risk of harm to self or others. In those cases, it is also important to consider the risks delaying GAMSTs poses to a TGD person's mental and physical health (Byne et al., 2018).

In general, social and medical transition of TDG people are both associated with a reduction in mental health problems (Aldridge et al., 2020; Bouman et al., 2017; Durwood et al., 2017; Glynn et al., 2016; Hughto & Reisner, 2016; Wilson et al., 2015; Witcomb et al., 2018). Unfortunately, the loss of social support and the physical and financial stress that can be associated with the initiation of GAMSTs may exacerbate pre-existing mental health problems and warrant additional support from the treating HCP (Budge et al., 2013; Yang, Wang et al., 2016). An assessment of mental health symptoms can improve transition outcomes, particularly when the assessment is used to facilitate access to psychological and social support during transition (Byne et al., 2012). A delay of transition in rare circumstances may be considered if, for example, the TGD person is unable to engage with the process of transition or would be unable to manage aftercare following surgery, even with support. Where a delay in GAMST as a last resort has been found to be necessary, the HCP should offer resources and support to improve mental health and facilitate re-engagement with the GAMST process as soon as practicable. It should be noted access to medical transition for TGD people facilitates social transition and improves safety in public (Rood et al., 2017). In turn, the degree to which TGD people's appearance conforms to their gender identity is the best predictor of quality of life and mental health outcomes following medical transition (Austin & Goodman, 2017). Delaying access to GAMSTs due to the presence of mental health problems may exacerbate symptoms (Owen-Smith et al., 2018) and damage rapport; consequently, this should be done only when all other avenues have been exhausted.

Statement 5.3.e

Ensure any physical health conditions that could negatively impact the outcome of gender-affirming medical treatments are assessed, with risks and benefits discussed, before a decision is made regarding treatment.

In rare cases, GAMSTs, such as hormonal and surgical interventions, may have iatrogenic consequences or may exacerbate pre-existing physical health conditions (Hembree et al., 2017). In these instances, care should be taken, whenever possible, to manage pre-existing physical health conditions while initiating (if appropriate) or continuing gender-affirming treatments. Any interruptions in treatment should be as brief as possible and with treatment re-initiated as soon as practicable. Limited data and inconsistent findings suggest an association between cardiovascular and metabolic risks and hormone therapy in TGD adults (Getahun, 2018; Iwamoto, Defreyne et al., 2019; Iwamoto et al., 2021; Spanos et al., 2020). Because of the possible harm related to long-term treatment and the probable benefits expected from the preventive measures applied before and during hormone treatment, a careful assessment of physical health conditions prior to initiation of treatment is important. Some specific conditions, such as a history of hormone-sensitive cancer, may require further assessment and management that may preclude hormone treatment (Center of Excellence for Transgender Health, 2016; Hembree et al., 2017).

Similar concerns may be present for TGD adults who wish to access surgical interventions. Each gender-affirming surgical intervention has specific risks and potentially unfavorable consequences (Bryson & Honig, 2019; Nassiri et al., 2020; Remington et al., 2018). However, intervention-specific risks associated with the presence of specific physical conditions have not been well researched. Thus, the kinds of medical concerns raised by TGD people during the assessment are typically no different from those of any other surgical candidate.

Taking into consideration the mental and physical health disparities (Brown & Jones, 2016) and barriers to health care (Safer et al., 2016) experienced by TGD people, the assessment of physical conditions by HCPs should not be limited to a history of medical interventions. If the TGD person has physical health conditions, it is important these conditions are managed while initiating or continuing GAMSTs whenever possible. Any interruption in treatment should be made with a view toward re-initiating treatment as soon as practicable. It is also important HCPs develop a treatment strategy for managing physical conditions that facilitates health and promotes consistent adherence to a treatment plan.

Statement 5.3.f

Assess the capacity to consent for the specific gender-affirming treatments prior to the initiation of this treatment.

The practice of informed consent to treatment is central to the provision of health care. Informed consent is couched in the ethical principle that recipients of health care should understand the health care they receive and any potential consequences that could result. The importance of informed consent is embedded in many legislative and regulatory practices that guide HCPs around the world (Jefford & Moore, 2008). It is not possible to know all the potential consequences of a health care treatment; instead, considering what would be "reasonable" to expect is often used as a minimum criterion for consent (Jefford & Moore, 2008; Spatz et al., 2016) and remains the case with GAMSTs. Being able to consent to a health care procedure or clinical intervention requires several complex cognitive processes. Consent requires the cognitive capacity to understand the risks and benefits of a treatment and the potential negative and positive outcomes in addition to the ability to retain that information for the purposes of making the decision (using aids as necessary) and the cognitive ability to use that understanding to make an informed decision (American Medical Association, 2021; Applebaum, 2007). It is vital the TGD person and the assessing HCP consider a priori the nature of the treatment sought and the potential positive and negative effects it may have on the biological, psychological, and social domains of the TGD person's life.

It is important to recognize mental illness, in particular symptoms of cognitive impairment or psychosis, can impact a person's ability to grant consent for GAMSTs (Hostiuc et al., 2018). However, the presence of such symptoms does not necessarily equate to an inability to give consent because many people with significant mental health symptoms are able to understand the risks and benefits of treatment enough to make an informed decision (Carpenter et al., 2000). Instead, it is important a careful assessment is carried out that examines each TGD person's ability to comprehend the nature of the specific GAMST being considered, consider treatment options, including risks and benefits, appreciate the potential short- and long-term consequences of the decision, and communicate their choice in order to receive the treatment (Grootens-Wiegers et al., 2017).

There may be instances in which an individual lacks the capacity to consent to health care, such as during an acute episode of psychosis or in situations where an individual has long-term cognitive impairment. However, limits to capacity to consent to treatment should not prevent individuals from receiving appropriate GAMSTs. For some, understanding the risks and benefits may require the use of repeated explanations in jargon-free language over time or the use of diagrams to facilitate explanation and aid comprehension. A comprehensive and thorough assessment undertaken by the multidisciplinary health care team can further inform this process. For others, an alternative decision maker, such as a legal guardian or regulator-approved,

independent decision maker may need to be appointed. These situations need to be considered on a case-by-case basis with the aim of ensuring the most affirmative and least restrictive health care is provided to the individual. Also see Chapter 11—Institutional Environments.

Statement 5.3.g

Assess the capacity of the gender diverse and transgender adult to understand the effect of gender-affirming treatment on reproduction and explore reproductive options with the individual prior to the initiation of gender-affirming treatment.

As gender-affirming medical interventions often affect reproductive capacity, HCPs should ensure a TGD person is aware of the implications for reproduction of the treatments and is familiar with gamete storage and assistive reproductive options. Gender-affirming hormone treatments have been shown to impact reproductive functions and fertility, although the consequences are heterogenous for people of all birth-assigned sexes (Adeleye et al., 2019; Jindarak et al., 2018; Taub et al., 2020). There may be individual differences and fluctuations in these effects on TGD adults. It is therefore essential that HCPs inform a TGD person about the possible impact of the treatment on their reproductive potential during the assessment and as part of the evaluation of the person's capacity to consent for GAMSTs. Reproductive options should be considered and discussed prior to the initiation of gender-affirming treatments. Because the literature is unclear about the possibility of conception while on hormone therapy, information about the necessity of using contraception to avoid unwanted pregnancy and the different methods of contraception available may need to be provided (Light et al., 2014; Schubert & Carey,2020).

Cross-sectional studies in clinical and nonclinical samples from different populations consistently report TGD adults express parental desire and wish to pursue fertility preservation with varying rates that are related to age, gender, and the duration of gender-affirming hormone treatment (Auer et al., 2018; De Sutter et al., 2002; Defreyne, Van Schuvlenbergh et al., 2020; Wierckx, Stuyver et al., 2012). In a small sample, provision of fertility information was found to have an influence on decision-making related to the use of fertility preservation (Chen et al., 2019). Although there was no comparison made between groups who did and did not receive fertility counseling, high fertility preservation rates occurred following comprehensive fertility counseling among transgender individuals (Amir et al., 2020). Further, one study suggested consultation with a specialist reduced regret related to the decision about whether to pursue fertility preservation procedures (Vyas et al., 2021). For more information see Chapter 16—Reproductive Health.

Statement 5.4

We suggest, as part of the assessment for gender-affirming hormonal or surgical treatment, professionals who have competencies in the assessment of transgender and gender diverse people wishing gender-related medical treatment consider the role of social transition together with the individual.

Social transition can be extremely beneficial to many TGD people although not all TGD people are able to socially transition or wish to socially transition (Bränström & Pachankis, 2021; Koehler et al., 2018; Nieder, Eyssel et al., 2020). Consequently, some TGD people seek gender-affirming interventions after social transition, some before, some during, and some in the absence of social transition.

Social transition and gender identity disclosure can improve the mental health of a TGD person seeking gender-affirming interventions (Hughto et al., 2020; McDowell et al., 2019). In addition, chest and facial surgeries prior to hormone therapy can facilitate social transition (Altman, 2012; Davis & Colton Meier, 2014; Olson-Kennedy, Warus et al. 2018; Van Boerum et al., 2019). As part of the assessment process, HCPs should discuss which social role is most comfortable for the TGD person, if a social transition is planned, and the timing for any planned social transition (Barker & Wylie, 2008). It is imperative during the assessment process, HCPs are respectful of the wide diversity of gendered social roles, including nonbinary as well as binary identities and presentations, which vary

according to cultural, local community, and individual understandings.

Not everyone who requests GAMSTs will wish to or be able to socially transition. Little is known about TGD people who do not socially transition before, during, or after medical treatment, as this has not been systematically studied. The most frequent reasons that have been identified for avoiding social transition are fear of being abandoned by family or friends, fearing economic loss (Bradford et al., 2013), and being discriminated against and stigmatized (Langenderfer-Magruder et al., 2016; McDowell et al., 2019; White Hughto et al., 2015). However, some people do not pursue social transition because they feel hormonal or surgical treatments offer enough subjective improvement to reduce gender dysphoria.

If there is no clear plan for social transition or if social transition is unwanted, additional assessment is important to determine the specific nature and advisability of the treatment request, especially if surgical treatment is requested. Additional assessment can offer the TGD person an opportunity to consider the possible effects of not socially transitioning while still obtaining GAMSTs. Given the lack of data on health outcomes for TGD people who do not socially transition (Evans et al., 2021; Levine, 2009; Turban, Loo et al., 2021), GAMSTs should be approached cautiously in such circumstances.

Statement 5.5

We recommend transgender and gender diverse adults who fulfill the criteria for gender-affirming medical and surgical treatment require a single opinion for the initiation of this treatment from a professional who has competencies in the assessment of transgender and gender diverse people wishing gender-related medical and surgical treatment.

Previous versions of the SOC guidelines have required TGD individuals to be assessed for GAMSTs by two qualified HCPs. It was believed having two independent opinions was best practice as it ensured safety for both TGD people and HCPs. For example, it was assumed that seeing two HCPs offered assuredness for both TGD people and their assessing HCPs when pursuing irreversible medical interventions.

However, the limited research in the area indicates two opinions are largely unnecessary. For example, Jones, Brewin et al. (2017) reviewed the case notes of experienced HCPs working within a state-funded gender service and found there was an overwhelming correlation between both opinions—arguably making one of them redundant. Further, Bouman et al. (2014) determined the requirement for two independent assessors reflected paternalism in health care services and raised a potential breach of the autonomy of TGD individuals. The authors posited when clients are adequately prepared and assessed under the care of a multidisciplinary team, a second independent assessment is unnecessary.

Consequently, if written documentation or a letter is required to recommend gender-affirming medical and surgical treatment (GAMST), TGD people seeking treatments including hormones, and genital, chest, facial and other gender-affirming surgeries require a single written opinion/signature from an HCP competent to independently assess and diagnose (Bouman et al., 2014; Yuan et al, 2021). Further written opinions/signatures may be requested where there is a specific clinical need.

Statement 5.6

We suggest health care professionals assessing transgender and gender diverse people seeking gonadectomy consider a minimum of 6 months of hormone therapy as appropriate to the TGD person's gender goals before the TGD person undergoes irreversible surgical intervention (unless hormones are not clinically indicated for the individual).

The Endocrine Society Clinical Practice Guidelines advise a period of consistent hormone treatment prior to genital surgery (Hembree et al., 2017). While there was limited supportive research, this recommendation was considered to be good clinical practice as it allows a more reversible experience prior to the irreversible experience of surgery. For example, there can be changes in sexual desire after genital surgery that removes the testicles (Lawrence, 2005; Wierckx, Van de Peer et al., 2014). In this context, reversible testosterone suppression can offer a TGD person a period of time to experience the absence of testosterone and decide if this feels right for

them. It should be noted the effects of reduced estrogen on a TGD person's sexual desire and functioning following an oophorectomy is less well documented.

Surgery that removes gonads is an irreversible procedure that leads to loss of fertility and loss of the effects of endogenous sex steroids. Both effects must be discussed as a component of the assessment process. For additional information see Chapter 16—Reproductive Health. Of course, hormones are not clinically indicated for TGD adults who do not want them or in cases where they are contraindicated due to health reasons. For more information see Chapter 13—Surgery and Postoperative Care.

Statement 5.7

We recommend health care professionals assessing adults who wish to detransition and seek gender-related hormone intervention, surgical intervention, or both, utilize a comprehensive multidisciplinary assessment that will include additional viewpoints from experienced health care professionals in transgender health and that considers, together with the individual, the role of social transition as part of the assessment process.

Many TGD adults may consider a range of identities and elements of gender presentation while they are exploring their gender identity and are considering transition options. Accordingly, people may spend some time in a gender identity or presentation before they discover it does not feel comfortable and later adapt it or shift to an earlier identity or presentation (Turban, King et al., 2021). Some TGD adults may also experience a change in gender identity over time so that their needs for medical treatment evolve. This is a healthy and reasonable process for determining the most comfortable and congruent way of living, which is informed by the person's gender identity and the context of their life. This process of identity exploration should not necessarily be equated with regret, confusion, or poor decision-making because a TGD adult's gender identity may change without devaluing previous transition decisions (MacKinnon et al., 2021; Turban, Loo et al., 2021). TGD adults should be assisted in this exploration and any other changes in their identity (Expósito-Campos, 2021). While exploration continues, gender-affirming treatments that are irreversible should be avoided until clarity about long-term goals and outcomes is achieved.

The decision to detransition appears to be rare (Defreyne, Motmans et al., 2017; Hadje-Moussa et al., 2019; Wiepjes et al., 2018). Estimates of the number of people who detransition due to a change in identity are likely to be overinflated due to research blending different cohorts (Expósito-Campos, 2021). For example, detransition research cohorts often include TGD adults who chose to detransition because of a change in their identity as well as TGD adults who chose to detransition without a change in identity. While little research has been conducted to systematically examine variables that correlate with a TGD adult's decision to halt a transition process or to detransition, a recent study found the vast majority of TGD people who opted to detransition did so due to external factors, such as stigma and lack of social support and not because of changes in gender identity (Turban, King et al., 2021). TGD adults who have not experienced a change in identity may choose to halt transition or to detransition because of oppression, violence, and social/relational conflict, surgical complications, health concerns, physical contraindications, a lack of resources, or dissatisfaction with the results (Expósito-Campos, 2021). In such cases, MHPs are well placed to assist the TGD person with these challenges.

While the choice to detransition is proportionally rare, it is expected an overall increase in the number of adults who identify as TGD would result in an increase in the absolute number of people seeking to halt or reverse a transition. However, while the absolute numbers may increase, the percentage of people seeking to halt or reverse permanent physical changes should remain static and low. The existence of these rare requests must not be used as a justification to interrupt critical, medically necessary care, including hormone and surgical treatments, for the vast majority of TGD adults.

Due to the limited research in this area, clinical guidance is based primarily on individual case studies and the expert opinion of HCPs

working with TGD adults (Expósito-Campos, 2021; Richards & Barrett, 2020). Accordingly, if a TGD adult has undergone permanent physical changes and seeks to undo them, the assessing HCP should be a member of a comprehensive multidisciplinary assessment team. A multidisciplinary team allows for the contribution of additional viewpoints from HCPs experienced in transgender health. In collaboration with the TGD adult, the multidisciplinary team is encouraged to thoroughly understand the motivations for the original treatment and for the decision to detransition. Any concerns with the previous physical changes should be carefully explored and a significant effort made to ensure similar concerns are not replicated by the reversal.

To ensure the greatest likelihood of satisfaction and comfort with a reversal of permanent physical changes, the TGD adult and the multidisciplinary team should explore the role of social transition in the assessment and in preparation for the reversal. In such instances, it is highly likely a prolonged period of living in role will be necessary before further physical changes are recommended. HCPs should support the TGD adult through any social changes, as well as any feelings of failure, shame, depression, or guilt in deciding to make such a change. In addition, people should be supported in coping with any prejudice or social difficulties they may have experienced that could have led to a decision to detransition or that may have resulted from such a decision. It is also important to help the person remain engaged with health care throughout the process (Narayan et al., 2021).

While available research shows consistent positive outcomes for the majority of TGD adults who choose to transition (Aldridge et al., 2020; Byne et al., 2012; Gorin-Lazard et al., 2012; Owen-Smith et al., 2018; White Hughto & Reisner, 2016), some TGD adults may decompensate or experience a worsened condition following transition. Little research has been conducted to systematically examine variables that correlate with poor or worsened biological, psychological, or social conditions following transition (Hall et al., 2021; Littman, 2021); however, this occurrence appears to be rare (Hall et al., 2021; Wiepjes et al., 2018). In cases where people decompensate after physical or social transition and then remain in a poorer biological, psychological, or social state than they were in prior to transition, serious consideration should be given as to whether transition is helpful at this time, for this person, or both. In cases where treatment is no longer supported, assistance should be arranged to support the person to manage the process of stopping treatment and to manage any concomitant difficulties (Narayan et al., 2021).

It is vital that people who detransition, for any reason, be supported. It should be remembered, however, this is a rare occurrence and the literature shows consistently positive outcomes for the vast majority of TGD adults who transition to a gender that is comfortable for them, including those who receive GAMSTs (Byne et al., 2012; Green & Fleming, 1990; Lawrence, 2003; Motmans et al., 2012; Van de Grift, Elaut et al., 2018).

CHAPTER 6 Adolescents

Historical context and changes since previous Standards of Care

Specialized health care for transgender adolescents began in the 1980s when a few specialized gender clinics for youth were developed around the world that served relatively small numbers of children and adolescents. In more recent years, there has been a sharp increase in the number of adolescents requesting gender care (Arnoldussen et al., 2019; Kaltiala, Bergman et al., 2020). Since then, new clinics have been founded, but clinical services in many places have not kept pace with the increasing number of youth seeking care. Hence, there are often long waitlists for services, and barriers to care exist for many transgender youth around the world (Tollit et al., 2018).

Until recently, there was limited information regarding the prevalence of gender diversity among adolescents. Studies from high school samples indicate much higher rates than earlier thought, with reports of up to 1.2% of participants identifying as transgender (Clark et al., 2014) and up to 2.7% or more (e.g., 7–9%) experiencing some level of self-reported gender diversity (Eisenberg et al., 2017; Kidd et al., 2021; Wang et al., 2020). These studies suggest gender diversity in youth should no longer be viewed as rare. Additionally, a pattern of uneven ratios by assigned sex has been reported in gender clinics, with adolescents assigned female at birth (AFAB) initiating care 2.5–7.1 times more frequently as compared to adolescents who are assigned male at birth (AMAB) (Aitken et al., 2015; Arnoldussen et al., 2019; Bauer et al., 2021; de Graaf, Carmichael et al., 2018; Kaltiala et al., 2015; Kaltiala, Bergman et al., 2020).

A specific World Professional Association for Transgender Health's (WPATH) Standards of Care section dedicated to the needs of children and adolescents was first included in the 1998 WPATH Standards of Care, 5th version (Levine et al., 1998). Youth aged 16 or older were deemed potentially eligible for gender-affirming medical care, but only in select cases. The subsequent 6th (Meyer et al., 2005) and 7th (Coleman et al., 2012) versions divided medical-affirming treatment for adolescents into three categories and presented eligibility criteria regarding age/puberty stage—namely fully reversible puberty delaying blockers as soon as puberty had started; partially reversible hormone therapy (testosterone, estrogen) for adolescents at the age of majority, which was age 16 in certain European countries; and irreversible surgeries at age 18 or older, except for chest "masculinizing" mastectomy, which had an age minimum of 16 years. Additional eligibility criteria for gender-related medical care included a persistent, long (childhood) history of gender "non-conformity"/dysphoria, emerging or intensifying at the onset of puberty; absence or management of psychological, medical, or social problems that interfere with treatment; provision of support for commencing the intervention by the parents/caregivers; and provision of informed consent. A chapter dedicated to transgender and gender diverse (TGD) adolescents, distinct from the child chapter, has been created for this 8th edition of the Standards of Care given 1) the exponential growth in adolescent referral rates; 2) the increased number of studies specific to adolescent gender diversity-related care; and 3) the unique developmental and gender-affirming care issues of this age group.

Non-specific terms for gender-related care are avoided (e.g., gender-affirming model, gender exploratory model) as these terms do not represent unified practices, but instead heterogenous care practices that are defined differently in various settings.

Adolescence overview

Adolescence is a developmental period characterized by relatively rapid physical and psychological maturation, bridging childhood and adulthood (Sanders, 2013). Multiple developmental processes occur simultaneously, including pubertal-signaled changes. Cognitive, emotional, and social systems mature, and physical changes associated with puberty progress. These processes do not all begin and end at the same time for a given individual, nor do they occur at the same age for all persons. Therefore, the lower and upper borders of adolescence are imprecise and cannot be defined exclusively by age. For example, physical pubertal changes may

begin in late childhood and executive control neural systems continue to develop well into the mid-20s (Ferguson et al., 2021). There is a lack of uniformity in how countries and governments define the age of majority (i.e., legal decision-making status; Dick et al., 2014). While many specify the age of majority as 18 years of age, in some countries it is as young as 15 years (e.g., Indonesia and Myanmar), and in others as high as 21 years (e.g., the U.S. state of Mississippi and Singapore).

For clarity, this chapter applies to adolescents from the start of puberty until the legal age of majority (in most cases 18 years), however there are developmental elements of this chapter, including the importance of parental/caregiver involvement, that are often relevant for the care of transitional-aged young adults and should be considered appropriately.

Cognitive development in adolescence is often characterized by gains in abstract thinking, complex reasoning, and metacognition (i.e., a young person's ability to think about their own feelings in relation to how others perceive them; Sanders, 2013). The ability to reason hypothetical situations enables a young person to conceptualize implications regarding a particular decision. However, adolescence is also often associated with increased risk-taking behaviors. Along with these notable changes, adolescence is often characterized by individuation from parents and the development of increased personal autonomy. There is often a heightened focus on peer relationships, which can be both positive and detrimental (Gardner & Steinberg, 2005). Adolescents often experience a sense of urgency that stems from hypersensitivity to reward, and their sense of timing has been shown to be different from that of older individuals (Van Leijenhorst et al., 2010). Social-emotional development typically advances during adolescence, although there is a great variability among young people in terms of the level of maturity applied to inter- and intra-personal communication and insight (Grootens-Wiegers et al., 2017). For TGD adolescents making decisions about gender-affirming treatments—decisions that may have lifelong consequences—it is critical to understand how all these aspects of development may impact decision-making for a given young person within their specific cultural context.

Gender identity development in adolescence

Our understanding of gender identity development in adolescence is continuing to evolve. When providing clinical care to gender diverse young people and their families, it is important to know what is and is not known about gender identity during development (Berenbaum, 2018). When considering treatments, families may have questions regarding the development of their adolescent's gender identity, and whether or not their adolescent's declared gender will remain the same over time. For some adolescents, a declared gender identity that differs from the assigned sex at birth comes as no surprise to their parents/caregivers as their history of gender diverse expression dates back to childhood (Leibowitz & de Vries, 2016). For others, the declaration does not happen until the emergence of pubertal changes or even well into adolescence (McCallion et al., 2021; Sorbara et al., 2020).

Historically, social learning and cognitive developmental research on gender development was conducted primarily with youth who were not gender diverse in identity or expression and was carried out under the assumption that sex correlated with a specific gender; therefore, little attention was given to gender identity development. In addition to biological factors influencing gender development, this research demonstrated psychological and social factors also play a role (Perry & Pauletti, 2011). While there has been less focus on gender identity development in TGD youth, there is ample reason to suppose, apart from biological factors, psychosocial factors are also involved (Steensma, Kreukels et al., 2013). For some youth, gender identity development appears fixed and is often expressed from a young age, while for others there may be a developmental process that contributes to gender identity development over time.

Neuroimaging studies, genetic studies, and other hormone studies in intersex individuals demonstrate a biological contribution to the development of gender identity for some

individuals whose gender identity does not match their assigned sex at birth (Steensma, Kreukels et al., 2013). As families often have questions about this very issue, it is important to note it is not possible to distinguish between those for whom gender identity may seem fixed from birth and those for whom gender identity development appears to be a developmental process. Since it is impossible to definitively delineate the contribution of various factors contributing to gender identity development for any given young person, a comprehensive clinical approach is important and necessary (see Statement 3). Future research would shed more light on gender identity development if conducted over long periods of time with diverse cohort groups. Conceptualization of gender identity by shifting from dichotomous (e.g., binary) categorization of male and female to a dimensional gender spectrum along a continuum (APA, 2013) would also be necessary.

Adolescence may be a critical period for the development of gender identity for gender diverse young people (Steensma, Kreukels et al., 2013). Dutch longitudinal clinical follow-up studies of adolescents with childhood gender dysphoria who received puberty suppression, gender-affirming hormones, or both, found that none of the youth in adulthood regretted the decisions they had taken in adolescence (Cohen-Kettenis & van Goozen, 1997; de Vries et al., 2014). These findings suggest adolescents who were comprehensively assessed and determined emotionally mature enough to make treatment decisions regarding gender- affirming medical care presented with stability of gender identity over the time period when the studies were conducted.

When extrapolating findings from the longer-term longitudinal Dutch cohort studies to present-day gender diverse adolescents seeking care, it is critical to consider the societal changes that have occurred over time in relation to TGD people. Given the increase in visibility of TGD identities, it is important to understand how increased awareness may impact gender development in different ways (Kornienko et al., 2016). One trend identified is that more young people are presenting to gender clinics with nonbinary identities (Twist & de Graaf, 2019). Another phenomenon occurring in clinical practice is the increased number of adolescents seeking care who have not seemingly experienced, expressed (or experienced and expressed) gender diversity during their childhood years. One researcher attempted to study and describe a specific form of later-presenting gender diversity experience (Littman, 2018). However, the findings of the study must be considered within the context of significant methodological challenges, including 1) the study surveyed parents and not youth perspectives; and 2) recruitment included parents from community settings in which treatments for gender dysphoria are viewed with scepticism and are criticized. However, these findings have not been replicated. For a select subgroup of young people, susceptibility to social influence impacting gender may be an important differential to consider (Kornienko et al., 2016). However, caution must be taken to avoid assuming these phenomena occur prematurely in an individual adolescent while relying on information from datasets that may have been ascertained with potential sampling bias (Bauer et al., 2022; WPATH, 2018). It is important to consider the benefits that social connectedness may have for youth who are linked with supportive people (Tuzun et al., 2022)(see Statement 4).

Given the emerging nature of knowledge regarding adolescent gender identity development, an individualized approach to clinical care is considered both ethical and necessary. As is the case in all areas of medicine, each study has methodological limitations, and conclusions drawn from research cannot and should not be universally applied to all adolescents. This is also true when grappling with common parental questions regarding the stability versus instability of a particular young person's gender identity development. While future research will help advance scientific understanding of gender identity development, there may always be some gaps. Furthermore, given the ethics of self-determination in care, these gaps should not leave the TGD adolescent without important and necessary care.

Research evidence of gender-affirming medical treatment for transgender adolescents

A key challenge in adolescent transgender care is the quality of evidence evaluating the effectiveness of medically necessary gender-affirming medical

and surgical treatments (GAMSTs) (see medically necessary statement in the Global chapter, Statement 2.1), over time. Given the lifelong implications of medical treatment and the young age at which treatments may be started, adolescents, their parents, and care providers should be informed about the nature of the evidence base. It seems reasonable that decisions to move forward with medical and surgical treatments should be made carefully. Despite the slowly growing body of evidence supporting the effectiveness of early medical intervention, the number of studies is still low, and there are few outcome studies that follow youth into adulthood. Therefore, a systematic review regarding outcomes of treatment in adolescents is not possible. A short narrative review is provided instead.

At the time of this chapter's writing, there were several longer-term longitudinal cohort follow-up studies reporting positive results of early (i.e., adolescent) medical treatment; for a significant period of time, many of these studies were conducted through one Dutch clinic (e.g., Cohen-Kettenis & van Goozen, 1997; de Vries, Steensma et al., 2011; de Vries et al., 2014; Smith et al., 2001, 2005). The findings demonstrated the resolution of gender dysphoria is associated with improved psychological functioning and body image satisfaction. Most of these studies followed a pre-post methodological design and compared baseline psychological functioning with outcomes after the provision of medical gender-affirming treatments. Different studies evaluated individual aspects or combinations of treatment interventions and included 1) gender-affirming hormones and surgeries (Cohen-Kettenis & van Goozen, 1997; Smith et al., 2001, 2005); 2) puberty suppression (de Vries, Steensma et al., 2011); and 3) puberty suppression, affirming hormones, and surgeries (de Vries et al., 2014). The 2014 long-term follow-up study is the only study that followed youth from early adolescence (pretreatment, mean age of 13.6) through young adulthood (posttreatment, mean age of 20.7). This was the first study to show gender-affirming treatment enabled transgender adolescents to make age-appropriate developmental transitions while living as their affirmed gender with satisfactory objective and subjective outcomes in adulthood (de Vries et al., 2014). While the study employed a small (n = 55), select, and socially supported sample, the results were convincing. Of note, the participants were part of the Dutch clinic known for employing a multidisciplinary approach, including provision of comprehensive, ongoing assessment and management of gender dysphoria, and support aimed at emotional well-being.

Several more recently published longitudinal studies followed and evaluated participants at different stages of their gender-affirming treatments. In these studies, some participants may not have started gender-affirming medical treatments, some had been treated with puberty suppression, while still others had started gender-affirming hormones or had even undergone gender-affirming surgery (GAS) (Achille et al., 2020; Allen et al., 2019; Becker-Hebly et al., 2021; Carmichael et al., 2021; Costa et al., 2015; Kuper et al., 2020, Tordoff et al., 2022). Given the heterogeneity of treatments and methods, this type of design makes interpreting outcomes more challenging. Nonetheless, when compared with baseline assessments, the data consistently demonstrate improved or stable psychological functioning, body image, and treatment satisfaction varying from three months to up to two years from the initiation of treatment.

Cross-sectional studies provide another design for evaluating the effects of gender-affirming treatments. One such study compared psychological functioning in transgender adolescents at baseline and while undergoing puberty suppression with that of cisgender high school peers at two different time points. At baseline, the transgender youth demonstrated lower psychological functioning compared with cisgender peers, whereas when undergoing puberty suppression, they demonstrated better functioning than their peers (van der Miesen et al., 2020). Grannis et al. (2021) demonstrated transgender males who started testosterone had lower internalizing mental health symptoms (depression and anxiety) compared with those who had not started testosterone treatment.

Four additional studies followed different outcome designs. In a retrospective chart study, Kaltiala, Heino et al. (2020) reported transgender

adolescents with few or no mental health challenges prior to commencing gender-affirming hormones generally did well during the treatment. However, adolescents with more mental health challenges at baseline continued to experience the manifestations of those mental health challenges over the course of gender-affirming medical treatment. Nieder et al. (2021) studied satisfaction with care as an outcome measure and demonstrated transgender adolescents were more satisfied the further they progressed with the treatments they initially started. Hisle-Gorman et al. (2021) compared health care utilization pre- and post-initiation of gender-affirming pharmaceuticals as indicators of the severity of mental health conditions among 3,754 TGD adolescents in a large health care data set. Somewhat contrary to the authors' hypothesis of improved mental health, mental health care use did not significantly change, and psychotropic medication prescriptions increased. In a large non-probability sample of transgender-identified adults, Turban et al. (2022) found those who reported access to gender-affirming hormones in adolescence had lower odds of past-year suicidality compared with transgender people accessing gender- affirming hormones in adulthood.

Providers may consider the possibility an adolescent may regret gender-affirming decisions made during adolescence, and a young person will want to stop treatment and return to living in the birth-assigned gender role in the future. Two Dutch studies report low rates of adolescents (1.9% and 3.5%) choosing to stop puberty suppression (Brik et al., 2019; Wiepjes et al., 2018). Again, these studies were conducted in clinics that follow a protocol that includes a comprehensive assessment before the gender-affirming medical treatment is started. At present, no clinical cohort studies have reported on profiles of adolescents who regret their initial decision or detransition after irreversible affirming treatment. Recent research indicate there are adolescents who detransition, but do not regret initiating treatment as they experienced the start of treatment as a part of understanding their gender-related care needs (Turban, 2018). However, this may not be the predominant perspective of people who detransition (Littman, 2021; Vandenbussche, 2021). Some adolescents may regret the steps they have taken (Dyer, 2020). Therefore, it is important to present the full range of possible outcomes when assisting transgender adolescents. Providers may discuss this topic in a collaborative and trusting manner (i.e., as a "potential future experience and consideration") with the adolescent and their parents/caregivers before gender-affirming medical treatments are started. Also, providers should be prepared to support adolescents who detransition. In an internet convenience sample survey of 237 self-identified detransitioners with a mean age of 25.02 years, which consisted of over 90% of birth assigned females, 25% had medically transitioned before age 18 and 14% detransitioned before age 18 (Vandenbussche, 2021). Although an internet convenience sample is subject to selection of respondents, this study suggests detransitioning may occur in young transgender adolescents and health care professionals should be aware of this. Many of them expressed difficulties finding help during their detransition process and reported their detransition was an isolating experience during which they did not receive either sufficient or appropriate support (Vandenbussche, 2021).

To conclude, although the existing samples reported on relatively small groups of youth (e.g., n = 22-101 per study) and the time to follow-up varied across studies (6 months–7 years), this emerging evidence base indicates a general improvement in the lives of transgender adolescents who, following careful assessment, receive medically necessary gender-affirming medical treatment. Further, rates of reported regret during the study monitoring periods are low. Taken as a whole, the data show early medical intervention—as part of broader combined assessment and treatment approaches focused on gender dysphoria and general well-being—can be effective and helpful for many transgender adolescents seeking these treatments.

Ethical and human rights perspectives

Medical ethics and human rights perspectives were also considered while formulating the

Statements of Recommendations

6.1- We recommend health care professionals working with gender diverse adolescents:
6.1.a- Are licensed by their statutory body and hold a postgraduate degree or its equivalent in a clinical field relevant to this role granted by a nationally accredited statutory institution.
6.1.b- Receive theoretical and evidenced-based training and develop expertise in general child, adolescent, and family mental health across the developmental spectrum.
6.1.c- Receive training and have expertise in gender identity development, gender diversity in children and adolescents, have the ability to assess capacity to assent/consent, and possess general knowledge of gender diversity across the life span.
6.1.d- Receive training and develop expertise in autism spectrum disorders and other neurodevelopmental presentations or collaborate with a developmental disability expert when working with autistic/neurodivergent gender diverse adolescents.
6.1.e- Continue engaging in professional development in all areas relevant to gender diverse children, adolescents, and families.
6.2- We recommend health care professionals working with gender diverse adolescents facilitate the exploration and expression of gender openly and respectfully so that no one particular identity is favored.
6.3- We recommend health care professionals working with gender diverse adolescents undertake a comprehensive biopsychosocial assessment of adolescents who present with gender identity-related concerns and seek medical/surgical transition-related care, and that this be accomplished in a collaborative and supportive manner.
6.4- We recommend health care professionals work with families, schools, and other relevant settings to promote acceptance of gender diverse expressions of behavior and identities of the adolescent.
6.5- We recommend against offering reparative and conversion therapy aimed at trying to change a person's gender and lived gender expression to become more congruent with the sex assigned at birth.
6.6- We suggest health care professionals provide transgender and gender diverse adolescents with health education on chest binding and genital tucking, including a review of the benefits and risks.
6.7- We recommend providers consider prescribing menstrual suppression agents for adolescents experiencing gender incongruence who may not desire testosterone therapy, who desire but have not yet begun testosterone therapy, or in conjunction with testosterone therapy for breakthrough bleeding.
6.8- We recommend health care professionals maintain an ongoing relationship with the gender diverse and transgender adolescent and any relevant caregivers to support the adolescent in their decision-making throughout the duration of puberty suppression treatment, hormonal treatment, and gender- related surgery until the transition is made to adult care.
6.9- We recommend health care professionals involve relevant disciplines, including mental health and medical professionals, to reach a decision about whether puberty suppression, hormone initiation, or gender-related surgery for gender diverse and transgender adolescents are appropriate and remain indicated throughout the course of treatment until the transition is made to adult care.
6.10- We recommend health care professionals working with transgender and gender diverse adolescents requesting gender-affirming medical or surgical treatments inform them, prior to initiating treatment, of the reproductive effects including the potential loss of fertility and available options to preserve fertility within the context of the youth's stage of pubertal development.
6.11- We recommend when gender-affirming medical or surgical treatments are indicated for adolescents, health care professionals working with transgender and gender diverse adolescents involve parent(s)/guardian(s) in the assessment and treatment process, unless their involvement is determined to be harmful to the adolescent or not feasible.

The following recommendations are made regarding the requirements for gender-affirming medical and surgical treatment (All of them must be met):
6.12- We recommend health care professionals assessing transgender and gender diverse adolescents only recommend gender-affirming medical or surgical treatments requested by the patient when:
6.12.a- The adolescent meets the diagnostic criteria of gender incongruence as per the ICD-11 in situations where a diagnosis is necessary to access health care. In countries that have not implemented the latest ICD, other taxonomies may be used although efforts should be undertaken to utilize the latest ICD as soon as practicable.
6.12.b- The experience of gender diversity/incongruence is marked and sustained over time.
6.12.c- The adolescent demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment.
6.12.d- The adolescent's mental health concerns (if any) that may interfere with diagnostic clarity, capacity to consent, and gender-affirming medical treatments have been addressed.
6.12.e- The adolescent has been informed of the reproductive effects, including the potential loss of fertility and the available options to preserve fertility, and these have been discussed in the context of the adolescent's stage of pubertal development.
6.12.f- The adolescent has reached Tanner stage 2 of puberty for pubertal suppression to be initiated.
6.12.g- The adolescent had at least 12 months of gender-affirming hormone therapy or longer, if required, to achieve the desired surgical result for gender-affirming procedures, including breast augmentation, orchiectomy, vaginoplasty, hysterectomy, phalloplasty, metoidioplasty, and facial surgery as part of gender-affirming treatment unless hormone therapy is either not desired or is medically contraindicated.

adolescent SOC statements. For example, allowing irreversible puberty to progress in adolescents who experience gender incongruence is not a neutral act given that it may have immediate and lifelong harmful effects for the transgender young person (Giordano, 2009; Giordano & Holm, 2020; Kreukels & Cohen-Kettenis, 2011). From a human rights perspective, considering gender diversity as a normal and expected variation within the broader diversity of the human experience, it is an adolescent's right to participate in their own decision-making

process about their health and lives, including access to gender health services (Amnesty International, 2020).

Short summary of statements and unique issues in adolescence

These guidelines are designed to account for what is known and what is not known about gender identity development in adolescence, the evidence for gender-affirming care in adolescence, and the unique aspects that distinguish adolescence from other developmental stages.

Identity exploration: A defining feature of adolescence is the solidifying of aspects of identity, including gender identity. Statement 6.2 addresses identity exploration in the context of gender identity development. Statement 6.12.b accounts for the length of time needed for a young person to experience a gender diverse identity, express a gender diverse identity, or both, so as to make a meaningful decision regarding gender-affirming care.

Consent and decision-making: In adolescence, consent and decision-making require assessment of the individual's emotional, cognitive, and psychosocial development. Statement 6.12.c directly addresses emotional and cognitive maturity and describes the necessary components of the evaluation process used to assess decision-making capacity.

Caregivers/parent involvement: Adolescents are typically dependent on their caregivers/parents for guidance in numerous ways. This is also true as the young person navigates through the process of deciding about treatment options. Statement 6.11 addresses the importance of involving caregivers/parents and discusses the role they play in the assessment and treatment. No set of guidelines can account for every set of individual circumstances on a global scale.

Statement 6.1

We recommend health care professionals working with gender diverse adolescents:

a. **Are licensed by their statutory body and hold a postgraduate degree or its equivalent in a clinical field relevant to this role granted by a nationally accredited statutory institution.**
b. **Receive theoretical and evidenced-based training and develop expertise in general child, adolescent, and family mental health across the developmental spectrum.**
c. **Receive training and have expertise in gender identity development, gender diversity in children and adolescents, have the ability to assess capacity to assent/consent, and possess general knowledge of gender diversity across the life span.**
d. **Receive training and develop expertise in autism spectrum disorders and other neurodevelopmental presentations or collaborate with a developmental disability expert when working with autistic/neurodivergent gender diverse adolescents.**
e. **Continue engaging in professional development in all areas relevant to gender diverse children, adolescents, and families.**

When assessing and supporting TGD adolescents and their families, care providers/health care professionals (HCPs) need both general as well as gender-specific knowledge and training. Providers who are trained to work with adolescents and families play an important role in navigating aspects of adolescent development and family dynamics when caring for youth and families (Adelson et al., 2012; American Psychological Association, 2015; Hembree et al., 2017). Other chapters in these standards of care describe these criteria for professionals who provide gender care in more detail (see Chapter 5—Assessment for Adults; Chapter 7—Children; or Chapter 13—Surgery and Postoperative Care). Professionals working with adolescents should understand what is and is not known regarding adolescent gender identity development, and how this knowledge base differs from what applies to adults and prepubertal children. Among HCPs, the mental health professional (MHP) has the most appropriate training and dedicated clinical time to conduct an assessment and elucidate treatment priorities and goals when working with transgender youth, including those seeking gender-affirming medical/surgical care. Understanding and managing the dynamics of family members who may share differing perspectives regarding the history and needs of the

young person is an important competency that MHPs are often most prepared to address.

When access to professionals trained in child and adolescent development is not possible, HCPs should make a commitment to obtain training in the areas of family dynamics and adolescent development, including gender identity development. Similarly, considering autistic/neurodivergent transgender youth represent a substantial minority subpopulation of youth served in gender clinics globally, it is important HCPs seek additional training in the field of autism and understand the unique elements of care autistic gender diverse youth may require (Strang, Meagher et al., 2018). If these qualifications are not possible, then consultation and collaboration with a provider who specializes in autism and neurodiversity is advised.

Statement 6.2

We recommend health care professionals working with gender diverse adolescents facilitate the exploration and expression of gender openly and respectfully so that no one particular identity is favored.

Adolescence is a developmental period that involves physical and psychological changes characterized by individuation and the transition to independence from caregivers (Berenbaum et al., 2015; Steinberg, 2009). It is a period during which young people may explore different aspects of identity, including gender identity.

Adolescents differ regarding the degree to which they explore and commit to aspects of their identity (Meeus et al., 2012). For some adolescents, the pace to achieving consolidation of identity is fast, while for others it is slower. For some adolescents, physical, emotional, and psychological development occur over the same general timeline, while for others, there are certain gaps between these aspects of development. Similarly, there is variation in the timeline for gender identity development (Arnoldussen et al., 2020; Katz-Wise et al., 2017). For some young people, gender identity development is a clear process that starts in early childhood, while for others pubertal changes contribute to a person's experience of themselves as a particular gender (Steensma, Kreukels et al., 2013), and for many others a process may begin well after pubertal changes are completed. Given these variations, there is no one particular pace, process, or outcome that can be predicted for an individual adolescent seeking gender-affirming care.

Therefore, HCPs working with adolescents should promote supportive environments that simultaneously respect an adolescent's affirmed gender identity and also allows the adolescent to openly explore gender needs, including social, medical, and physical gender-affirming interventions should they change or evolve over time.

Statement 6.3

We recommend health care professionals working with gender diverse adolescents undertake a comprehensive biopsychosocial assessment of adolescents who present with gender identity-related concerns and seek medical/surgical transition-related care, and that this be accomplished in a collaborative and supportive manner.

Given the many ways identity may unfold during adolescence, we recommend using a comprehensive biopsychosocial assessment to guide treatment decisions and optimize outcomes. This assessment should aim to understand the adolescent's strengths, vulnerabilities, diagnostic profile, and unique needs to individualize their care. As mentioned in Statement 6.1, MHPs have the most appropriate training, experience, and dedicated clinical time required to obtain the information discussed here. The assessment process should be approached collaboratively with the adolescent and their caregiver(s), both separately and together, as described in more detail in Statement 6.11. An assessment should occur prior to any medically necessary medical or surgical intervention under consideration (e.g., puberty blocking medication, gender-affirming hormones, surgeries). See medically necessary statement in Chapter 2—Global Applicability, Statement 2.1; see also Chapter 12—Hormone Therapy and Chapter 13—Surgery and Postoperative Care.

Youth may experience many different gender identity trajectories. Sociocultural definitions and experiences of gender continue to evolve over time, and youth are increasingly presenting with a range of identities and ways of describing their experiences and gender-related needs (Twist & de

Graaf, 2019). For example, some youth will realize they are transgender or more broadly gender diverse and pursue steps to present accordingly. For some youth, obtaining gender-affirming medical treatment is important while for others these steps may not be necessary. For example, a process of exploration over time might not result in the young person self-affirming or embodying a different gender in relation to their assigned sex at birth and would not involve the use of medical interventions (Arnoldussen et al., 2019).

The most robust longitudinal evidence supporting the benefits of gender-affirming medical and surgical treatments in adolescence was obtained in a clinical setting that incorporated a detailed comprehensive diagnostic assessment process over time into its delivery of care protocol (de Vries & Cohen-Kettenis, 2012; de Vries et al., 2014). Given this research and the ongoing evolution of gender diverse experiences in society, a comprehensive diagnostic biopsychosocial assessment during adolescence is both evidence-based and preserves the integrity of the decision-making process. In the absence of a full diagnostic profile, other mental health entities that need to be prioritized and treated may not be detected. There are no studies of the long-term outcomes of gender-related medical treatments for youth who have not undergone a comprehensive assessment. Treatment in this context (e.g., with limited or no assessment) has no empirical support and therefore carries the risk that the decision to start gender-affirming medical interventions may not be in the long-term best interest of the young person at that time.

As delivery of health care and access to specialists varies globally, designing a particular assessment process to adapt existing resources is often necessary. In some cases, a more extended assessment process may be useful, such as for youth with more complex presentations (e.g., complicating mental health histories (Leibowitz & de Vries, 2016)), co-occurring autism spectrum characteristics (Strang, Powers et al., 2018), and/or an absence of experienced childhood gender incongruence (Ristori & Steensma, 2016). Given the unique cultural, financial, and geographical factors that exist for specific populations, providers should design assessment models that are flexible and allow for appropriately timed care for as many young people as possible, so long as the assessment effectively obtains information about the adolescent's strengths, vulnerabilities, diagnostic profile, and individual needs. Psychometrically validated psychosocial and gender measures can also be used to provide additional information.

The multidisciplinary assessment for youth seeking gender-affirming medical/surgical interventions includes the following domains that correspond to the relevant statements:

- **Gender Identity Development:** Statements 6.12.a and 6.12.b elaborate on the factors associated with gender identity development within the specific cultural context when assessing TGD adolescents.
- **Social Development and Support; Intersectionality:** Statements 6.4 and 6.11 elaborate on the importance of assessing gender minority stress, family dynamics, and other aspects contributing to social development and intersectionality.
- **Diagnostic Assessment of Possible Co-Occurring Mental Health and/or Developmental Concerns:** Statement 6.12.d elaborates on the importance of understanding the relationship that exists, if at all, between any co-occurring mental health or developmental concerns and the young person's gender identity/gender diverse expression.
- **Capacity for Decision-Making:** Statement 6.12.c elaborates on the assessment of a young person's emotional maturity and the relevance when an adolescent is considering gender affirming-medical/surgical treatments.

Statement 6.4

We recommend health care professionals work with families, schools, and other relevant settings to promote acceptance of gender diverse expressions of behavior and identities of the adolescent.

Multiple studies and related expert consensus support the implementation of approaches that promote acceptance and affirmation of gender diverse youth across all settings, including families, schools, health care facilities, and all other organizations and communities with which they

interact (e.g., Pariseau et al., 2019; Russell et al., 2018; Simons et al., 2013; Toomey et al., 2010; Travers et al., 2012). Acceptance and affirmation are accomplished through a range of approaches, actions, and policies we recommend be enacted across the various relationships and settings in which a young person exists and functions. It is important for the family members and community members involved in the adolescent's life to work collaboratively in these efforts unless their involvement is considered harmful to the adolescent. Examples proposed by Pariseau et al. (2019) and others of acceptance and affirmation of gender diversity and contemplation and expression of identity that can be implemented by family, staff, and organizations include:

1. Actions that are supportive of youth drawn to engaging in gender-expansive (e.g., nonconforming) activities and interests;
2. Communications that are supportive when youth express their experiences about their gender and gender exploration;
3. Use of the youth's asserted name/pronouns;
4. Support for youth wearing clothing/uniforms, hairstyles, and items (e.g., jewelry, makeup) they feel affirm their gender;
5. Positive and supportive communication with youth about their gender and gender concerns;
6. Education about gender diversity issues for people in the young person's life (e.g., family members, health care providers, social support networks), as needed, including information about how to advocate for gender diverse youth in community, school, health care, and other settings;
7. Support for gender diverse youth to connect with communities of support (e.g., LGBTQ groups, events, friends);
8. Provision of opportunities to discuss, consider, and explore medical treatment options when indicated;
9. Antibullying policies that are enforced;
10. Inclusion of nonbinary experiences in daily life, reading materials, and curricula (e.g., books, health, and sex education classes, assigned essay topics that move beyond the binary, LGBTQ, and ally groups);
11. Gender inclusive facilities that the youth can readily access without segregation from nongender diverse peers (e.g., bathrooms, locker rooms).

We recommend HCPs work with parents, schools, and other organizations/groups to promote acceptance and affirmation of TGD identities and expressions, whether social or medical interventions are implemented or not as acceptance and affirmation are associated with fewer negative mental health and behavioral symptoms and more positive mental health and behavioral functioning (Day et al., 2015; de Vries et al., 2016; Greytak et al., 2013; Pariseau et al., 2019; Peng et al., 2019; Russell et al., 2018; Simons et al., 2013; Taliaferro et al., 2019; Toomey et al., 2010; Travers et al., 2012). Russell et al. (2018) found mental health improvement increases with more acceptance and affirmation across more settings (e.g., home, school, work, and friends). Rejection by family, peers, and school staff (e.g., intentionally using the name and pronoun the youth does not identify with, not acknowledging affirmed gender identity, bullying, harassment, verbal and physical abuse, poor relationships, rejection for being TGD, eviction) was strongly linked to negative outcomes, such as anxiety, depression, suicidal ideation, suicide attempts, and substance use (Grossman et al., 2005; Klein & Golub; 2016; Pariseau et al., 2019; Peng et al., 2019; Reisner, Greytak et al., 2015; Roberts et al., 2013). It is important to be aware that negative symptoms increase with increased levels of rejection and continue into adulthood (Roberts et al., 2013).

Neutral or indifferent responses to a youth's gender diversity and exploration (e.g., letting a child tell others their chosen name but not using the name, not telling family or friends when the youth wants them to disclose, not advocating for the child about rejecting behavior from school staff or peers, not engaging or participating in other support mechanisms (e.g., with psychotherapists and support groups) have also been found to have negative consequences, such as increased depressive symptoms (Pariseau et al., 2019). For these reasons, it is important not to ignore a youth's gender questioning or delay consideration of the youth's gender-related

care needs. There is particular value in professionals recognizing youth need individualized approaches, support, and consideration of needs around gender expression, identity, and embodiment over time and across domains and relationships. Youth may need help coping with the tension of tolerating others' processing/adjusting to an adolescent's identity exploration and changes (e.g., Kuper, Lindley et al., 2019). It is important professionals collaborate with parents and others as they process their concerns and feelings and educate themselves about gender diversity because such processes may not necessarily reflect rejection or neutrality but may rather represent efforts to develop attitudes and gather information that foster acceptance (e.g., Katz-Wise et al., 2017).

Statement 6.5

We recommend against offering reparative and conversion therapy aimed at trying to change a person's gender and lived gender expression to become more congruent with the sex assigned at birth.

Some health care providers, secular or religious organizations, and rejecting families may undertake efforts to thwart an adolescent's expression of gender diversity or assertion of a gender identity other than the expression and behavior that conforms to the sex assigned at birth. Such efforts at blocking reversible social expression or transition may include choosing not to use the youth's identified name and pronouns or restricting self-expression in clothing and hairstyles (Craig et al., 2017; Green et al., 2020). These disaffirming behaviors typically aim to reinforce views that a young person's gender identity/expression must match the gender associated with the sex assigned at birth or expectations based on the sex assigned at birth. Activities and approaches (sometimes referred to as "treatments") aimed at trying to change a person's gender identity and expression to become more congruent with the sex assigned at birth have been attempted, but these approaches have not resulted in changes in gender identity (Craig et al., 2017; Green et al., 2020). We recommend against such efforts because they have been found to be ineffective and are associated with increases in mental illness and poorer psychological functioning (Craig et al., 2017; Green et al., 2020; Turban, Beckwith et al., 2020).

Much of the research evaluating "conversion therapy" and "reparative therapy" has investigated the impact of efforts to change gender expression (masculinity or femininity) and has conflated sexual orientation with gender identity (APA, 2009; Burnes et al., 2016; Craig et al., 2017). Some of these efforts have targeted both gender identity and expression (AACAP, 2018). Conversion/reparative therapy has been linked to increased anxiety, depression, suicidal ideation, suicide attempts, and health care avoidance (Craig et al., 2017; Green et al., 2020; Turban, Beckwith et al., 2020). Although some of these studies have been criticized for their methodologies and conclusions (e.g., D'Angelo et al., 2020), this should not detract from the importance of emphasizing efforts undertaken a priori to change a person's identity are clinically and ethically unsound. We recommend against any type of conversion or attempts to change a person's gender identity because 1) both secular and religion-based efforts to change gender identity/expression have been associated with negative psychological functioning that endures into adulthood (Turban, Beckwith et al., 2020); and 2) larger ethical reasons exist that should underscore respect for gender diverse identities.

It is important to note potential factors driving a young person's gender-related experience and report of gender incongruence, when carried out in the context of supporting an adolescent with self-discovery, is not considered reparative therapy as long as there is no a priori goal to change or promote one particular gender identity or expression (AACAP, 2018; see Statement 6.2). To ensure these explorations are therapeutic, we recommend employing affirmative consideration and supportive tone in discussing what steps have been tried, considered, and planned for a youth's gender expression. These discussion topics may include what felt helpful or affirming, what felt unhelpful or distressing and why. We recommend employing affirmative responses to these steps and discussions, such as those identified in SOC-8 Statement 6.4.

Statement 6.6

We suggest health care professionals provide transgender and gender diverse adolescents with health education on chest binding and genital tucking, including review of the benefits and risks.

TGD youth may experience distress related to chest and genital anatomy. Practices such as chest binding, chest padding, genital tucking, and genital packing are reversible, nonmedical interventions that may help alleviate this distress (Callen-Lorde, 2020a, 2020b; Deutsch, 2016a; Olson-Kennedy, Rosenthal et al., 2018; Transcare BC, 2020). It is important to assess the degree of distress related to physical development or anatomy, educate youth about potential nonmedical interventions to address this distress, and discuss the safe use of these interventions.

Chest binding involves compression of the breast tissue to create a flatter appearance of the chest. Studies suggest that up to 87% of trans masculine patients report a history of binding (Jones, 2015; Peitzmeier, 2017). Binding methods may include the use of commercial binders, sports bras, layering of shirts, layering of sports bras, or the use of elastics or other bandages (Peitzmeier, 2017). Currently, most youth report learning about binding practices from online communities composed of peers (Julian, 2019). Providers can play an important role in ensuring youth receive accurate and reliable information about the potential benefits and risks of chest binding. Additionally, providers can counsel patients about safe binding practices and monitor for potential negative health effects. While there are potential negative physical impacts of binding, youth who bind report many benefits, including increased comfort, improved safety, and lower rates of misgendering (Julian, 2019). Common negative health impacts of chest binding in youth include back/chest pain, shortness of breath, and overheating (Julian, 2019). More serious negative health impacts such as skin infections, respiratory infections, and rib fractures are uncommon and have been associated with chest binding in adults (Peitzmeier, 2017). If binding is employed, youth should be advised to use only those methods considered safe for binding—such as binders specifically designed for the gender diverse population—to reduce the risk of serious negative health effects. Methods that are considered unsafe for binding include the use of duct tape, ace wraps, and plastic wrap as these can restrict blood flow, damage skin, and restrict breathing. If youth report negative health impacts from chest binding, these should ideally be addressed by a gender-affirming medical provider with experience working with TGD youth.

Genital tucking is the practice of positioning the penis and testes to reduce the outward appearance of a genital bulge. Methods of tucking include tucking the penis and testes between the legs or tucking the testes inside the inguinal canal and pulling the penis back between the legs. Typically, genitals are held in place by underwear or a gaff, a garment that can be made or purchased. Limited studies are available on the specific risks and benefits of tucking in adults, and none have been carried out in youth. Previous studies have reported tight undergarments are associated with decreased sperm concentration and motility. In addition, elevated scrotal temperatures can be associated with poor sperm characteristics, and genital tucking could theoretically affect spermatogenesis and fertility (Marsh, 2019) although there are no definitive studies evaluating these adverse outcomes. Further research is needed to determine the specific benefits and risks of tucking in youth.

Statement 6.7

We recommend providers consider prescribing menstrual suppression agents for adolescents experiencing gender incongruence who may not desire testosterone therapy, who desire but have not yet begun testosterone therapy, or in conjunction with testosterone therapy for breakthrough bleeding.

When discussing the available options of menstrual-suppressing medications with gender diverse youth, providers should engage in shared decision-making, use gender-inclusive language (e.g., asking patients which terms they utilize to refer to their menses, reproductive organs, and genitalia) and perform physical exams in a sensitive, gender-affirmative manner (Bonnington et al., 2020; Krempasky et al., 2020). There is no formal research evaluating how menstrual

suppression may impact gender incongruence and/or dysphoria. However, the use of menstrual suppression can be an initial intervention that allows for further exploration of gender-related goals of care, prioritization of other mental health care, or both, especially for those who experience a worsening of gender dysphoria from unwanted uterine bleeding (see Statement 6.12d; Mehringer & Dowshen, 2019). When testosterone is not used, menstrual suppression can be achieved via a progestin. To exclude any underlying menstrual disorders, it is important to obtain a detailed menstrual history and evaluation prior to implementing menstrual-suppressing therapy (Carswell & Roberts, 2017). As part of the discussion about menstrual-suppressing medications, the need for contraception and information regarding the effectiveness of menstrual-suppressing medications as methods of contraception also need to be addressed (Bonnington et al., 2020). A variety of menstrual suppression options, such as combined estrogen-progestin medications, oral progestins, depot and subdermal progestin, and intrauterine devices (IUDs), should be offered to allow for individualized treatment plans while properly considering availability, cost and insurance coverage, as well as contraindications and side effects (Kanj et al., 2019).

Progestin-only hormonal medication are options, especially in trans masculine or nonbinary youth who are not interested in estrogen-containing medical therapies as well as those at risk for thromboembolic events or who have other contraindications to estrogen therapy (Carswell & Roberts, 2017). Progestin-only hormonal medications include oral progestins, depo-medroxyprogesterone injection, etonogestrel implant, and levonorgestrel IUD (Schwartz et al., 2019). Progestin-only hormonal options vary in terms of efficacy in achieving menstrual suppression and have lower rates of achieving amenorrhea than combined oral contraception (Pradhan & Gomez-Lobo, 2019). A more detailed description of the relevant clinical studies is presented in Chapter 12—Hormone Therapy. HCPs should not make assumptions regarding the individual's preferred method of administration as some trans masculine youth may prefer vaginal rings or IUD implants (Akgul et al., 2019). Although hormonal medications require monitoring for potential mood lability, depressive effects, or both, the benefits and risks of untreated menstrual suppression in the setting of gender dysphoria should be evaluated on an individual basis. Some patients may opt for combined oral contraception that includes different combinations of ethinyl estradiol, with ranging doses, and different generations of progestins (Pradhan & Gomez-Lobo, 2019). Lower dose ethinyl estradiol components of combined oral contraceptive pills are associated with increased breakthrough uterine bleeding. Continuous combined oral contraceptives may be used to allow for continuous menstrual suppression and can be delivered as transdermal or vaginal rings.

The use of gonadotropin releasing hormone (GnRH) analogues may also result in menstrual suppression. However, it is recommended gender diverse youth meet the eligibility criteria (as outlined in Statement 6.12) before this medication is considered solely for this purpose (Carswell & Roberts, 2017; Pradhan & Gomez-Lobo, 2019). Finally, menstrual-suppression medications may be indicated as an adjunctive therapy for breakthrough uterine bleeding that may occur while on exogenous testosterone or as a bridging medication while awaiting menstrual suppression with testosterone therapy. When exogenous testosterone is employed as a gender-affirming hormone, menstrual suppression is typically achieved in the first six months of therapy (Ahmad & Leinung, 2017). However, it is vital adolescents be counseled ovulation and pregnancy can still occur in the setting of amenorrhea (Gomez et al., 2020; Kanj et al., 2019).

Statement 6.8

We recommend health care professionals maintain an ongoing relationship with the gender diverse and transgender adolescent and any relevant caregivers to support the adolescent in their decision-making throughout the duration of puberty suppression treatment, hormonal treatment, and gender-related surgery until the transition is made to adult care.

HCPs with expertise in child and adolescent development, as described in Statement 6.1, play an important role in the continuity of care for

young people over the course of their gender-related treatment needs. Supporting adolescents and their families necessitates approaching care using a developmental lens through which understanding a young person's evolving emotional maturity and care needs can take place over time. As gender-affirming treatment pathways differ based on the needs and experiences of individual TGD adolescents, decision-making for these treatments (puberty suppression, estrogens/androgens, gender-affirmation surgeries) can occur at different points in time within a span of several years. Longitudinal research demonstrating the benefits of pubertal suppression and gender-affirming hormone treatment (GAHT) was carried out in a setting where an ongoing clinical relationship between the adolescents/families and the multidisciplinary team was maintained (de Vries et al., 2014).

Clinical settings that offer longer appointment times provide space for adolescents and caregivers to share important psychosocial aspects of emotional well-being (e.g., family dynamics, school, romantic, and sexual experiences) that contextualize individualized gender-affirming treatment needs and decisions as described elsewhere in the chapter. An ongoing clinical relationship can take place across settings, whether that be within a multidisciplinary team or with providers in different locations who collaborate with one another. Given the wide variability in the ability to obtain access to specialized gender care centers, particularly for marginalized groups who experience disparities with access, it is important for the HCP to appreciate the existence of any barriers to care while maintaining flexibility when defining how an ongoing clinical relationship can take place in that specific context.

An ongoing clinical relationship that increases resilience in the youth and provides support to parents/caregivers who may have their own treatment needs may ultimately lead to increased parental acceptance—when needed—which is associated with better mental health outcomes in youth (Ryan, Huebner et al., 2009).

Statement 6.9

We recommend health care professionals involve relevant disciplines, including mental health and medical professionals, to reach a decision about whether puberty suppression, hormone initiation, or gender-related surgery for gender diverse and transgender adolescents are appropriate and remain indicated throughout the course of treatment until the transition is made to adult care.

TGD adolescents with gender dysphoria/gender incongruence who seek gender-affirming medical and surgical treatments benefit from the involvement of health care professionals (HCPs) from different disciplines. Providing care to TGD adolescents includes addressing 1) diagnostic considerations (see Statements 6.3, 6.12a, and 6.12b) conducted by a specialized gender HCP (as defined in Statement 6.1) whenever possible and necessary; and 2) treatment considerations when prescribing, managing, and monitoring medications for gender-affirming medical and surgical care, requiring the training of the relevant medical/surgical professional. The list of key disciplines includes but is not limited to adolescent medicine/primary care, endocrinology, psychology, psychiatry, speech/language pathology, social work, support staff, and the surgical team.

The evolving evidence has shown a clinical benefit for transgender youth who receive their gender-affirming treatments in multidisciplinary gender clinics (de Vries et al., 2014; Kuper et al., 2020; Tollit et al., 2019). Finally, adolescents seeking gender-affirming care in multidisciplinary clinics are presenting with significant complexity necessitating close collaboration between mental health, medical, and/or surgical professionals (McCallion et al., 2021; Sorbara et al., 2020; Tishelman et al., 2015).

As not all patients and families are in the position or in a location to access multidisciplinary care, the lack of available disciplines should not preclude a young person from accessing needed care in a timely manner. When disciplines are available, particularly in centers with existing multidisciplinary teams, disciplines, or both, it is recommended efforts be made to include the relevant providers when developing a gender care team. However, this does not mean all disciplines are necessary to provide care to a particular youth and family.

If written documentation or a letter is required to recommend gender-affirming medical and surgical treatment (GAMST) for an adolescent, only one letter of assessment from a member of the multidisciplinary team is needed. This letter needs to reflect the assessment and opinion from the team that involves both medical HCPs and MHPs (American Psychological Association, 2015; Hembree et al., 2017; Telfer et al., 2018). Further assessment results and written opinions may be requested when there is a specific clinical need or when team members are in different locations or choose to write their own summaries. For further information see Chapter 5—Assessment for Adults, Statement 5.5.

Statement 6.10

We recommend health care professionals working with transgender and gender diverse adolescents requesting gender-affirming medical or surgical treatments inform them, prior to the initiation of treatment, of the reproductive effects, including the potential loss of fertility and available options to preserve fertility within the context of the youth's stage of pubertal development.

While assessing adolescents seeking gender-affirming medical or surgical treatments, HCPs should discuss the specific ways in which the required treatment may affect reproductive capacity. Fertility issues and the specific preservation options are more thoroughly discussed in Chapter 12—Hormone Therapy and Chapter 16—Reproductive Health.

It is important HCPs understand what fertility preservation options exist so they can relay the information to adolescents. Parents are advised to be involved in this process and should also understand the pros and cons of the different options. HCPs should acknowledge adolescents and parents may have different views around reproductive capacity and may therefore come to different decisions (Quain et al., 2020), which is why HCPs can be helpful in guiding this process.

HCPs should specifically pay attention to the developmental and psychological aspects of fertility preservation and decision-making competency for the individual adolescent. While adolescents may think they have made up their minds concerning their reproductive capacity, the possibility their opinions about having biologically related children in the future might change over time needs to be discussed with an HCP who has sufficient experience, is knowledgeable about adolescent development, and has experience working with parents.

Addressing the long-term consequences on fertility of gender-affirming medical treatments and ensuring transgender adolescents have realistic expectations concerning fertility preservation options or adoption cannot not be addressed with a one-time discussion but should be part of an ongoing conversation. This conversation should occur not only before initiating any medical intervention (puberty suppression, hormones, or surgeries), but also during further treatment and during transition.

Currently, there are only preliminary results from retrospective studies evaluating transgender adults and the decisions they made when they were young regarding the consequences of medical-affirming treatment on reproductive capacity. It is important not to make assumptions about what future adult goals an adolescent may have. Research in childhood cancer survivors found participants who acknowledged missed opportunities for fertility preservation reported distress and regret surrounding potential infertility (Armuand et al., 2014; Ellis et al., 2016; Lehmann et al., 2017). Furthermore, individuals with cancer who did not prioritize having biological children before treatment have reported "changing their minds" in survivorship (Armuand et al., 2014).

Given the complexities of the different fertility preservation options and the challenges HCPs may experience discussing fertility with the adolescent and the family (Tishelman et al., 2019), a fertility consultation is an important consideration for every transgender adolescent who pursues medical-affirming treatments unless the local situation is such that a fertility consultation is not covered by insurance or public health care plans, is not available locally, or the individual circumstances make this unpreferable.

Statement 6.11

We recommend when gender-affirming medical or surgical treatments are indicated for adolescents, health care professionals working with transgender and gender diverse adolescents

involve parent(s)/guardian(s) in the assessment and treatment process, unless their involvement is determined to be harmful to the adolescent or not feasible.

When there is an indication an adolescent might benefit from a gender-affirming medical or surgical treatment, involving the parent(s) or primary caregiver(s) in the assessment process is recommended in almost all situations (Edwards-Leeper & Spack, 2012; Rafferty et al., 2018). Exceptions to this might include situations in which an adolescent is in foster care, child protective services, or both, and custody and parent involvement would be impossible, inappropriate, or harmful. Parent and family support of TGD youth is a primary predictor of youth well-being and is protective of the mental health of TGD youth (Gower, Rider, Coleman et al., 2018; Grossman et al., 2019; Lefevor et al., 2019; McConnell et al., 2015; Pariseau et al., 2019; Ryan, 2009; Ryan et al., 2010; Simons et al., 2013; Wilson et al., 2016). Therefore, including parent(s)/caregiver(s) in the assessment process to encourage and facilitate increased parental understanding and support of the adolescent may be one of the most helpful practices available.

Parent(s)/caregiver(s) may provide key information for the clinical team, such as the young person's gender and overall developmental, medical, and mental health history as well as insights into the young person's level of current support, general functioning, and well-being. Concordance or divergence of reports given by the adolescent and their parent(s)/caregiver(s) may be important information for the assessment team and can aid in designing and shaping individualized youth and family supports (De Los Reyes et al., 2019; Katz-Wise et al., 2017). Knowledge of the family context, including resilience factors and challenges, can help providers know where special supports would be needed during the medical treatment process. Engagement of parent(s)/caregiver(s) is also important for educating families about various treatment approaches, ongoing follow-up and care needs, and potential treatment complications. Through psychoeducation regarding clinical gender care options and participation in the assessment process, which may unfold over time, parent(s)/caregiver(s) may better understand their adolescent child's gender-related experience and needs (Andrzejewski et al., 2020; Katz-Wise et al., 2017).

Parent/caregiver concerns or questions regarding the stability of gender-related needs over time and implications of various gender-affirming interventions are common and should not be dismissed. It is appropriate for parent(s)/caregiver(s) to ask these questions, and there are cases in which the parent(s)/caregiver(s)' questions or concerns are particularly helpful in informing treatment decisions and plans. For example, a parent/caregiver report may provide critical context in situations in which a young person experiences very recent or sudden self-awareness of gender diversity and a corresponding gender treatment request, or when there is concern for possible excessive peer and social media influence on a young person's current self-gender concept. Contextualization of the parent/caregiver report is also critical, as the report of a young person's gender history as provided by parent(s)/caregiver(s) may or may not align with the young person's self-report. Importantly, gender histories may be unknown to parent(s)/caregiver(s) because gender may be internal experience for youth, not known by others unless it is discussed. For this reason, an adolescent's report of their gender history and experience is central to the assessment process.

Some parents may present with unsupportive or antagonistic beliefs about TGD identities, clinical gender care, or both (Clark et al., 2020). Such unsupportive perspectives are an important therapeutic target for families. Although challenging parent perspectives may in some cases seem rigid, providers should not assume this is the case. There are many examples of parent(s)/caregiver(s) who, over time with support and psychoeducation, have become increasingly accepting of their TGD child's gender diversity and care needs.

Helping youth and parent(s)/caregiver(s) work together on important gender care decisions is a primary goal. However, in some cases, parent(s)/caregiver(s) may be too rejecting of their adolescent child and their child's gender needs to be part of the clinical evaluation process. In these situations, youth may require the engagement of larger systems of advocacy and support to move

forward with the necessary support and care (Dubin et al., 2020).

Statement 6.12

We recommend health care professionals assessing transgender and gender diverse adolescents only recommend gender-affirming medical or surgical treatments requested by the patient when:

Statement 6.12.a

The adolescent meets the diagnostic criteria of gender incongruence as per the ICD-11 in situations where a diagnosis is necessary to access health care. In countries that have not implemented the latest ICD, other taxonomies may be used although efforts should be undertaken to utilize the latest ICD as soon as practicable.

When working with TGD adolescents, HCPs should realize while a classification may give access to care, pathologizing transgender identities may be experienced as stigmatizing (Beek et al., 2016). Assessments related to gender health and gender diversity have been criticized, and controversies exist around diagnostic systems (Drescher, 2016).

HCPs should assess the overall gender-related history and gender care-related needs of youth. Through this assessment process, HCPs may provide a diagnosis when it is required to get access to transgender-related care.

Gender incongruence and gender dysphoria are the two diagnostic terms used in the World Health Organization's International Classification of Diseases (ICD) and the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM), respectively. Of these two widely used classification systems, the DSM is for psychiatric classifications only and the ICD contains all diseases and conditions related to physical as well as mental health. The most recent versions of these two systems, the DSM-5 and the ICD-11, reflect a long history of reconceptualizing and de-psychopathologizing gender-related diagnoses (American Psychiatric Association, 2013; World Health Organization, 2019a). Compared with the earlier version, the DSM-5 replaced gender identity disorder with gender dysphoria, acknowledging the distress experienced by some people stemming from the incongruence between experienced gender identity and the sex assigned at birth. In the most recent revision, the DSM-5-TR, no changes in the diagnostic criteria for gender dysphoria are made. However, terminology was adapted into the most appropriate current language (e.g., birth-assigned gender instead of natal-gender and gender-affirming treatment instead of gender reassignment (American Psychiatric Association, 2022). Compared with the ICD 10th edition, the gender incongruence classification was moved from the Mental Health chapter to the Conditions Related to Sexual Health chapter in the ICD-11. When compared with the DSM-5 classification of gender dysphoria, one important reconceptualization is distress is not a required indicator of the ICD-11 classification of gender incongruence (WHO, 2019a). After all, when growing up in a supporting and accepting environment, the distress and impairment criterion, an inherent part of every mental health condition, may not be applicable (Drescher, 2012). As such, the ICD-11 classification of gender incongruence may better capture the fullness of gender diversity experiences and related clinical gender needs.

Criteria for the ICD-11 classification gender incongruence of adolescence or adulthood require a marked and persistent incongruence between an individual´s experienced gender and the assigned sex, which often leads to a need to "transition" to live and be accepted as a person of the experienced gender. For some, this includes hormonal treatment, surgery, or other health care services to enable the individual´s body to align as much as required, and to the extent possible, with the person's experienced gender. Relevant for adolescents is the indicator that a classification cannot be assigned "prior to the onset of puberty." Finally, it is noted "that gender variant behaviour and preferences alone are not a basis for assigning the classification" (WHO, ICD-11, 2019a).

Criteria for the DSM-5 and DSM-5-TR classification of gender dysphoria in adolescence and adulthood denote "a marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration' (criterion A, fulfilled when 2 of 6 subcriteria are manifest; DSM-5, APA, 2013; DSM 5-TR, APA, 2022).

Of note, although a gender-related classification is one of the requirements for receiving medical gender-affirming care, such a classification alone does not indicate a person needs medical-affirming care. The range of youth experiences of gender incongruence necessitates professionals provide a range of treatments or interventions based on the individual's needs. Counseling, gender exploration, mental health assessment and, when needed, treatment with MHPs trained in gender development may all be indicated with or without the implementation of medical-affirming care.

Statement 6.12.b

The experience of gender diversity/incongruence is marked and sustained over time.

Identity exploration and consolidation are experienced by many adolescents (Klimstra et al., 2010; Topolewska-Siedzik & Cieciuch, 2018). Identity exploration during adolescence may include a process of self-discovery around gender and gender identity (Steensma, Kreukels et al., 2013). Little is known about how processes that underlie consolidation of gender identity during adolescence (e.g., the process of commitment to specific identities) may impact a young person's experience(s) or needs over time.

Therefore, the level of reversibility of a gender-affirming medical intervention should be considered along with the sustained duration of a young person's experience of gender incongruence when initiating treatment. Given potential shifts in gender-related experiences and needs during adolescence, it is important to establish the young person has experienced several years of persistent gender diversity/incongruence prior to initiating less reversible treatments such as gender-affirming hormones or surgeries. Puberty suppression treatment, which provides more time for younger adolescents to engage their decision-making capacities, also raises important considerations (see Statement 6.12f and Chapter 12—Hormone Therapy) suggesting the importance of a sustained experience of gender incongruence/diversity prior to initiation. However, in this age group of younger adolescents, several years is not always practical nor necessary given the premise of the treatment as a means to buy time while avoiding distress from irreversible pubertal changes. For youth who have experienced a shorter duration of gender incongruence, social transition-related and/or other medical supports (e.g., menstrual suppression/androgen blocking) may also provide some relief as well as furnishing additional information to the clinical team regarding a young person's broad gender care needs (see Statements 6.4, 6.6, and 6.7).

Establishing evidence of persistent gender diversity/incongruence typically requires careful assessment with the young person over time (see Statement 6.3). Whenever possible and when appropriate, the assessment and discernment process should also include the parent(s)/caregiver(s) (see Statement 6.11). Evidence demonstrating gender diversity/incongruence sustained over time can be provided via history obtained directly from the adolescent and parents/caregivers when this information is not documented in the medical records.

The research literature on continuity versus discontinuity of gender-affirming medical care needs/requests is complex and somewhat difficult to interpret. A series of studies conducted over the last several decades, including some with methodological challenges (as noted by Temple Newhook et al., 2018; Winters et al., 2018) suggest the experience of gender incongruence is not consistent for all children as they progress into adolescence. For example, a subset of youth who experienced gender incongruence or who socially transitioned prior to puberty over time can show a reduction in or even full discontinuation of gender incongruence (de Vries et al., 2010; Olson et al., 2022; Ristori & Steensma, 2016; Singh et al., 2021; Wagner et al., 2021). However, there has been less research focused on rates of continuity and discontinuity of gender incongruence and gender-related needs in pubertal and adolescent populations. The data available regarding broad unselected gender-referred pubertal/adolescent cohorts (from the Amsterdam transgender clinic) suggest that, following extended assessments over time, a subset of adolescents with gender incongruence presenting for gender care elect not to pursue gender-affirming medical care

(Arnoldussen et al., 2019; de Vries, Steensma et al., 2011). Importantly, findings from studies of gender incongruent pubertal/adolescent cohorts, in which participants who have undergone comprehensive gender evaluation over time, have shown persistent gender incongruence and gender-related need and have received referrals for medical gender care, suggest low levels of regret regarding gender-related medical care decisions (de Vries et al., 2014; Wiepjes et al., 2018). Critically, these findings of low regret can only currently be applied to youth who have demonstrated sustained gender incongruence and gender-related needs over time as established through a comprehensive and iterative assessment (see Statement 6.3).

Statement 6.12.c

The adolescent demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment.

The process of informed consent includes communication between a patient and their provider regarding the patient's understanding of a potential intervention as well as, ultimately, the patient's decision whether to receive the intervention. In most settings, for minors, the legal guardian is integral to the informed consent process: if a treatment is to be given, the legal guardian (often the parent[s]/caregiver[s]) provides the informed consent to do so. In most settings, assent is a somewhat parallel process in which the minor and the provider communicate about the intervention and the provider assesses the level of understanding and intention.

A necessary step in the informed consent/assent process for considering gender-affirming medical care is a careful discussion with qualified HCPs trained to assess the emotional and cognitive maturity of adolescents. The reversible and irreversible effects of the treatment, as well as fertility preservation options (when applicable), and all potential risks and benefits of the intervention are important components of the discussion. These discussions are required when obtaining informed consent/assent. Assessment of cognitive and emotional maturity is important because it helps the care team understand the adolescent's capacity to be informed.

The skills necessary to assent/consent to any medical intervention or treatment include the ability to 1) comprehend the nature of the treatment; 2) reason about treatment options, including the risks and benefits; 3) appreciate the nature of the decision, including the long-term consequences; and 4) communicate choice (Grootens-Wiegers et al., 2017). In the case of gender- affirming medical treatments, a young person should be well-informed about what the treatment may and may not accomplish, typical timelines for changes to appear (e.g., with gender-affirming hormones), and any implications of stopping the treatment. Gender-diverse youth should fully understand the reversible, partially reversible, and irreversible aspects of a treatment, as well as the limits of what is known about certain treatments (e.g., the impact of pubertal suppression on brain development (Chen and Loshak, 2020)). Gender-diverse youth should also understand, although many gender-diverse youth begin gender- affirming medical care and experience that care as a good fit for them long-term, there is a subset of individuals who over time discover this care is not a fit for them (Wiepjes et al., 2018). Youth should know such shifts are sometimes connected to a change in gender needs over time, and in some cases, a shift in gender identity itself. Given this information, gender diverse youth must be able to reason thoughtfully about treatment options, considering the implications of the choices at hand. Furthermore, as a foundation for providing assent, the gender-diverse young person needs to be able to communicate their choice.

The skills needed to accomplish the tasks required for assent/consent may not emerge at specific ages per se (Grootens-Wiegers et al., 2017). There may be variability in these capacities related to developmental differences and mental health presentations (Shumer & Tishelman, 2015) and dependent on the opportunities a young person has had to practice these skills (Alderson, 2007). Further, assessment of emotional and cognitive maturity must be conducted separately for each gender-related treatment decision (Vrouenraets et al., 2021).

The following questions may be useful to consider in assessing a young person's emotional and

cognitive readiness to assent or consent to a specific gender-affirming treatment:

- Can the young person think carefully into the future and consider the implications of a partially or fully irreversible intervention?
- Does the young person have sufficient self-reflective capacity to consider the possibility that gender-related needs and priorities can develop over time, and gender-related priorities at a certain point in time might change?
- Has the young person, to some extent, thought through the implications of what they might do if their priorities around gender do change in the future?
- Is the young person able to understand and manage the day-to-day short- and long-term aspects of a specific medical treatment (e.g., medication adherence, administration, and necessary medical follow-ups)?

Assessment of emotional and cognitive maturity may be accomplished over time as the care team continues to engage in conversations about the treatment options and affords the young person the opportunity to practice thinking into the future and flexibly consider options and implications. For youth with neurodevelopmental and/or some types of mental health differences, skills for future thinking, planning, big picture thinking, and self-reflection may be less-well developed (Dubbelink & Geurts, 2017). In these cases, a more careful approach to consent and assent may be required, and this may include additional time and structured opportunities for the young person to practice the skills necessary for medical decision-making (Strang, Powers et al., 2018).

For unique situations in which an adolescent minor is consenting for their own treatment without parental permission (see Statement 6.11), extra care must be taken to support the adolescent's informed decision-making. This will typically require greater levels of engagement of and collaboration between the HCPs working with the adolescent to provide the young person appropriate cognitive and emotional support to consider options, weigh benefits and potential challenges/costs, and develop a plan for any needed (and potentially ongoing) supports associated with the treatment.

Statement 6.12.d

The adolescent's mental health concerns (if any) that may interfere with diagnostic clarity, capacity to consent, and/or gender-affirming medical treatments have been addressed.

Evidence indicates TGD adolescents are at increased risk of mental health challenges, often related to family/caregiver rejection, non-affirming community environments, and neurodiversity-related factors (e.g., de Vries et al., 2016; Pariseau et al., 2019; Ryan et al., 2010; Weinhardt et al., 2017). A young person's mental health challenges may impact their conceptualization of their gender development history and gender identity-related needs, the adolescent's capacity to consent, and the ability of the young person to engage in or receive medical treatment. Additionally, like cisgender youth, TGD youth may experience mental health concerns irrespective of the presence of gender dysphoria or gender incongruence. In particular, depression and self-harm may be of specific concern; many studies reveal depression scores and emotional and behavioral problems comparable to those reported in populations referred to mental health clinics (Leibowitz & de Vries, 2016). Higher rates of suicidal ideation, suicide attempts, and self-harm have also been reported (de Graaf et al., 2020). In addition, eating disorders occur more frequently than expected in non-referred populations (Khatchadourian et al., 2013; Ristori et al., 2019; Spack et al., 2012). Importantly, TGD adolescents show high rates of autism spectrum disorder/characteristics (Øien et al., 2018; van der Miesen et al., 2016; see also Statement 6.1d). Other neurodevelopmental presentations and/or mental health challenges may also be present, (e.g., ADHD, intellectual disability, and psychotic disorders (de Vries, Doreleijers et al., 2011; Meijer et al., 2018; Parkes & Hall, 2006).

Of note, many transgender adolescents are well-functioning and experience few if any mental health concerns. For example, socially transitioned pubertal adolescents who receive medical

gender- affirming treatment at specialized gender clinics may experience mental health outcomes equivalent to those of their cisgender peers (e.g., de Vries et al., 2014; van der Miesen et al., 2020). A provider's key task is to assess the direction of the relationships that exist between any mental health challenges and the young person's self-understanding of gender care needs and then prioritize accordingly.

Mental health difficulties may challenge the assessment and treatment of gender-related needs of TGD adolescents in various ways:

1. First, when a TGD adolescent is experiencing acute suicidality, self-harm, eating disorders, or other mental health crises that threaten physical health, safety must be prioritized. According to the local context and existing guidelines, appropriate care should seek to mitigate the threat or crisis so there is sufficient time and stabilization for thoughtful gender-related assessment and decision-making. For example, an actively suicidal adolescent may not be emotionally able to make an informed decision regarding gender-affirming medical/surgical treatment. If indicated, safety-related interventions should not preclude starting gender-affirming care.
2. Second, mental health can also complicate the assessment of gender development and gender identity-related needs. For example, it is critical to differentiate gender incongruence from specific mental health presentations, such as obsessions and compulsions, special interests in autism, rigid thinking, broader identity problems, parent/child interaction difficulties, severe developmental anxieties (e.g., fear of growing up and pubertal changes unrelated to gender identity), trauma, or psychotic thoughts. Mental health challenges that interfere with the clarity of identity development and gender-related decision-making should be prioritized and addressed.
3. Third, decision-making regarding gender-affirming medical treatments that have life-long consequences requires thoughtful, future-oriented thinking by the adolescent, with support from the parents/caregivers, as indicated (see Statement 6.11). To be able to make such an informed decision, an adolescent should be able to understand the issues, express a choice, appreciate and give careful thought regarding the wish for medical-affirming treatment (see Statement 6.12c). Neurodevelopmental differences, such as autistic features or autism spectrum disorder (see Statement 6.1d, e.g., communication differences; a preference for concrete or rigid thinking; differences in self-awareness, future thinking and planning), may challenge the assessment and decision-making process; neurodivergent youth may require extra support, structure, psychoeducation, and time built into the assessment process (Strang, Powers et al., 2018). Other mental health presentations that involve reduced communication and self-advocacy, difficulty engaging in assessment, memory and concentration difficulties, hopelessness, and difficulty engaging in future-oriented thinking may complicate assessment and decision-making. In such cases, extended time is often necessary before any decisions regarding medical-affirming treatment can be made.
4. Finally, while addressing mental health concerns is important during the course of medical treatment, it does not mean all mental health challenges can or should be resolved completely. However, it is important any mental health concerns are addressed sufficiently so that gender -affirming medical treatment can be provided optimally (e.g., medication adherence, attending follow-up medical appointments, and self-care, particularly during a postoperative course).

Statement 6.12.e

The adolescent has been informed of the reproductive effects, including the potential loss of fertility, and available options to preserve fertility, and these have been discussed in the context of the adolescent's stage of pubertal development.

For guidelines regarding the clinical approach, the scientific background, and the rationale, see Chapter 12—Hormone Therapy and Chapter 16—Reproductive Health.

Statement 6.12.f

The adolescent has reached Tanner stage 2 of puberty for pubertal suppression to be initiated.

The onset of puberty is a pivotal point for many gender diverse youth. For some, it creates an intensification of their gender incongruence, and for others, pubertal onset may lead to gender fluidity (e.g., a transition from binary to nonbinary gender identity) or even attenuation of a previously affirmed gender identity (Drummond et al., 2008; Steensma et al., 2011, Steensma, Kreukels et al., 2013; Wallien & Cohen-Kettenis, 2008). The use of puberty-blocking medications, such as GnRH analogues, is not recommended until children have achieved a minimum of Tanner stage 2 of puberty because the experience of physical puberty may be critical for further gender identity development for some TGD adolescents (Steensma et al., 2011). Therefore, puberty blockers should not be implemented in prepubertal gender diverse youth (Waal & Cohen-Kettenis, 2006). For some youth, GnRH agonists may be appropriate in late stages or in the post-pubertal period (e.g., Tanner stage 4 or 5), and this should be highly individualized. See Chapter 12—Hormone Therapy for a more comprehensive review of the use of GnRH agonists.

Variations in the timing of pubertal onset is due to multiple factors (e.g., sex assigned at birth, genetics, nutrition, etc.). Tanner staging refers to five stages of pubertal development ranging from prepubertal (Tanner stage 1) to post-pubertal, and adult sexual maturity (Tanner stage 5) (Marshall & Tanner, 1969, 1970). For assigned females at birth, pubertal onset (e.g., gonadarche) is defined by the occurrence of breast budding (Tanner stage 2), and for birth-assigned males, the achievement of a testicular volume of greater than or equal to 4 mL (Roberts & Kaiser, 2020). An experienced medical provider should be relied on to differentiate the onset of puberty from physical changes such as pubic hair and apocrine body odor due to sex steroids produced by the adrenal gland (e.g., adrenarche) as adrenarche does not warrant the use of puberty-blocking medications (Roberts & Kaiser, 2020). Educating parents and families about the difference between adrenarche and gonadarche helps families understand the timing during which shared decision-making about gender-affirming medical therapies should be undertaken with their multidisciplinary team.

The importance of addressing other risks and benefits of pubertal suppression, both hypothetical and actual, cannot be overstated. Evidence supports the existence of surgical implications for transgender girls who proceed with pubertal suppression (van de Grift et al., 2020). Longitudinal data exists to demonstrate improvement in romantic and sexual satisfaction for adolescents receiving puberty suppression, hormone treatment and surgery (Bungener et al., 2020). A study on surgical outcomes of laparoscopic intestinal vaginoplasty (performed because of limited genital tissue after the use of puberty blockers) in transgender women revealed that the majority experienced orgasm after surgery (84%), although a specific correlation between sexual pleasure outcomes and the timing of pubertal suppression initiation was not discussed in the study (Bouman, van der Sluis et al., 2016), nor does the study apply to those who would prefer a different surgical procedure. This underscores the importance of engaging in discussions with families about the future unknowns related to surgical and sexual health outcomes.

Statement 6.12.g

The adolescent had at least 12 months of gender-affirming hormone therapy or longer, if required, to achieve the desired surgical result for gender-affirming procedures, including breast augmentation, orchiectomy, vaginoplasty, hysterectomy, phalloplasty, metoidioplasty, and facial surgery as part of gender-affirming treatment unless hormone therapy is either not desired or is medically contraindicated.

GAHT leads to anatomical, physiological, and psychological changes. The onset of the anatomic effects (e.g., clitoral growth, breast growth, vaginal mucosal atrophy) may begin early after the initiation of therapy, and the peak effect is expected at 1–2 years (T'Sjoen et al., 2019). To

ensure sufficient time for psychological adaptations to the physical change during an important developmental time for the adolescent, 12 months of hormone treatment is suggested. Depending upon the surgical result required, a period of hormone treatment may need to be longer (e.g., sufficient clitoral virilization prior to metoidioplasty/phalloplasty, breast growth and skin expansion prior to breast augmentation, softening of skin and changes in facial fat distribution prior to facial GAS) (de Blok et al., 2021).

For individuals who are not taking hormones prior to surgical interventions, it is important surgeons review the impact of hormone therapy on the proposed surgery. In addition, for individuals undergoing gonadectomy who are not taking hormones, a plan for hormone replacement can be developed with their prescribing professional prior to surgery.

Consideration of ages for gender-affirming medical and surgical treatment for adolescents

Age has a strong, albeit imperfect, correlation with cognitive and psychosocial development and may be a useful objective marker for determining the potential timing of interventions (Ferguson et al., 2021). Higher (i.e., more advanced) ages may be required for treatments with greater irreversibility, complexity, or both. This approach allows for continued cognitive/emotional maturation that may be required for the adolescent to fully consider and consent to increasingly complex treatments (see Statement 6.12c).

A growing body of evidence indicates providing gender-affirming treatment for gender diverse youth who meet criteria leads to positive outcomes (Achille et al., 2020; de Vries et al., 2014; Kuper et al., 2020). There is, however, limited data on the optimal timing of gender-affirming interventions as well as the long-term physical, psychological, and neurodevelopmental outcomes in youth (Chen et al., 2020; Chew et al., 2018; Olson-Kennedy et al., 2016). Currently, the only existing longitudinal studies evaluating gender diverse youth and adult outcomes are based on a specific model (i.e., the Dutch approach) that involved a comprehensive initial assessment with follow-up. In this approach, pubertal suppression was considered at age 12, GAHT at age 16, and surgical interventions after age 18 with exceptions in some cases. It is not clear if deviations from this approach would lead to the same or different outcomes. Longitudinal studies are currently underway to better define outcomes as well as the safety and efficacy of gender-affirming treatments in youth (Olson-Kennedy, Garofalo et al., 2019; Olson-Kennedy, Rosenthal et al., 2019). While the long-term effects of gender-affirming treatments initiated in adolescence are not fully known, the potential negative health consequences of delaying treatment should also be considered (de Vries et al., 2021). As the evidence base regarding outcomes of gender-affirming interventions in youth continues to grow, recommendations on the timing and readiness for these interventions may be updated.

Previous guidelines regarding gender-affirming treatment of adolescents recommended partially reversible GAHT could be initiated at approximately 16 years of age (Coleman et al., 2012; Hembree et al., 2009). More recent guidelines suggest there may be compelling reasons to initiate GAHT prior to the age of 16, although there are limited studies on youth who have initiated hormones prior to 14 years of age (Hembree et al., 2017). A compelling reason for earlier initiation of GAHT, for example, might be to avoid prolonged pubertal suppression, given potential bone health concerns and the psychosocial implications of delaying puberty as described in more detail in Chapter 12—Hormone Therapy (Klink, Caris et al., 2015; Schagen et al., 2020; Vlot et al., 2017; Zhu & Chan, 2017). Puberty is a time of significant brain and cognitive development. The potential neurodevelopmental impact of extended pubertal suppression in gender diverse youth has been specifically identified as an area in need of continued study (Chen et al., 2020). While GnRH analogs have been shown to be safe when used for the treatment of precocious puberty, there are concerns delaying exposure to sex hormones (endogenous or exogenous) at a time of peak bone mineralization may lead to decreased bone mineral density. The potential decrease in bone mineral density as well as the clinical significance of any decrease requires continued study (Klink, Caris et al., 2015; Lee, Finlayson et al.,

2020; Schagen et al., 2020). The potential negative psychosocial implications of not initiating puberty with peers may place additional stress on gender diverse youth, although this has not been explicitly studied. When considering the timing of initiation of gender-affirming hormones, providers should compare the potential physical and psychological benefits and risks of starting treatment with the potential risks and benefits of delaying treatment. This process can also help identify compelling factors that may warrant an individualized approach.

Studies carried out with trans masculine youth have demonstrated chest dysphoria is associated with higher rates of anxiety, depression, and distress and can lead to functional limitations, such as avoiding exercising or bathing (Mehringer et al., 2021; Olson-Kennedy, Warus et al., 2018; Sood et al., 2021). Testosterone unfortunately does little to alleviate this distress, although chest masculinization is an option for some individuals to address this distress long-term. Studies with youth who sought chest masculinization surgery to alleviate chest dysphoria demonstrated good surgical outcomes, satisfaction with results, and minimal regret during the study monitoring period (Marinkovic & Newfield, 2017; Olson-Kennedy, Warus et al., 2018). Chest masculinization surgery can be considered in minors when clinically and developmentally appropriate as determined by a multidisciplinary team experienced in adolescent and gender development (see relevant statements in this chapter). The duration or current use of testosterone therapy should not preclude surgery if otherwise indicated. The needs of some TGD youth may be met by chest masculinization surgery alone. Breast augmentation may be needed by trans feminine youth, although there is less data about this procedure in youth, possibly due to fewer individuals requesting this procedure (Boskey et al., 2019; James, 2016). GAHT, specifically estrogen, can help with development of breast tissue, and it is recommended youth have a minimum of 12 months of hormone therapy, or longer as is surgically indicated, prior to breast augmentation unless hormone therapy is not clinically indicated or is medically contraindicated.

Data are limited on the optimal timing for initiating other gender-affirming surgical treatments in adolescents. This is partly due to the limited access to these treatments, which varies in different geographical locations (Mahfouda et al., 2019). Data indicate rates of gender-affirming surgeries have increased since 2000, and there has been an increase in the number of TGD youth seeking vaginoplasty (Mahfouda et al., 2019; Milrod & Karasic, 2017). A 2017 study of 20 WPATH-affiliated surgeons in the US reported slightly more than half had performed vaginoplasty in minors (Milrod & Karasic, 2017). Limited data are available on the outcomes for youth undergoing vaginoplasty. Small studies have reported improved psychosocial functioning and decreased gender dysphoria in adolescents who have undergone vaginoplasty (Becker et al., 2018; Cohen-Kettenis & van Goozen, 1997; Smith et al.,2001). While the sample sizes are small, these studies suggest there may be a benefit for some adolescents to having these procedures performed before the age of 18. Factors that may support pursuing these procedures for youth under 18 years of age include the increased availability of support from family members, greater ease of managing postoperative care prior to transitioning to tasks of early adulthood (e.g., entering university or the workforce), and safety concerns in public spaces (i.e., to reduce transphobic violence) (Boskey et al., 2018; Boskey et al., 2019; Mahfouda et al., 2019). Given the complexity and irreversibility of these procedures, an assessment of the adolescent's ability to adhere to postsurgical care recommendations and to comprehend the long-term impacts of these procedures on reproductive and sexual function is crucial (Boskey et al., 2019). Given the complexity of phalloplasty, and current high rates of complications in comparison to other gender-affirming surgical treatments, it is not recommended this surgery be considered in youth under 18 at this time (see Chapter 13—Surgery and Postoperative Care).

Additional key factors that should be taken into consideration when discussing the timing of interventions with youth and families are addressed in detail in statements 6.12a-f. For a summary of the criteria/recommendations for medically necessary gender-affirming medical treatment in adolescents, see Appendix D.

CHAPTER 7 Children

These Standards of Care pertain to prepubescent gender diverse children and are based on research, ethical principles, and accumulated expert knowledge. The principles underlying these standards include the following 1) childhood gender diversity is an expected aspect of general human development (Endocrine Society and Pediatric Endocrine Society, 2020; Telfer et al., 2018); 2) childhood gender diversity is not a pathology or mental health disorder (Endocrine Society and Pediatric Endocrine Society, 2020; Oliphant et al., 2018; Telfer et al., 2018); 3) diverse gender expressions in children cannot always be assumed to reflect a transgender identity or gender incongruence (Ehrensaft, 2016; Ehrensaft, 2018; Rael et al., 2019); 4) guidance from mental health professionals (MHPs) with expertise in gender care for children can be helpful in supporting positive adaptation as well as discernment of gender-related needs over time (APA, 2015; Ehrensaft, 2018; Telfer et al., 2018); 5) conversion therapies for gender diversity in children (i.e., any "therapeutic" attempts to compel a gender diverse child through words, actions, or both to identify with, or behave in accordance with, the gender associated with the sex assigned at birth are harmful and we repudiate their use (APA, 2021; Ashley, 2019b, Paré, 2020; SAMHSA, 2015; Telfer et al., 2018; UN Human Rights Council, 2020).

Throughout the text, the term "health care professional" (HCP) is used broadly to refer to professionals working with gender diverse children. Unlike pubescent youth and adults, prepubescent gender diverse children are not eligible to access medical intervention (Pediatric Endocrine Society, 2020); therefore, when professional input is sought, it is most likely to be from an HCP specialized in psychosocial supports and gender development. Thus, this chapter is uniquely focused on developmentally appropriate psychosocial practices, although other HCPs, such as pediatricians and family practice HCPs may also find these standards useful as they engage in professional work with gender diverse children and their families.

This chapter employs the term "gender diverse" given that gender trajectories in prepubescent children cannot be predicted and may evolve over time (Steensma, Kreukels et al., 2013). At the same time, this chapter recognizes some children will remain stable in a gender identity they articulate early in life that is discrepant from the sex assigned at birth (Olson et al., 2022). The term, "gender diverse" includes transgender binary and nonbinary children, as well as gender diverse children who will ultimately not identify as transgender later in life. Terminology is inherently culturally bound and evolves over time. Thus, it is possible terms used here may become outdated and we will find better descriptors.

This chapter describes aspects of medical necessary care intended to promote the well-being and gender-related needs of children (see medically necessary statement in the Global Applicability chapter, Statement 2.1). This chapter advocates everyone employs these standards, to the extent possible. There may be situations or locations in which the recommended resources are not fully available. HCPs/teams lacking resources need to work toward meeting these standards. However, if unavoidable limitations preclude components of these recommendations, this should not hinder providing the best services currently available. In those locations where some but not all recommended services exist, choosing not to implement potentially beneficial care services risks harm to a child (Murchison et al., 2016; Telfer et al., 2018; Riggs et al., 2020). Overall, it is imperative to prioritize a child's best interests.

A vast empirical psychological literature indicates early childhood experiences frequently set the stage for lifelong patterns of risk and/or resilience and contribute to a trajectory of development more or less conducive to well-being and a positive quality of life (Anda et al., 2010; Masten & Cicchetti, 2010; Shonkoff & Garner, 2012). The available research indicates, in general, gender diverse youth are at greater risk for experiencing psychological difficulties (Ristori & Steensma, 2016) than age- matched cisgender peers as a result of encountering destructive experiences, including trauma and maltreatment stemming from gender diversity-related rejection and other harsh, non-accepting interactions (Barrow & Apostle, 2018; Giovanardi et al., 2018; Gower, Rider, Brown et al., 2018; Grossman & D'Augelli, 2006; Hendricks & Testa, 2012; Reisner, Greytak

et al., 2015; Roberts et al., 2014; Tishelman & Neumann-Mascis, 2018). Further, literature indicates prepubescent children who are well accepted in their gender diverse identities are generally well-adjusted (Malpas et al., 2018; Olson et al., 2016). Assessment and treatment of children typically emphasizes an *ecological* approach, recognizing children need to be safe and nurtured in each setting they frequent (Belsky, 1993; Bronfenbrenner, 1979; Kaufman & Tishelman, 2018; Lynch & Cicchetti, 1998; Tishelman et al., 2010; Zielinski & Bradshaw, 2006). Thus, the perspective of this chapter draws on basic psychological literature and knowledge of the unique risks to gender diverse children and emphasizes the integration of an ecological approach to understanding their needs and to facilitating positive mental health in all gender care. This perspective prioritizes fostering well-being and quality of life for a child throughout their development. Additionally, this chapter also embraces the viewpoint, supported by the substantial psychological research cited above, that psychosocial gender-affirming care (Hidalgo et al., 2013) for prepubescent children offers a window of opportunity to promote a trajectory of well-being that will sustain them over time and during the transition to adolescence. This approach potentially can mitigate some of the common mental health risks faced by transgender and gender diverse (TGD) teens, as frequently described in literature (Chen et al., 2021; Edwards-Leeper et al., 2017; Haas et al., 2011; Leibowitz & de Vries, 2016; Reisner, Bradford et al., 2015; Reisner, Greytak et al., 2015).

Developmental research has focused on understanding various aspects of gender development in the earliest years of childhood based on a general population of prepubescent children. This research has typically relied on the assumption that child research participants are cisgender (Olezeski et al., 2020) and has reported gender identity stability is established in the preschool years for the general population of children, most of whom are likely not gender diverse (Kohlberg, 1966; Steensma, Kreukels et al., 2013). Recently, developmental research has demonstrated gender diversity can be observed and identified in young prepubescent children (Fast & Olson, 2018; Olson & Gülgöz, 2018; Robles et al., 2016). Nonetheless, empirical study in this area is limited, and at this time there are no psychometrically sound assessment measures capable of reliably and/or fully ascertaining a prepubescent child's self-understanding of their own gender and/or gender-related needs and preferences (Bloom et al., 2021). Therefore, this chapter emphasizes the importance of a nuanced and individualized clinical approach to gender assessment, consistent with the recommendations from various guidelines and literature (Berg & Edwards-Leeper, 2018; de Vries & Cohen-Kettenis, 2012; Ehrensaft, 2018; Steensma & Wensing-Kruger, 2019). Research and clinical experience have indicated gender diversity in prepubescent children may, for some, be fluid; there are no reliable means of predicting an individual child's gender evolution (Edwards-Leeper et al., 2016; Ehrensaft, 2018; Steensma, Kreukels et al., 2013), and the gender-related needs for a particular child may vary over the course of their childhood.

It is important to understand the meaning of the term "assessment" (sometimes used synonymously with the term "evaluation"). There are multiple contexts for assessment (Krishnamurthy et al., 2004) including rapid assessments that take place during an immediate crisis (e.g., safety assessment when a child may be suicidal) and focused assessments when a family may have a circumscribed question, often in the context of a relatively brief consultation (Berg & Edwards-Leeper, 2018). The term assessment is also often used in reference to "diagnostic assessment," which can also be called an "intake" and is for the purpose of determining whether there is an issue that is diagnosable and/or could benefit from a therapeutic process. This chapter focus on comprehensive assessments, useful for understanding a child and family's needs and goals (APA, 2015; de Vries & Cohen-Kettenis, 2012; Srinath et al., 2019; Steensma & Wensing-Kruger, 2019). This type of psychosocial assessment is not necessary for all gender diverse children, but may be requested for a number of reasons. Assessments may present a useful opportunity to start a process of support for a gender diverse child and their family, with the understanding that gender diverse children benefit when their family dynamics include

Statements of Recommendations

7.1- We recommend health care professionals working with gender diverse children receive training and have expertise in gender development and gender diversity in children and possess a general knowledge of gender diversity across the life span.
7.2- We recommend health care professionals working with gender diverse children receive theoretical and evidenced-based training and develop expertise in general child and family mental health across the developmental spectrum.
7.3- We recommend health care professionals working with gender diverse children receive training and develop expertise in autism spectrum disorders and other neurodiversity or collaborate with an expert with relevant expertise when working with autistic/neurodivergent, gender diverse children.
7.4- We recommend health care professionals working with gender diverse children engage in continuing education related to gender diverse children and families.
7.5- We recommend health care professionals conducting an assessment with gender diverse children access and integrate information from multiple sources as part of the assessment.
7.6- We recommend health care professionals conducting an assessment with gender diverse children consider relevant developmental factors, neurocognitive functioning, and language skills.
7.7- We recommend health care professionals conducting an assessment with gender diverse children consider factors that may constrain accurate reporting of gender identity/gender expression by the child and/or family/caregiver(s).
7.8- We recommend health care professionals consider consultation, psychotherapy, or both for a gender diverse child and family/caregivers when families and health care professionals believe this would benefit the well-being and development of a child and/or family.
7.9- We recommend health care professionals offering consultation, psychotherapy, or both to gender diverse children and families/caregivers work with other settings and individuals important to the child to promote the child's resilience and emotional well-being.
7.10- We recommend health care professionals offering consultation, psychotherapy, or both to gender diverse children and families/caregivers provide both parties with age-appropriate psychoeducation about gender development.
7.11- We recommend that health care professionals provide information to gender diverse children and their families/caregivers as the child approaches puberty about potential gender affirming medical interventions, the effects of these treatments on future fertility, and options for fertility preservation.
7.12- We recommend parents/caregivers and health care professionals respond supportively to children who desire to be acknowledged as the gender that matches their internal sense of gender identity.
7.13- We recommend health care professionals and parents/caregivers support children to continue to explore their gender throughout the pre-pubescent years, regardless of social transition.
7.14- We recommend the health care professionals discuss the potential benefits and risks of a social transition with families who are considering it.
7.15- We suggest health care professionals consider working collaboratively with other professionals and organizations to promote the well-being of gender diverse children and minimize the adversities they may face.

acceptance of their gender diversity and parenting guidance when requested. Comprehensive assessments are appropriate when solicited by a family requesting a full understanding of the child's gender and mental health needs in the context of gender diversity.

In these circumstances, family member mental health issues, family dynamics, and social and cultural contexts, all of which impact a gender diverse child, should be taken into consideration (Barrow & Apostle, 2018; Brown & Mar, 2018; Cohen-Kettenis et al., 2003; Hendricks & Testa, 2012; Kaufman & Tishelman, 2018; Ristori & Steensma, 2016; Tishelman & Neumann-Mascis, 2018). This is further elaborated upon in the text below.

It is important HCPs working with gender diverse children strive to understand the child and the family's various aspects of identity and experience: racial, ethnic, immigrant/refugee status, religious, geographic, and socio-economic, for example, and be respectful and sensitive to cultural context in clinical interactions (Telfer et al., 2018). Many factors may be relevant to culture and gender, including religious beliefs, gender-related expectations, and the degree to which gender diversity is accepted (Oliphant et al., 2018). Intersections between gender diversity, sociocultural diversity, and minority statuses can be sources of strength, social stress, or both (Brown & Mar, 2018; Oliphant et al., 2018; Riggs & Treharne, 2016).

Each child, family member, and family dynamic is unique and potentially encompasses multiple cultures and belief patterns. Thus, HCPs of all disciplines should avoid stereotyping based on preconceived ideas that may be incorrect or biased (e.g., that a family who belongs to a religious organization that is opposed to appreciating gender diversity will necessarily be unsupportive of their child's gender diversity) (Brown & Mar, 2018). Instead, it is essential to approach each family openly and understand each family member and family pattern as distinct.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 7.1

We recommend the health care professionals working with gender diverse children receive training and have expertise in gender development and gender diversity in children and possess general knowledge of gender diversity across the life span.

HCPs working with gender diverse children should acquire and maintain the necessary training and credentials relevant to the scope of their role as professionals. This includes licensure, certification, or both by appropriate national and/or regional accrediting bodies. We recognize the specifics of credentialing and regulation of professionals vary globally. Importantly, basic licensure, certification, or both may be insufficient in and of itself to ensure competency working with gender diverse children, as HCPs specifically require in-depth training and supervised experience in childhood gender development and gender diversity to provide appropriate care.

Statement 7. 2

We recommend health care professionals working with gender diverse children receive theoretical and evidenced-based training and develop expertise in general child and family mental health across the developmental spectrum.

HCPs should receive training and supervised expertise in general child and family mental health across the developmental spectrum from toddlerhood through adolescence, including evidence-based assessment and intervention approaches. Gender diversity is not a mental health disorder; however, as cited above, we know mental health can be adversely impacted for gender diverse children (e.g., through gender minority stress) (Hendricks & Testa, 2012) that may benefit from exploration and support; therefore, mental health expertise is highly recommended. Working with children is a complex endeavor, involving an understanding of a child's developmental needs at various ages, the ability to comprehend the forces impacting a child's well-being both inside and outside the family (Kaufman & Tishelman, 2018), and an ability to fully assess when a child is unhappy or experiencing significant mental health difficulties, related or unrelated to gender. Research has indicated high levels of adverse experiences and trauma in the gender diverse community of children, including susceptibility to rejection or even maltreatment (APA, 2015; Barrow & Apostle, 2018; Giovanardi et al., 2018; Reisner, Greytak et al., 2015; Roberts et al., 2012; Tishelman & Neumann-Mascis, 2018). HCPs need to be cognizant of the potential for adverse experiences and be able to initiate effective interventions to prevent harm and promote positive well-being.

Statement 7.3

We recommend health care professionals working with gender diverse children receive training and develop expertise in autism spectrum disorders and other neurodiversity or collaborate with an expert with relevant expertise when working with autistic/neurodivergent, gender diverse children.

The experience of gender diversity in autistic children as well as in children with other forms of neurodivergence may present extra clinical complexities (de Vries et al., 2010; Strang, Meagher et al., 2018). For example, autistic children may find it difficult to self-advocate for their gender-related needs and may communicate in highly individualistic ways (Kuvalanka et al., 2018; Strang, Powers et al., 2018). They may have varied interpretations of gender-related experiences given common differences in communication and thinking style. Because of the unique needs of gender diverse neurodivergent children, they may be at high risk for being misunderstood (i.e., for their communications to be misinterpreted). Therefore, professionals providing support to these children can best serve them by receiving training and developing expertise in autism and related neurodevelopmental presentations and/or collaborating with autism specialists (Strang, Meagher et al., 2018). Such training is especially relevant as research has documented

higher rates of autism among gender diverse youth than in the general population (de Vries et al., 2010; Hisle-Gorman et al., 2019; Shumer et al., 2015).

Statement 7.4

We recommend health care professionals working with gender diverse children engage in continuing education related to gender diverse children and families.

Continuing professional development regarding gender diverse children and families may be acquired through various means, including through readings (journal articles, books, websites associated with gender knowledgeable organizations), attending on-line and in person trainings, and joining peer supervision/consultation groups (Bartholomaeus et al., 2021).

Continuing education includes 1) maintaining up-to-date knowledge of available and relevant research on gender development and gender diversity in prepubescent children and gender diversity across the life span; 2) maintaining current knowledge regarding best practices for assessment, support, and treatment approaches with gender diverse children and families. This is a relatively new area of practice and health care professionals need to adapt as new information emerges through research and other avenues (Bartholomaeus et al., 2021).

Statement 7.5

We recommend health care professionals conducting an assessment with gender diverse children access and integrate information from multiple sources as part of the assessment.

A comprehensive assessment, when requested by a family and/or an HCP can be useful for developing intervention recommendations, as needed, to benefit the well-being of the child and other family members. Such an assessment can be beneficial in a variety of situations when a child and/or their family/guardians, in coordination with providers, feel some type of intervention would be helpful. Neither assessments nor interventions should ever be used as a means of covertly or overtly discouraging a child's gender diverse expressions or identity. Instead, with appropriately trained providers, assessment can be an effective means of better understanding how to support a child and their family without privileging any particular gender identity or expression. An assessment can be especially important for some children and their families by collaborating to promote a child's gender health, well-being, and self-fulfillment.

A comprehensive assessment can facilitate the formation of an individualized plan to assist a gender diverse prepubescent children and family members (de Vries & Cohen-Kettenis, 2012; Malpas et al., 2018; Steensma & Wensing-Kruger, 2019; Telfer et al., 2018; Tishelman & Kaufman, 2018). In such an assessment, integrating information from multiple sources is important to 1) best understand the child's gender needs and make recommendations; and 2) identify areas of child, family/caregiver, and community strengths and supports specific to the child's gender status and development as well as risks and concerns for the child, their family/caregivers and environment. Multiple informants for both evaluation and support/intervention planning purposes may include the child, parents/caregivers, extended family members, siblings, school personnel, HCPs, the community, broader cultural and legal contexts and other sources as indicated (Berg & Edwards-Leeper, 2018; Srinath, 2019).

An HCP conducting an assessment of gender diverse children needs to explore gender-related issues but must also take a broad view of the child and the environment, consistent with the ecological model described above (Bronfenbrenner, 1979) to fully understand the factors impacting a child's well-being and areas of gender support and risk (Berg & Edwards-Leeper, 2018; Hendricks & Testa, 2012; Kaufman & Tishelman, 2018; Tishelman & Neumann-Mascis, 2018). This includes understanding the strengths and challenges experienced by the child/family and that are present in the environment. We advise HCPs conducting an assessment with gender diverse children to consider incorporating multiple assessment domains, depending on the child and the family's needs and circumstances. Although some of the latter listed domains below do not directly address the child's gender (see items 7–12 below), they need to be accounted for in a gender assessment, as indicated by clinical judgment, to understand the complex web of factors

that may be affecting the child's well-being in an integrated fashion, including gender health, consistent with evaluation best practices a (APA, 2015; Berg & Edwards-Leeper, 2018; Malpas et al., 2018) and develop a multi-pronged intervention when needed.

Summarizing from relevant research and clinical expertise, assessment domains often include 1) a child's asserted gender identity and gender expression, currently and historically; 2) evidence of dysphoria, gender incongruence, or both; 3) strengths and challenges related to the child, family, peer and others' beliefs and attitudes about gender diversity, acceptance and support for child; 4) child and family experiences of gender minority stress and rejection, hostility, or both due to the child's gender diversity; 5) level of support related to gender diversity in social contexts (e.g., school, faith community, extended family); 6) evaluation of conflict regarding the child's gender and/or parental/caregiver/sibling concerning behavior related to the child's gender diversity; 7) child mental health, communication and/or cognitive strengths and challenges, neurodivergence, and/or behavioral challenges causing significant functional difficulty; 8) relevant medical and developmental history; 9) areas that may pose risks (e.g., exposure to domestic and/or community violence, any form of child maltreatment; history of trauma; safety and/or victimization with peers or in any other setting; suicidality); 10) co-occurring significant family stressors, such as chronic or terminal illness, homelessness or poverty; 11) parent/caregiver and/or sibling mental health and/or behavioral challenges causing significant functional difficulty; and 12) child's and family's strengths and challenges.

A thorough assessment incorporating multiple forms of information gathering is helpful for understanding the needs, strengths, protective factors, and risks for a specific child and family across environments (e.g., home/school). Methods of information gathering often include 1) interviews with the child, family members and others (e.g., teachers), structured and unstructured; 2) caregiver and child completed standardized measures related to gender; general child well-being; child cognitive and communication skills and developmental disorders/disabilities; support and acceptance by parent/caregiver, sibling, extended family and peers; parental stress; history of childhood adversities; and/or other issues as appropriate (APA, 2020; Berg & Edwards-Leeper, 2018; Kaufman & Tishelman, 2018; Srinath, 2019).

Depending on the family characteristics, the developmental profile of the child, or both, methods of information gathering also may also benefit from including the following 1) child and/or family observation, structured and unstructured; and 2) structured and visually supported assessment techniques (worksheets; self-portraits; family drawings, etc.) (Berg & Edwards-Leeper, 2018).

Statement 7.6

We recommend that health care professionals conducting an assessment with gender diverse children consider relevant developmental factors, neurocognitive functioning and language skills.

Given the complexities of assessing young children who, unlike adults, are in the process of development across a range of domains (cognitive, social, emotional, physiological), it is important to consider the developmental status of a child and gear assessment modalities and interactions to the individualized abilities of the child. This includes tailoring the assessment to a child's developmental stage and abilities (preschoolers, school age, early puberty prior to adolescence), including using language and assessment approaches that prioritize a child's comfort, language skills, and means of self-expression (Berg & Edwards-Leeper, 2018; Srinath, 2019). For example, relevant developmental factors, such as neurocognitive differences (e.g., autism spectrum conditions), and receptive and expressive language skills should be considered in conducting the assessment. Health care professionals may need to consult with specialists for guidance in cases in which they do not possess the specialized skills themselves (Strang et al., 2021).

Statement 7.7

We recommend health care professionals conducting an assessment with gender diverse children consider factors that may constrain accurate reporting of gender identity/gender expression by the child and/or family/caregiver(s).

HCPs conducting an assessment with gender diverse children and families need to account for developmental, emotional, and environmental factors that may constrain a child's, caregiver's, sibling or other's report or influence their belief systems related to gender (Riggs & Bartholomaeus, 2018). As with all child psychological assessments, environmental and family/caregiver reactions (e.g., punishment), and/or cognitive and social factors may influence a child's comfort and/or ability to directly discuss certain factors, including gender identity and related issues (Srinath, 2019). Similarly, family members may feel constrained in freely expressing their concerns and ideas depending on family conflicts or dynamics and/or other influences (e.g., cultural/religious; extended family pressure) (Riggs & Bartholomaeus, 2018).

Statement 7.8

We recommend health care professionals consider consultation, psychotherapy, or both for a gender diverse child and family/caregivers when families and health care professionals believe this would benefit the well-being and development of a child and/or family.

The goal of psychotherapy should never be aimed at modifying a child's gender identity (APA, 2021; Ashley, 2019b; Paré, 2020; SAMHSA, 2015; UN Human Rights Council, 2020), either covertly or overtly. Not all gender diverse children or their families need input from MHPs as gender diversity is not a mental health disorder (Pediatric Endocrine Society, 2020; Telfer et al., 2018). Nevertheless, it is often appropriate and helpful to seek psychotherapy when there is distress or concerns are expressed by parents to improve psychosocial health and prevent further distress (APA, 2015). Some of the common reasons for considering psychotherapy for a gender diverse child and family include the following 1) A child is demonstrating significant conflicts, confusion, stress or distress about their gender identity or needs a protected space to explore their gender (Ehrensaft, 2018; Spivey and Edwards-Leeper, 2019); 2) A child is experiencing external pressure to express their gender in a way that conflicts with their self-knowledge, desires, and beliefs (APA, 2015); 3) A child is struggling with mental health concerns, related to or independent of their gender (Barrow & Apostle, 2018); 4) A child would benefit from strengthening their resilience in the face of negative environmental responses to their gender identity or presentation (Craig & Auston, 2018; Malpas et al., 2018); 5) A child may be experiencing mental health and/or environmental concerns, including family system problems that can be misinterpreted as gender congruence or incongruence (Berg & Edwards-Leeper, 2018); and 6) A child expresses a desire to meet with an MHP to get gender-related support. In these situations, the psychotherapy will focus on supporting the child with the understanding that the child's parent(s)/caregiver(s) and potentially other family members will be included as necessary (APA, 2015; Ehrensaft, 2018; McLaughlin & Sharp, 2018). Unless contraindicated, it is extremely helpful for parents/guardians to participate in some capacity in the psychotherapy process involving prepubescent children as family factors are often central to a child's well-being. Although relatively unexplored in research involving gender diverse children, it may be important to attend to the relationship between siblings and the gender diverse child (Pariseau et al., 2019; Parker & Davis-McCabe, 2021).

HCPs should employ interventions tailor-made to the individual needs of the child that are designed to 1) foster protective social and emotional coping skills to promote resilience in the face of potential negative reactions to the child's gender identity, expressions, or both (Craig & Austin, 2016; Malpas et al., 2018; Spencer, Berg et al., 2021); 2) collaboratively problem-solve social challenges to reduce gender minority stress (Barrow & Apostle, 2018; Tishelman & Neumann-Mascis, 2018); 3) strengthen environmental supports for the child and/or members of the immediate and extended family (Kaufman & Tishelman, 2018); and 4) provide the child an opportunity to further understand their internal gender experiences (APA, 2015; Barrow& Apostle, 2018; Ehrensaft, 2018; Malpas et al., 2018; McLaughlin & Sharp, 2018). It is helpful for HCPs to develop a relationship with a gender diverse child and family that can endure over time as needed. This enables the child/family to establish a long-term trusting relationship throughout childhood whereby the HCP can offer support and guidance as a child matures and as potentially

different challenges or needs emerge for the child/family (Spencer, Berg et al., 2021; Murchison et al., 2016). In addition to the above and within the limits of available resources, when a child is neurodivergent, an HCP who has the skill set to address both neurodevelopmental differences and gender is most appropriate (Strang et al., 2021).

As outlined in the literature, there are numerous reasons parents/caregivers, siblings, and extended family members of a prepubescent child may find it useful to seek psychotherapy for themselves (Ehrensaft, 2018; Malpas et al., 2018; McLaughlin & Sharp, 2018). As summarized below, some of these common catalysts for seeking such treatment occur when one or more *family members* 1) desire education around gender development (Spivey & Edwards-Leeper, 2019); 2) are experiencing significant confusion or stress about the child's gender identity, expression, or both (Ashley, 2019c; Ehrensaft, 2018); 3) need guidance related to emotional and behavioral concerns regarding the gender diverse child (Barrow & Apostle, 2018; 4) need support to promote affirming environments outside of the home (e.g., school, sports, camps) (Kaufman & Tishelman, 2018); 5) are seeking assistance to make informed decisions about social transition, including how to do so in a way that is optimal for a child's gender development and health (Lev & Wolf-Gould, 2018); 6) are seeking guidance for dealing with condemnation from others, including political entities and accompanying legislation, regarding their support for their gender diverse child (negative reactions directed toward parents/caregivers can sometimes include rejection and/or harassment/abuse from the social environment arising from affirming decisions (Hidalgo & Chen, 2019); 7) are seeking to process their own emotional reactions and needs about their child's gender identity, including grief about their child's gender diversity and/or potential fears or anxieties for their child's current and future well-being (Pullen Sansfaçon et al., 2019); and 8) are emotionally distressed and/or in conflict with other family members regarding the child's gender diversity (as needed, HCPs can provide separate sessions for parents/caregivers, siblings and extended family members for support, guidance, and/or psychoeducation) (McLaughlin & Sharp, 2018; Pullen Sansfaçon et al., 2019; Spivey & Edwards-Leeper, 2019).

Statement 7.9

We recommend health care professionals offering consultation, psychotherapy, or both to gender diverse children and families/caregivers work with other settings and individuals important to the child to promote the child's resilience and emotional well-being.

Consistent with the ecological model described above and, as appropriate, based on individual/family circumstances, it can be extremely helpful for HCPs to prioritize coordination with important others (e.g., teachers, coaches, religious leaders) in a child's life to promote emotional and physical safety across settings (e.g., school settings, sports and other recreational activities, faith-based involvement) (Kaufman & Tishelman, 2018). Therapeutic and/or support groups are often recommended as a valuable resource for families/caregivers and/or gender diverse children themselves (Coolhart, 2018; Horton et al., 2021; Malpas et al., 2018; Murchison et al., 2016).

Statement 7.10

We recommend HCPs offering consultation, psychotherapy, or both to gender diverse children and families/caregivers provide both parties with age appropriate psycho-education about gender development.

Parents/caregivers and their gender diverse child should have the opportunity to develop knowledge regarding ways in which families/caregivers can best support their child to maximize resilience, self-awareness, and functioning (APA, 2015; Ehrensaft, 2018; Malpas, 2018; Spivey & Edwards-Leeper, 2019). It is neither possible nor is it the role of the HCP to predict with certainty the child's ultimate gender identity; instead, the HCP's task is to provide a safe space for the child's identity to develop and evolve over time without attempts to prioritize any particular developmental trajectory with regard to gender (APA, 2015; Spivey & Edwards-Leeper, 2019). Gender diverse children and early adolescents have different needs and experiences than older adolescents, socially and physiologically, and those differences should be reflected in the individualized approach HCPs

provide to each child/family (Keo-Meir & Ehrensaft, 2018; Spencer, Berg et al., 2021).

Parents/caregivers and their children should also have the opportunity to develop knowledge about gender development and gender literacy through age-appropriate psychoeducation (Berg & Edwards-Leeper, 2018; Rider, Vencill et al., 2019; Spencer, Berg et al., 2021). Gender literacy involves understanding the distinctions between sex designated at birth, gender identity, and gender expression, including the ways in which these three factors uniquely come together for a child (Berg & Edwards-Leeper, 2018; Rider, Vencill et al., 2019; Spencer, Berg et al., 2021). As a child gains gender literacy, they begin to understand their body parts do not necessarily define their gender identity and/or their gender expression (Berg & Edwards-Leeper, 2018; Rider, Vencill et al., 2019; Spencer, Berg et al., 2021). Gender literacy also involves learning to identify messages and experiences related to gender within society. As a child gains gender literacy, they may view their developing gender identity and gender expression more positively, promoting resilience and self-esteem, and diminishing risk of shame in the face of negative messages from the environment. Gaining gender literacy through psychoeducation may also be important for siblings and/or extended family members who are important to the child (Rider, Vencill et al., 2019; Spencer, Berg et al., 2021).

Statement 7.11

We recommend health care professionals provide information to gender diverse children and their families/caregivers as the child approaches puberty about potential gender-affirming medical interventions, the effects of these treatments on future fertility, and options for fertility preservation.

As a child matures and approaches puberty, HCPs should prioritize working with children and their parents/caregivers to integrate psychoeducation about puberty, engage in shared decision-making about potential gender-affirming medical interventions, and discuss fertility-related and other reproductive health implications of medical treatments (Nahata, Quinn et al., 2018; Spencer, Berg et al., 2021). Although only limited empirical research exists to evaluate such interventions, expert consensus and developmental psychological literature generally support the notion that open communication with children about their bodies and preparation for physiological changes of puberty, combined with gender-affirming acceptance, will promote resilience and help to foster positive sexuality as a child matures into adolescence (Spencer, Berg et al., 2019). All these discussions may be extended (e.g., starting earlier) to include neurodivergent children, to ensure there is enough time for reflection and understanding, especially as choices regarding future gender- affirming medical care potentially arise (Strang, Jarin et al., 2018). These discussions could include the following topics:

- Review of body parts and their different functions;
- The ways in which a child's body may change over time with and without medical intervention;
- The impact of medical interventions on later sexual functioning and fertility;
- The impact of puberty suppression on potential later medical interventions;
- Acknowledgment of the current lack of clinical data in certain areas related to the impacts of puberty suppression;
- The importance of appropriate sex education prior to puberty.

These discussions should employ developmentally appropriate language and teaching styles, and be geared to the specific needs of each individual child (Spencer, Berg et al., 2021).

Statement 7.12

We recommend parents/caregivers and health care professionals respond supportively to children who desire to be acknowledged as the gender that matches their internal sense of gender identity.

Gender social transition refers to a process by which a child is acknowledged by others and has the opportunity to live publicly, either in all situations or in certain situations, in the gender identity they affirm and has no singular set of parameters or actions (Ehrensaft et al., 2018).

Gender social transition has often been conceived in the past as binary—a girl transitions to a boy, a boy to a girl. The concept has expanded to include children who shift to a nonbinary or individually shaped iteration of gender identity (Chew et al., 2020; Clark et al., 2018). Newer research indicates the social transition process may serve a protective function for some prepubescent children and serve to foster positive mental health and well-being (Durwood et al., 2017; Gibson et al., 2021; Olson et al., 2016). Thus, recognition that a child's gender may be fluid and develop over time (Edwards-Leeper et al., 2016; Ehrensaft, 2018; Steensma, Kreukels et al., 2013) is not sufficient justification to negate or deter social transition for a prepubescent child when it would be beneficial. Gender identity evolution may continue even after a partial or complete social transition process has taken place (Ashley, 2019e; Edwards-Leeper et al., 2018; Ehrensaft, 2020; Ehrensaft et al., 2018; Spivey & Edwards-Leeper, 2019). Although empirical data remains limited, existing research has indicated children who are most assertive about their gender diversity are most likely to persist in a diverse gender identity across time, including children who socially transition prior to puberty (Olson et al., 2022; Rae et al., 2019; Steensma, McGuire et al., 2013). Thus, when considering a social transition, we suggest parents/caregivers and HCPs pay particular attention to children who consistently and often persistently articulate a gender identity that does not match the sex designated at birth. This includes those children who may explicitly request or desire a social acknowledgement of the gender that better matches the child's articulated gender identity and/or children who exhibit distress when their gender as they know it is experienced as incongruent with the sex designated at birth (Rae et al., 2019; Steensma, Kreukels et al., 2013).

Although there is a dearth of empirical literature regarding best practices related to the social transition process, clinical literature and expertise provides the following guidance that prioritizes a child's best interests (Ashley, 2019e; Ehrensaft, 2018; Ehrensaft et al, 2018; Murchison et al., 2016; Telfer et al., 2018): 1) social transition should originate from the child and reflect the child's wishes in the process of making the decision to initiate a social transition process; 2) an HCP may assist exploring the advantages/benefits, plus potential challenges of social transition; 3) social transition may best occur in all or in specific contexts/settings only (e.g., school, home); and 4) a child may or may not choose to disclose to others that they have socially transitioned, or may designate, typically with the help of their parents/caregivers, a select group of people with whom they share the information.

In summary, social transition, when it takes place, is likely to best serve a child's well-being when it takes place thoughtfully and individually for each child. A child's social transition (and gender as well) may evolve over time and is not necessarily static, but best reflects the cross-section of the child's established self-knowledge of their present gender identity and desired actions to express that identity (Ehrensaft et al., 2018).

A social transition process can include one or more of a number of different actions consistent with a child's affirmed gender (Ehrensaft et al., 2018), including:

- Name change;
- Pronoun change;
- Change in sex/gender markers (e.g., birth certificate; identification cards; passport; school and medical documentation; etc.);
- Participation in gender-segregated programs (e.g., sports teams; recreational clubs and camps; schools; etc.);
- Bathroom and locker room use;
- Personal expression (e.g., hair style; clothing choice; etc.);
- Communication of affirmed gender to others (e.g., social media; classroom or school announcements; letters to extended families or social contacts; etc.).

Statement 7.13

We recommend health care professionals and parents/caregivers support children to continue to explore their gender throughout the pre-pubescent years, regardless of social transition.

It is important children who have engaged in social transition be afforded the same opportunities as other children to continue considering

meanings and expressions of gender throughout their childhood years (Ashley 2019e; Spencer, Berg et al., 2021). Some research has found children may experience gender fluidity or even detransition after an initial social transition. Research has not been conclusive about when in the life span such detransition is most likely to occur, or what percentage of youth will eventually experience gender fluidity and/or a desire to detransition—due to gender evolution, or potentially other reasons (e.g., safety concerns; gender minority stress) (Olson et al., 2022; Steensma, Kreukels et al., 2013). A recent research report indicates in the US, detransition occurs with only a small percentage of youth five years after a binary social transition (Olson et al., 2022); further follow-up of these young people would be helpful. Replication of these findings is important as well since this study was conducted with a limited and self-selected participant pool in the US and thus may not be applicable to all gender diverse children. In summary, we have limited ability to know in advance the ways in which a child's gender identity and expressions may evolve over time and whether or why detransition may take place for some. In addition, not all gender diverse children wish to explore their gender (Telfer et al., 2018). Cisgender children are not expected to undertake this exploration, and therefore attempts to force this with a gender diverse child, if not indicated or welcomed, can be experienced as pathologizing, intrusive and/or cisnormative (Ansara & Hegarty, 2012; Bartholomaeus et al., 2021; Oliphant et al., 2018).

Statement 7.14

We recommend health care professionals discuss the potential benefits and risks of a social transition with families who are considering it.

Social transition in prepubescent children consists of a variety of choices, can occur as a process over time, is individualized based on both a child's wishes and other psychosocial considerations (Ehrensaft, 2018), and is a decision for which possible benefits and challenges should be weighted and discussed.

A social transition may have potential benefits as outlined in clinical literature (e.g., Ehrensaft et al., 2018) and supported by research (Fast & Olson, 2018; Rae et al., 2019). These include facilitating gender congruence while reducing gender dysphoria and enhancing psychosocial adjustment and well-being (Ehrensaft et al., 2018). Studies have indicated socially transitioned gender diverse children largely mirror the mental health characteristics of age matched cisgender siblings and peers (Durwood et al., 2017). These findings differ markedly from the mental health challenges consistently noted in prior research with gender diverse children and adolescents (Barrow & Apostle, 2018) and suggest the impact of social transition may be positive. Additionally, social transition for children typically can only take place with the support and acceptance of parents/caregivers, which has also been demonstrated to facilitate well-being in gender diverse children (Durwood et al., 2021; Malpas et al., 2018; Pariseau et al., 2019), although other forms of support, such as school-based support, have also been identified as important (Durwood et al., 2021; Turban, King et al., 2021). HCPs should discuss the potential benefits of a social transition with children and families in situations in which 1) there is a consistent, stable articulation of a gender identity that is incongruent with the sex assigned at birth (Fast & Olson, 2018). This should be differentiated from gender diverse expressions/behaviors/interests (e.g., playing with toys, expressing oneself through clothing or appearance choices, and/or engaging in activities socially defined and typically associated with the other gender in a binary model of gender) (Ehrensaft, 2018; Ehrensaft et al., 2018); 2) the child is expressing a strong desire or need to transition to the gender they have articulated as being their authentic gender (Ehrensaft et al., 2018; Fast & Olson, 2018; Rae et al., 2019); and 3) the child will be emotionally and physically safe during and following transition (Brown & Mar, 2018). Prejudice and discrimination should be considerations, especially in localities where acceptance of gender diversity is limited or prohibited (Brown & Mar, 2018; Hendricks & Testa, 2012; Turban, King et al., 2021). Of note, there can also be possible risks to a gender diverse child who does not socially transition, including 1) being ostracized or bullied for being perceived as not conforming to prescribed community

gender roles and/or socially expected patterns of behavior; and 2) living with the internal stress or distress that the gender they know themselves to be is incongruent with the gender they are being asked to present to the world.

To promote gender health, the HCP should discuss the potential challenges of a social transition. One concern often expressed relates to fear that a child will preclude considering the possible evolution of their gender identity as they mature or be reluctant to initiate another gender transition even if they no longer feel their social transition matches their current gender identity (Edwards-Leeper et al., 2016; Ristori & Steensma, 2016). Although limited, recent research has found some parents/caregivers of children who have socially transitioned may discuss with their children the option of new gender iterations (for example, reverting to an earlier expression of gender) and are comfortable about this possibility (Olson et al., 2019). Another often identified social transition concern is that a child may suffer negative sequelae if they revert to the former gender identity that matches their sex designated at birth (Chen et al., 2018; Edwards-Leeper et al., 2019; Steensma & Cohen-Kettenis, 2011). From this point of view, parents/caregivers should be aware of the potential developmental effect of a social transition on a child.

HCPs should provide guidance to parents/caregivers and supports to a child when a social gender transition is being considered or taking place by 1) providing consultation, assessment, and gender supports when needed and sought by the parents/caregivers; 2) aiding family members, as needed, to understand the child's desires for a social transition and the family members' own feelings about the child's expressed desires; 3) exploring with, and learning from, the parents/caregivers whether and how they believe a social transition would benefit their child both now and in their ongoing development; 4) providing guidance when parents/caregivers are not in agreement about a social transition and offering the opportunity to work together toward a consistent understanding of their child's gender status and needs; 5) providing guidance about safe and supportive ways to disclose their child's social transition to others and to facilitate their child transitioning in their various social environments (e.g., schools, extended family); 6) facilitating communication, when desired by the child, with peers about gender and social transition as well as fortifying positive peer relationships; 7) providing guidance when social transition may not be socially accepted or safe, either everywhere or in specific situations, or when a child has reservations about initiating a transition despite their wish to do so; there may be multiple reasons for reservations, including fears and anxieties; 8) working collaboratively with family members and MHPs to facilitate a social transition in a way that is optimal for the child's unfolding gender development, overall well-being, and physical and emotional safety; and 9) providing psychoeducation about the many different trajectories the child's gender may take over time, leaving pathways open to future iterations of gender for the child, and emphasizing there is no need to predict an individual child's gender identity in the future (Malpas et al., 2018).

All of these tasks incorporate enhancing the quality of communication between the child and family members and providing an opportunity for the child to be heard and listened to by all family members involved. These relational processes in turn facilitate the parents/caregivers' success in making informed decisions about the advisability and/or parameters of a social transition for their child (Malpas et al., 2018).

One role of HCPs is to provide guidance and support in situations in which children and parents/caregivers wish to proceed with a social transition but conclude that the social environment would not be accepting of those choices, by 1) helping parents/caregivers define and extend safe spaces in which the child can express their authentic gender freely; 2) discussing with parents/caregivers ways to advocate that increase the likelihood of the social environment being supportive in the future, if this is a realistic goal; 3) intervening as needed to help the child/family with any associated distress and/or shame brought about by the continued suppression of authentic gender identity and the need for secrecy; and 4) building both the child's and the family's resilience, instilling the understanding that if the social environment is having difficulty accepting a child's social transition and affirmed gender identity, it is not because of some shortcoming in the child but because of

insufficient gender literacy in the social environment (Ehrensaft et al., 2018).

Statement 7.15

We suggest health care professionals consider working collaboratively with other professionals and organizations to promote the well-being of gender diverse children and minimize the adversities they may face.

All children have the right to be supported and respected in their gender identities (Human Rights Campaign, 2018; Paré, 2020; SAMHSA, 2015). As noted above, gender diverse children are a particularly vulnerable group (Barrow & Apostle, 2018; Cohen-Kettenis et al., 2003; Giovanardi et al., 2018; Gower, Rider, Coleman et al., 2018; Grossman & D'Augelli, 2007; Hendricks & Testa, 2012; Reisner, Greytak et al., 2015; Ristori & Steensma, 2016; Roberts et al., 2012; Tishelman & Neumann-Mascis, 2018). The responsibilities of HCPs as advocates encompass acknowledging social determinants of health are critical for marginalized minorities (Barrow & Mar, 2018; Hendricks & Testa, 2012). Advocacy is taken up by all HCPs in the form of child and family support (APA, 2015; Malpas et al., 2018). Some HCPs may be called on to move beyond their individual offices or programs to advocate for gender diverse children in the larger community, often in partnership with stakeholders, including parents/caregivers, allies, and youth (Kaufman & Tishelman, 2018; Lopez et al., 2017; Vanderburgh, 2009). These efforts may be instrumental in enhancing children's gender health and promoting their civil rights (Lopez et al., 2017).

HCP's voices may be essential in schools, in parliamentary bodies, in courts of law, and in the media (Kuvalanka et al., 2019; Lopez et al., 2017; Whyatt-Sames, 2017; Vanderburgh, 2009). In addition, HCPs may have a more generalized advocacy role in acknowledging and addressing the frequent intentional or unintentional negating of the experience of gender diverse children that may be transmitted or communicated by adults, peers, and in media (Rafferty et al., 2018). Professionals who possess the skill sets and find themselves in appropriate situations can provide clear de-pathologizing statements on the needs and rights of gender diverse children and on the damage caused by discriminatory and transphobic rules, laws, and norms (Rafferty et al., 2018).

CHAPTER 8 Nonbinary

Nonbinary is used as an umbrella term referring to individuals who experience their gender as outside of the gender binary. The term nonbinary is predominantly but not exclusively associated with global north contexts and may sometimes be used to describe indigenous and non-Western genders. The term nonbinary includes people whose genders are comprised of more than one gender identity simultaneously or at different times (e.g., bigender), who do not have a gender identity or have a neutral gender identity (e.g., agender or neutrois), have gender identities that encompass or blend elements of other genders (e.g., polygender, demiboy, demigirl), and/or who have a gender that changes over time (e.g., genderfluid) (Kuper et al., 2014; Richards et al., 2016; Richards et al., 2017; Vincent, 2019). Nonbinary people may identify to varying degrees with binary-associated genders, e.g., nonbinary man/woman, or with multiple gender terms, e.g., nonbinary and genderfluid (James et al., 2016; Kuper et al., 2012). Nonbinary also functions as a gender identity in its own right (Vincent, 2020). It is important to acknowledge this is not an exhaustive list, the same identities can have different meanings for different people, and the use of terms can vary over time and by location.

Genderqueer, first used in the 1990s, is an identity category somewhat older than nonbinary—which first emerged in approximately the late 2000s (Nestle et al., 2002; Wilchins, 1995). Genderqueer may sometimes be used synonymously with nonbinary or may communicate a specific consciously politicized dimension to a person's gender. While transgender is used in many cultural contexts as an umbrella term inclusive of nonbinary people, not all nonbinary people consider themselves to be transgender for a range of reasons, including because they consider being transgender to be exclusively within the gender binary or because they do not feel "trans enough" to describe themselves as transgender (Garrison, 2018). Some nonbinary people are unsure or ambivalent about whether they would describe themselves as transgender (Darwin, 2020; Vincent, 2019).

In the context of the English language, nonbinary people may use the pronouns they/them/theirs, or neopronouns which include e/em/eir, ze/zir/hir, er/ers/erself among others (Moser & Devereux, 2019; Vincent, 2018). Some nonbinary people use a combination of pronouns (either deliberately mixing usage, allowing free choice, or changing with social context), or prefer to avoid gendered pronouns entirely, instead using their name. Additionally, some nonbinary people use she/her/hers, or he/him/his, sometimes or exclusively, whilst in some regions in the world descriptive language for nonbinary people does not (yet) exist. In contexts outside of English, a wide range of culturally specific linguistic adaptations and evolutions can be observed (Attig, 2022; Kirey-Sitnikova, 2021; Zimman, 2020). Also of note, some languages use one pronoun that is not associated with sex or gender while others gender all nouns. These variations in language are likely to influence nonbinary people's experience of gender and how they interact with others.

Recent studies suggest nonbinary people comprise roughly 25% to over 50% of the larger transgender population, with samples of youth reporting the highest percentage of nonbinary people (Burgwal et al., 2019; James et al., 2016; Watson, 2020). In recent studies of transgender adults, nonbinary people tend to be younger than transgender men and transgender women and in studies of both youth and adults, nonbinary people are more likely to have been assigned female at birth (AFAB). However, these findings should be interpreted with caution as there are likely a number of complex, sociocultural factors influencing the quality, representativeness, and accuracy of this data (Burgwal et al., 2019; James et al., 2016; Watson, 2020; Wilson & Meyer, 2021) (see also Chapter 3—Population Estimates).

Understanding gender identities and gender expressions as a non-linear spectrum

Nonbinary genders have long been recognized historically and cross-culturally (Herdt, 1994; McNabb, 2017; Vincent & Manzano, 2017). Many gender identity categories are culturally specific and cannot be easily translated from their context, either linguistically or in relation to the Western paradigm of gender. Historical settler colonial interactions with indigenous people with

non-Western genders remain highly relevant as cultural erasure and the intersections of racism and cisnormativity may detrimentally inform the social determinants of health of indigenous gender diverse people. From the 1950s, gender was used to reference the socially constructed categorization of behaviors, activities, appearance, etc. in relation to a binary model of male/man/masculine, and female/woman/feminine within contemporary Western contexts. However, gender now has a wider range of possible meanings, appreciating interrelated yet distinguishable concepts, including gendered biology (sex), gender roles, gender expression, and gender identity (Vincent, 2020). Aspects of gender expression that might traditionally be understood culturally as "masculine", "feminine", or "androgynous" may be legitimately expressed among people of any and all gender identities, whether nonbinary or not. For example, a nonbinary individual presenting in a feminine manner cannot be taken to imply they will necessarily later identify as a woman or access interventions associated with transgender women, such as vaginoplasty. A person's gender nonconformity in relation to cultural expectations should neither be viewed as a cause for concern nor assumed to be indicative of clinical complexity—for example, a nonbinary person assigned male at birth (AMAB) wearing feminine-coded clothing, using she/her pronouns, but keeping a masculine-coded first name.

Modeling gender as a spectrum offers greater nuance than a binary model. However, there remain significant limitations in a linear spectrum model that can lead to uncritical generalizations about gender. For example, while it is intuitive to position the "binary options" (man/male, woman/female) at either end of such a continuum, doing so situates masculinity as oppositional to femininity, failing to accommodate gender neutrality, the expression of masculinity and femininity simultaneously, and genderqueer or non-Western concepts of gender. It is essential HCPs do not view nonbinary genders as "partial" articulations of transgender manhood (in nonbinary people AFAB) or transgender womanhood (in nonbinary people AMAB), or definitively as "somewhere along the spectrum of masculinity/femininity"; some nonbinary individuals consider themselves outside male/female dichotomization altogether. A *non-linear* spectrum indicates differences of gender expression, identity, or needs around gender affirmation between clients should not be compared for the purposes of situating them along a linear spectrum. Additionally, the interpretation of gender expression is subjective and culturally defined, and what may be experienced or viewed as highly feminine by one person may not be viewed as such by another (Vincent, 2020). HCPs benefit from avoiding assumptions about how each client conceptualizes their gender and by being prepared to be led by a given client's personal understanding of gender as it relates to the client's gender identity, expression, and any need for medical care.

The gender development process experienced by all transgender and gender diverse (TGD) people regardless of their relationship to a gender binary appear to share similar themes (e.g., awareness, exploration, meaning making, integration), but the timing, progression, and personal experiences associated with each of these processes vary both within and across groups of transgender and nonbinary people (Kuper, Wright et al., 2018; Kuper, Lindley et al., 2019; Tatum et al., 2020). Sociocultural and intersectional perspectives can be helpful at contextualizing gender development and social transition, including how individual experiences are shaped by the social and cultural context and how they interact with additional domains of identity and personal experience.

The need for access to gender-affirming care

Some nonbinary people seek gender-affirming care to alleviate gender dysphoria or incongruence and increase body satisfaction through medically necessary interventions (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1). Some nonbinary people may feel a certain treatment is necessary for them—see also Chapter 5—Assessment of Adults (Beek et al., 2015; Jones et al., 2019; Köhler et al., 2018), whilst others do not (Burgwal & Motmans, 2021; Nieder, Eyssel et al., 2020), and the proportion of nonbinary people who seek gender-affirming care and the specific goals of

that care, remains unclear. It is the role of the health care professional to provide information about existing medical options (and their availability) that might help alleviate gender dysphoria or incongruence and increase body satisfaction without making assumptions about which treatment options may best fit each individual person.

Motivations for accessing (or not accessing) gender-affirming medical interventions, including hormone treatment, surgeries, or both are heterogeneous and potentially complex (Burgwal & Motmans, 2021; Vincent, 2019, 2020) and should be explored collaboratively before making decisions about physical interventions. The need of an individual to access gender-affirming medical procedures cannot be predicted by their gender role, expression, or identity. For example, some transgender women have no need of vaginoplasty, while some nonbinary individuals AMAB may need and benefit from that same intervention. Further, nonbinary people seeking gender-affirming care associated closely with a transition pathway from their assigned sex/gender to the other binarily-recognized category (i.e., estrogen therapy and vaginoplasty for someone AMAB) does not undermine the validity of their nonbinary identity.

While barriers to care remain widespread for many transgender people, nonbinary people appear to experience particularly high rates of difficulty accessing both mental health and gender-affirming medical care (Clark et al., 2018; James, 2016). Many nonbinary people report having experiences with health care professionals who were not affirming of their nonbinary gender, including experiences where health care professionals convey beliefs that their gender is not valid, or they are fundamentally more difficult to provide care for (Valentine, 2016; Vincent, 2020). Nonbinary people may face provider assumptions that they do not need or want gender-affirming treatment (Kcomt et al., 2020; Vincent, 2020) and have described experiencing pressure to present themselves as transgender men or transgender women (within a binary framework of gender) in order to access treatment (Bradford et al., 2019; Taylor et al., 2019). At times, nonbinary people find themselves educating the provider from whom they are seeking services despite the inappropriateness of providers relying primarily on their patients for education (Kcomt et al., 2020). In comparison to transgender men and transgender women, Burgwal and Motmans (2021) found that nonbinary people experienced more fear of prejudice from health care providers, less confidence in the services provided, and greater difficulty knowing where to go to for care. Studies in both Europe and US have shown that nonbinary individuals tend to delay care more often than binary transgender men or transgender women, with fear of insensitive or incompetent treatment being the most cited reason (Burgwal & Motmans, 2021; Grant et al., 2011). Nonbinary people also appear less likely to disclose their gender identity to their health care providers than other transgender people (Kcomt et al., 2020).

The need for an appropriate level of support

Providing gender-affirming care to nonbinary people goes beyond the provision of specific gender-affirming interventions such as hormone therapy or surgery and involves supporting the overall health and development of nonbinary people. Minority stress models have been adapted to conceptualize how the gender-related stressors experienced by transgender people are associated with physical and mental health disparities (Delozier et al., 2020; Testa et al., 2017). Nonbinary people appear to experience minority stressors that are both similar to and unique from those experienced by transgender men and transgender women. Johnson (2020) reported that experiences of invalidation are particularly high among nonbinary people, e.g., statements or actions conveying a belief that nonbinary identities are not "real" or are the result of a "fad" or "phase," and nonbinary people appear less likely than transgender men and transgender women to have their correct pronouns used by others. Similarly, nonbinary people have described feeling "invisible" to others (Conlin, 2019; Taylor, 2018) and one study found that nonbinary youth reported lower levels of self-esteem in comparison to young transgender men and transgender women (Thorne, Witcomb et al., 2019).

While many TGD people report experiences of discrimination, victimization, and interpersonal rejection (James, 2016) including bullying within

samples of youth (Human Rights Campaign, 2018; Witcomb et al., 2019), the prevalence of these experiences may vary across groups and appears influenced by additional intersecting characteristics. For example, Newcomb (2020) found transgender women and nonbinary youth AMAB experienced higher levels of victimization than transgender men and nonbinary youth AFAB, with nonbinary youth AMAB reporting the highest levels of traumatic stress. In a second study, Poquiz (2021) found transgender men and transgender women experienced higher levels of discrimination than nonbinary people. This intersectional complexity is also likely contributing to the variability in findings from studies comparing the physical and mental health of nonbinary and transgender men and transgender women, with some studies indicating more physical and mental health concerns among nonbinary people, some reporting less concerns, and some reporting no difference between groups (Scandurra, 2019).

Given nonbinary identity narratives may be less widely available than more binary-oriented identity narratives, nonbinary people may have less resources available to explore and articulate their gender-related sense of self. For example, this might include access to community spaces and interpersonal relationships where nonbinary identity can be explored, or access to language and concepts that allow more nuanced consideration of nonbinary experiences (Bradford et al., 2018; Fiani & Han, 2019; Galupo et al., 2019). Clinical guidance is now developing to assist providers in adapting gender-affirming therapeutic care to meet these unique experiences of nonbinary people (Matsuno, 2019; Rider, Vencill et al., 2019).

Gender-affirming medical interventions for nonbinary people

In contexts where a particular medical intervention does not have established precedent, it is important that before the intervention is considered, the individual is provided with an overview of the available information, including recognition of potential knowledge limits. It is equally important to undertake and document a comprehensive discussion of the physical changes needed and the potential limitations in achieving those attributes, as well as the implication that any given intervention may or may not enhance an individual's ability to express their gender.

With regards to estrogen therapy for nonbinary people AMAB, it is important to note the possibility of breast growth cannot be avoided (Seal, 2017). Although the extent of growth is highly variable, this should be made clear if a nonbinary person seeks some of the other changes associated with estrogen therapy (such as softening of skin and reduction in facial hair growth) but does not want or is ambivalent about breast growth. Likewise, for nonbinary people AFAB who may wish to access testosterone to acquire some changes but not others, it should be recognized that if facial hair development is needed, genital growth is inevitable (Seal, 2017). The time frame for taking testosterone means these changes are likely also to be accompanied by an irreversible vocal pitch drop, although the extent of each is individual (Vincent, 2019; Ziegler et al., 2018). A vocal pitch drop without the development of body hair is another such challenge. For some nonbinary people, hair removal is a very important part of their gender affirmation (Cocchetti, Ristori, Romani et al., 2020).

If hormonal therapy is discontinued and gonads are retained, many physical changes will revert to pre-hormone therapy status as gonadal hormones once again take effect, including reversal of amenorrhea and body hair development in nonbinary people AFAB and reduction in muscular definition and erectile dysfunction in nonbinary people AMAB. Other changes will be permanent such as "male-pattern" baldness, genital growth, and facial hair growth in nonbinary people AFAB or breast development in nonbinary people AMAB (Hembree et al., 2017). These will require further interventions to reverse, such as electrolysis or mastectomy and are sometimes described as "partially reversible" (Coleman et al., 2012). As the implications of using low-dose hormone therapy are not documented in this patient population, it is important to consider monitoring for cardiovascular risk and bone health if low-dose hormone therapy is used. For more detailed information see Chapter 12—Hormone Therapy.

If neither testosterone nor estrogen expression is needed, inhibition of estrogen and/or testosterone

Statements of Recommendations

8.1- We recommend health care professionals provide nonbinary people with individualized assessment and treatment that affirms their experience of gender.
8.2- We recommend health care professionals consider gender-affirming medical interventions (hormonal treatment or surgery) for nonbinary people in the absence of "social gender transition."
8.3- We recommend health care professionals consider gender-affirming surgical interventions in the absence of hormonal treatment, unless hormone therapy is required to achieve the desired surgical result.
8.4- We recommend health care professionals provide information to nonbinary people about the effects of hormonal therapies/surgery on future fertility and discuss the options for fertility preservation prior to starting hormonal treatment or undergoing surgery.

production is possible. The implications of this with regards to increased cardiovascular risk, reduced bone mineralization, and risk of depression should be discussed and measures taken to mitigate risk (Brett et al., 2007; Vale et al., 2010; Wassersug & Johnson, 2007). For more information see also Chapter 9—Eunuchs and Chapter 12—Hormone Therapy. Exploration of medical and/or social transition independently of each other and options to explore hormones, surgery, or both independently of each other should be available to everyone, whether the person is a transgender man, transgender woman, or a nonbinary person.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 8.1

We recommend health care professionals provide nonbinary people with individualized assessment and treatment that affirms their nonbinary experiences of gender.

An individualized assessment with a nonbinary person starts with an understanding of how they experience their own gender and how this impacts their goals for the care they are seeking. How individuals conceptualize their gender-related experiences are likely to vary across groups and cultures and may incorporate experiences associated with other intersecting aspects of identity (e.g., age, sexuality, race, ethnicity, socioeconomic status, disability status) (Kuper et al., 2014; Subramanian et al., 2016).

HCPs should avoid making a priori assumptions about any client's gender identity, expression, or needs for care. They should also be mindful that a client's nonbinary experience of gender may or may not be relevant to the assessment and treatment-related goals. The extent to which the client's gender is relevant to their treatment goals should determine the level of detail at which their gender identity is explored. For example, when seeking care for a presenting concern wholly unrelated to gender, simply determining the correct name and pronouns may be sufficient (Knutson et al., 2019). When addressing a concern for which current or past hormonal or surgical status is relevant, more detail may be needed, even if the concern is not specifically gender-related.

Clinical settings need to be welcoming, reflective of the diversity of genders, and affirm the experiences of gender of nonbinary people to be culturally competent. Ensuring clinic and provider information (e.g., websites), forms (e.g., intake surveys), and other materials are inclusive of nonbinary identities and experiences conveys that nonbinary people are welcome and recognized (Hagen & Galupo, 2014). Using free text fields for gender identity and pronouns is more inclusive than using a list of response options. Ensuring privacy at the reception desk, setting up alternatives for listing legal names in digital databases (in cultural contexts where this is necessary), installing gender-neutral toilets, and setting up alternatives to calling out the legal name in the waiting room are additional examples of transgender and gender diverse (TGD) cultural competency (Burgwal et al., 2021). In care settings, it is important preferences for names, pronouns, and other gender-related terms are asked and used both initially and on a regular basis as they may vary over time and circumstance.

HCPs are encouraged to adopt an approach that focuses on strengths and resilience.

Increasingly, critiques are emerging regarding HCPs over-focus on gender-related distress as it is also important to consider experiences of increased comfort, joy, and self-fulfilment that can result from self-affirmation and access to care (Ashley, 2019a; Benestad, 2010). In addition to utilizing diagnoses when/where required to facilitate access to care, HCPs are encouraged to collaboratively explore with clients this broader range of potential gender-related experiences and how they may fit with treatment options (Motmans et al., 2019). For all TGD people, resiliency factors such as supportive relationships, participation in communities that include similar others, and identity pride are essential to consider as they are associated with a range of positive health outcomes (Bowling et al., 2019; Budge, 2015; Johns et al., 2018).

Awareness of the limitations that exist in the tools providers have historically used to assess transgender people's experience of dysphoria is important as they may be particularly pronounced for many nonbinary people. Most gender-related measures assume clients experience their gender in a binary way, among other concerns (e.g., Recalled Gender Identity Scale, Utrecht Gender Dysphoria Scale). While several newer measures have been developed in an attempt to better capture the experiences of nonbinary people (McGuire et al., 2018; McGuire et al., 2020), open-ended discussion is likely to provide a deeper and more accurate understanding of each individual's unique experiences of dysphoria and their associated care needs. Similarly, while more recent iterations of diagnostic categories (i.e., "gender dysphoria" in the DSM 5 and "gender incongruence" in ICD-11) were intended to be inclusive of people with nonbinary experiences of gender, they may not adequately capture the full diversity and scope of experiences of gender-related distress, particularly for nonbinary people. In addition to distress associated with aspects of one's physical body and presentation (including features that may be existing or absent), distress may arise from how one experiences their own gender, how one's gender is perceived within social situations, and from experiences of minority stress associated with one's gender (Winters & Ehrbar, 2010). Nonbinary peoples' experiences in each of these areas may or may not be similar to those of transgender men or women.

A person-centered approach for affirming care includes specific discussion of how different interventions may or may not shift the client's comfort with their own experience of gender, and how their gender is perceived by others. Nonbinary people can face challenges in reconciling their personal identities with the limits of the medical treatments available and can also encounter confusion and intolerance from society regarding their gender presentations (Taylor et al., 2019). Emerging research suggests the medical treatment needs of nonbinary people are particularly diverse, with some reporting needs for treatments that have typically been associated with transition trajectories historically associated with transgender men and women and some reporting alternative approaches (e.g., low dose hormone therapy, surgery without hormone therapy), some reporting a lack of interest in medical treatment, and some reporting feeling unsure about their needs (Burgwal & Motmans, 2021; James et al., 2016). Conceptualizing assessment as an ongoing process is particularly important given gender-related experiences and associated needs may shift throughout the lifespan. Given the ongoing evolution in treatment options and knowledge of treatment effects, particularly for nonbinary people, clients will benefit from providers who regularly seek up-to-date knowledge and convey these updates to their clients.

Statement 8.2

We recommend health care professionals consider medical interventions (hormonal treatment or surgery) for nonbinary people in the absence of "social gender transition."

Previous requirements for accessing hormonal treatment and surgery, such as "living in a gender role that is congruent with one's gender identity," do not reflect the lived experiences of many TGD people (Coleman et al., 2012). Due to the entrenched nature of the gender binary in most contemporary Western cultures, one can typically only be understood by others as a man or woman within most settings (Butler, 1993). Hence, the visibility and understanding of nonbinary embodiments and expressions is limited. This is due to gendered cues

being almost always understood in reference to a gender binary (Butler, 1993). Presently, it can be difficult for nonbinary people to be reliably recognized as their gender via visual cues associated with their gender expression (e.g., clothing, hair). However, androgyny or gender nonconformity may be communicated by the mixing or combining of cultural markers with traditionally masculine or feminine connotations. Because there is no commonly recognized "nonbinary category" within most contemporary Western, global north cultural contexts, nonbinary visibility often necessitates explicit sharing of one's gender with others or the use of cues that may be interpreted as gender nonconformity (but not necessarily nonbinary).

For these reasons, framing access to medical care in the context of someone experiencing a "social gender transition" where they are "living in a gender role that is congruent with one's gender identity" is not in line with the way many TGD people understand themselves and their personal transition process. For some, "living in a gender role that is congruent with one's gender identity" does not involve changes in name, pronouns, or gender expression even as medical intervention may be necessary. Even if a person is able to live in ways that are congruent with their gender identity, it may be difficult for an outside observer to assess this without learning directly from that person how they understand their own experience in this regard. Expectation of "social gender transition" may be unhelpful when considering eligibility for gender- affirming care, such as hormones and surgery, and rigid expectations of what a "social gender role transition" "should" look like can be a barrier to care for nonbinary people. There is no logical requirement gender-affirming medical interventions can only be done once a person legally changes their name, changes the gender marker on their identity documents, or wears or refrains from wearing particular items of clothing. Nonbinary people may struggle to access recognition of their genders on formal documentation, which may negatively affect their mental health or well-being (Goetz & Arcomano, 2021). TGD people may benefit from specific support in accessing (or retaining) their gender marker of preference. A requirement that someone disclose their gender identity in all circles of their lives (family, work, school, etc.) in order to access medical care may not be consistent with their goals and can place them at risk if it is not safe to do so.

Statement 8.3

We recommend health care professionals consider gender-affirming surgical interventions in the absence of hormonal treatment unless hormone therapy is required to achieve the desired surgical result.

The trajectory of "hormones before surgery" is an option across a range of surgical interventions. Some nonbinary people will seek gender-affirming surgical treatment to alleviate gender incongruence and increase body satisfaction (Beek et al., 2015; Burgwal & Motmans, 2021; Jones et al., 2019; Koehler et al., 2018), but do not want hormonal treatment or are unable to undergo hormonal therapy due to other medical reasons (Nieder, Eyssel et al., 2020). Currently, it is unknown for which proportion of nonbinary people these options apply.

Perhaps the surgery which has some specific association with nonbinary people (rather than sought by transgender men or undergone by some cisgender women) is mastectomy in nonbinary people AFAB who have not taken testosterone—although testosterone is not a requirement for this type of surgery—and some nonbinary people AFAB may need breast reduction (McTernan et al., 2020). An example of a surgery for which at least a period of hormone therapy may be necessary is metoidioplasty that enhances the enlarged clitoris produced by testosterone therapy. See Chapter 13—Surgery and Postoperative Care for more detail on whether hormone therapy is necessary for various surgeries. Procedures addressing the internal reproductive system include hysterectomy, unilateral or bilateral salpingo-oophorectomy, and vaginectomy. Hormone therapy is not required for any of these procedures, but hormone replacement therapy (either with estrogens, testosterone, or both) is advisable in those individuals undergoing a total gonadectomy to prevent adverse effects on their cardiovascular and musculoskeletal systems (Hembree et al., 2017; Seal, 2017). For phalloplasty, while there is no surgical requirement per se for a minimum period of testosterone

treatment, virilization (or the absence of virilization) of the clitoris and labia minora may impact the choice of surgical technique and influence surgical options. For more information see Chapter 13—Surgery and Postoperative Care.

Nonbinary AMAB clients should be informed commencing estrogen therapy post-surgically with no prior history of estrogen therapy may influence (perhaps adversely) the surgical result (Kanhai, Hage, Asscheman et al., 1999; Kanhai, Hage, Karim et al., 1999). Nonbinary people AMAB requesting a bilateral orchiedectomy do not require estrogen therapy to achieve a better outcome (Hembree et al., 2017). In these contexts, it is good practice to inform clients of the risks and benefits of hormone replacement therapy (estrogens, testosterone, or both) in preventing adverse effects on the cardiovascular and musculoskeletal system as well as alternative treatment options, such as calcium plus vitamin D supplementation to prevent osteoporosis (Hembree et al., 2017; Seal, 2017; Weaver et al., 2016). See also Chapter 9—Eunuchs for those who choose to forgo hormone replacement therapy. In the case of vaginoplasty, individuals should be advised lack of testosterone-blocking therapy may cause postoperative hair growth in the vagina when hair-bearing skin graft and flaps have been used (Giltay & Gooren, 2000).

Additional surgical requests for nonbinary people AMAB include penile-preserving vaginoplasty, vaginoplasty with preservation of the testicle(s), and procedures resulting in an absence of external primary sexual characteristics (i.e., penectomy, scrotectomy, orchiectomy, etc.). The surgeon and individual seeking treatment are advised to engage in discussions so as to understand the individual's goals and expectations as well as the benefits and limitations of the intended (or requested) procedure, to make decisions on an individualized basis and collaborate with other health care providers who are involved (if any).

Statement 8.4.

We recommend health care professionals provide information to nonbinary people about the effects of hormonal therapies/surgery on future fertility and discuss the options for fertility preservation prior to starting hormonal treatment or undergoing surgery.

All nonbinary individuals who seek gender-affirming hormonal therapies should be offered information and guidance about fertility options (Hembree et al., 2017; De Roo et al., 2016; Defreyne, Elaut et al., 2020; Defreyne, van Schuvlenbergh et al., 2020; Nahata et al., 2017; Quinn et al., 2021). It is important to discuss the potential impact of hormone therapy on fertility prior to initiation. This discussion should include fertility preservation options, the extent to which fertility may or may not be regained if hormone therapy is ceased, and the fact that hormone therapy per se is not birth control. For more information see Chapter 16—Reproductive Health.

Recent studies suggest that nonbinary individuals are less likely to access care and make their needs for potential interventions heard (Beek et al., 2015; Taylor et al., 2019). As such, it stands to reason that any gender diverse individual should be offered information on current options and techniques for fertility preservation, ideally prior to commencing hormonal treatment as the quality of the sperm or eggs may be impacted by exposure to hormones (Hamada et al., 2015; Payer et al., 1979). However, this should in no way preclude making inquiries and seeking more information at a later time, as there is evidence that fertility is still possible for individuals taking estrogen and testosterone (Light et al., 2014). A decision by a nonbinary or gender diverse person that fertility preservation or counseling is not needed should not be used as a basis for denying or delaying access to hormonal treatment.

CHAPTER 9 Eunuchs

Among the many people who benefit from gender-affirming medical care, those who identify as eunuchs are among the least visible. The 8th version of the Standards of Care (SOC) includes a discussion of eunuch individuals because of their unique presentation and their need for medically necessary gender-affirming care (see Chapter 2—Global Applicability, Statement 2.1).

Eunuch individuals are those assigned male at birth (AMAB) and wish to eliminate masculine physical features, masculine genitals, or genital functioning. They also include those whose testicles have been surgically removed or rendered nonfunctional by chemical or physical means and who identify as eunuch. This identity-based definition for those who embrace the term eunuch does not include others, such as men who have been treated for advanced prostate cancer and reject the designation of eunuch. We focus here on those who identify as eunuchs as part of the gender diverse umbrella.

As with other gender diverse individuals, eunuchs may also seek castration to better align their bodies with their gender identity. As such, eunuch individuals are gender nonconforming individuals who have needs requiring medically necessary gender-affirming care (Brett et al., 2007; Johnson et al., 2007; Roberts et al., 2008).

Eunuch individuals identify their gender identities in various ways. Many eunuch individuals see their status as eunuch as their distinct gender identity with no other gender or transgender affiliation. The focus of this chapter is on the treatment and care for those who identify as eunuchs. Health care professionals (HCPs) will encounter eunuchs requesting hormonal interventions, castration, or both to become eunuchs. These individuals may also benefit from a eunuch community because of the identification—with or without actual castration.

While there is a 4000-year history of eunuchs in society, the greatest wealth of information about contemporary eunuch-identified people is found within the large online peer-support community that congregates on sites such as the Eunuch Archive (www.eunuch.org), which was established in 1998. The moderators of this site attempt to maintain both medical and historical accuracy in its discussion forums, although there is certainly misinformation as well. According to the website, as of January 2022, there have been over 130,000 registered members from various parts of the world and frequently over 90% of those reading the site are "guests" rather than members. The website lists over 23,000 threads and nearly 220,000 posts. For example, two threads giving instructions for self-castration by injection of different toxins directly into the testicles have about 2,500 posts each, and each has been read well over one million times. Beginning in 2001, there have been 20 annual international gatherings of the Eunuch Archive community in Minneapolis in addition to many regional gatherings elsewhere. While the topic of castration is of interest to the great majority of people who participate in the discussions, it is a minority of the membership who seriously seek or have undergone castration. Many former Eunuch Archive members have achieved their goals and no longer participate.

Because of misconceptions and prejudice about historic eunuchs, the invisibility of contemporary eunuchs, and the social stigma that affects all gender and sexual minorities, few eunuch individuals come out publicly as eunuch and many will tell no one and will share only with like-minded people in an online community or are known as such only to close family and friends (Wassersug & Lieberman, 2010). The stereotypes of eunuchs are often highly negative (Lieberman 2018), and eunuchs may suffer the same minority stress as other stigmatized groups (Wassersug & Lieberman, 2010). Research into minority stress affecting gender diverse people should therefore include eunuchs.

The current set of recommendations is directed at professionals working with individuals who identify as eunuchs (Johnson & Wassersug, 2016; Vale et al., 2010) requesting medically necessary gender-affirming medical and/or surgical treatments (GAMSTs). Although not a specific diagnostic category in the ICD or DSM, eunuch is a useful construct as it speaks to the specifics of eunuch experience while also connecting it to the experience of gender incongruence more broadly. Eunuch individuals will present themselves clinically in various ways. They wish for

Statements of Recommendations

9.1- We recommend health care professionals and other users of the Standards of Care 8th guidelines should apply the recommendations in ways that meet the needs of eunuch individuals
9.2- We recommend health care professionals should consider medical intervention, surgical intervention, or both for eunuch individuals when there is a high risk that withholding treatment will cause individuals harm through self-surgery, surgery by unqualified practitioners, or unsupervised use of medications that affect hormones.
9.3- We recommend health care professionals who are assessing eunuch individuals for treatment have demonstrated competency in assessing them.
9.4- We suggest health care professionals providing care to eunuch individuals include sexuality education and counseling.

a body that is compatible with their eunuch identity—a body that does not have fully functional male genitalia. Some other eunuch individuals feel acute discomfort with their male genitals and need to have them removed to feel comfortable in their bodies (Johnson et al., 2007; Roberts et al., 2008). Others are indifferent to having male external genitalia as long as they are only physically present and do not function to produce androgens and male secondary sexual features (Brett et al., 2007). Hormonal means may be used to suppress the production of androgens, although orchiectomy provides a permanent solution for those not wishing genital functioning (Wibowo et al., 2016). Some eunuch individuals desire lower testosterone levels achieved with orchiectomy, but many will elect some form of hormone replacement to prevent adverse effects associated with hypogonadism. Most who elect hormone therapy choose either a full or partial replacement dose of testosterone. A smaller number elect estrogen.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 9.1.

We recommend health care professionals and other users of the Standards of Care, Version 8 guidelines should apply the recommendations in ways that meet the needs of eunuch individuals.

Eunuch individuals are part of the population of gender diverse people who experience gender incongruence and may also seek gender-affirming care. Like other transgender and gender diverse (TGD) individuals, eunuchs require access to affirming care to gain comfort with their gendered self. Each section of the SOC addresses the needs of diverse individuals, and eunuchs can be included within that group. They may have commonality with some nonbinary individuals in that social transition may not be a desired option, and hormone therapy may not play the same role as it might in a social transition or transition within the binary (Wassersug & Lieberman, 2010).

Like other gender diverse individuals, eunuch individuals may be aware of their identity in childhood or adolescence. Due to the lack of research into the treatment of children who may identify as eunuchs, we refrain from making specific suggestions.

Eunuch individuals may seek medical or surgical care (hormone suppression, orchiectomy, and, in some cases, penectomy) to achieve physical, psychological, or sexual changes (Wassersug & Johnson, 2007). It is important all patients, including both eunuchs and those seeking castration, establish and maintain a relationship with an HCP that is built upon trust and mutual understanding. Given a lack of awareness of eunuchs within the general medical community and the fear among many individuals seeking castration they will not be accepted, many do not receive appropriate primary care and screening tests (Jäggi et al., 2018). Increased awareness and education among medical providers will help address the need to be informed about the need to include eunuchs in discussions of gender diversity (Deutsch, 2016a). It goes without saying that eunuchs require and deserve the same primary care services as the general population. The topic of screening tests for cancers, such as prostate and breast, is an important area for

discussion as the risks of hormone-related cancers are likely different among male-assigned people whose testosterone and estrogen levels are not in the male range. Due to a lack of studies looking at the prevalence and incidence of hormone-related cancers in the eunuch population, there is no evidence to guide how often to screen for hormone-related cancers with prostate exams, PSA measurements, mammograms, etcetera.

The large literature on prostate cancer patients who have been medically or surgically castrated provides information about some of the effects of post-pubertal castration (such as potential osteoporosis, depression, or metabolic syndrome), but voluntary eunuchs may interpret the results very differently from those castrated for medical reasons. Chemical or surgical castration may be experienced as a source of distress to cis men with prostate cancer, while the same treatment may be affirming and a source of comfort for eunuch individuals. Similarly, transmasculine people who have a mastectomy to gain comfort with their bodies experience that surgery differently from ciswomen who undergo mastectomy to treat breast cancer (Koçan & Gürsoy, 2016; van de Grift et al., 2016). The prostate cancer information is well summarized by Wassersug et al. (2021) who provide references that explore the large literature on the subject. Such information on the effects of castration should be made available to those seeking castration.

Following an assessment as per the SOC-8, medical options requested by the patient can be considered and prescribed, if appropriate. These options can be tailored to the individual to create a plan that reflects their specific needs and preferences. The number and type of interventions applied and the order in which these take place may differ from person to person. These options are consistent with both the assessment and surgery chapters of the SOC-8. Treatment options for eunuchs to consider include:

- Hormone suppression to explore the effects of androgen deficiency for eunuch individuals wishing to become asexual, nonsexual, or androgynous;
- Orchiectomy to stop testicular production of testosterone;
- Orchiectomy with or without penectomy to alter their body to match their self-image;
- Orchiectomy followed by hormone replacement with testosterone or estrogen.

Per statement 5.6 in Chapter 5—Assessment of Adults, eunuch individuals seeking gonadectomy consider a minimum of 6 months of hormone therapy as appropriate to the TGD person's gender goals before the TGD person undergoes irreversible surgical intervention (unless hormones are not clinically indicated for the individual).

Statement 9.2.

We recommend health care professionals consider medical intervention, surgical intervention, or both for eunuch individuals when there is a high risk that withholding treatment will cause individuals harm through self-surgery, surgery by unqualified practitioners, or unsupervised use of medications that affect hormones.

The same assessment process recommended in the SOC-8 ought to apply to eunuchs (see Chapter 5—Assessment of Adults). The Eunuch Archive has a large number of posts from individuals finding great difficulty in seeking medical providers who will perform castration surgery. There are a large number of eunuch individuals who have performed self-surgery or have had surgery performed by people who are not credentialed medical providers (Johnson & Irwig, 2014). There are also clinical reports of eunuch individuals who have self-castrated and accounts of patients who have misled medical providers to obtain castration (Hermann & Thorstenson, 2015; Mukhopadhyay & Chowdhury, 2009). There is no doubt when members of this population are denied access to quality medical treatment, they will take actions that may cause them great harm, such as bleeding and infection that may require hospital admission (Hay, 2021; Jackowich et al., 2014; Johnson & Irwig, 2014). Because of these serious problems and harm caused through self-surgery, surgery by unqualified practitioners or the unsupervised use of medications that affect hormones, it is important health care providers create a welcoming environment and consider various treatment options after careful assessment

to avoid the problems that lack of access to treatment and withholding treatment will cause.

When desired, castration can be achieved either chemically or surgically. For some, chemical castration can be an appropriate trial prior to undergoing surgical castration to determine how the individual feels when hypogonadal (Vale et al., 2010). Chemical castration is usually reversible if the medications are discontinued (Wassersug et al., 2021). The most common types of medications used to lower testosterone levels are antiandrogens and estrogen.

The two most commonly used antiandrogens, cyproterone acetate and spironolactone, are oral. Estrogen is sometimes prescribed for prostate cancer patients to lower serum testosterone levels via negative feedback at the hypothalamus and pituitary gland. Estrogens and antiandrogens may not fully suppress testosterone levels into the female or castrate range, and oral estrogens increase the risk of venous thromboembolism. Although not commonly used due to cost, gonadotropin releasing hormone (GnRH) agonists are a very effective method for suppressing the production of sex steroids and fertility (Hembree et al., 2017). When selecting a medication, we advise using those which have been studied in multiple transgender populations (i.e., estrogen, cyproterone acetate, GnRH agonists) rather than medications with little to no peer-reviewed scientific studies (i.e., bicalutamide, rectal progesterone, etc.) (Angus et al., 2021; Butler et al., 2017; Efstathiou et al., 2019; Tosun et al., 2019).

Many eunuch individuals pursue hormone replacement therapy following castration as they do not desire the complete suppression of hormone levels and consequent problems, such as the increased risk of osteoporosis. The two main options for replacement of sex steroids are testosterone and estrogen that may be used in full or partial replacement doses. The majority elect testosterone as they present as male and are not interested in feminization. A minority elect estrogen at a high enough dose to prevent osteoporosis, but low enough avoid most feminization. They may identify as nonbinary, agender, or other (Johnson et al., 2007; Johnson & Wassersug, 2016).

Although studies on hormone replacement therapy in eunuchs are lacking, findings from cisgender men treated for prostate cancer can be informative regarding the effects of hormone therapy. In a randomized controlled trial of 1,694 cisgender men treated for locally advanced or metastatic prostate cancer, one group received a GnRH agonist and the other received transdermal estrogen (Langley et al., 2021). Cisgender men who received the GnRH agonist developed signs and symptoms of both androgen and estrogen deficiency, whereas men who received the estrogen patch only developed androgen-depleting symptoms. Both groups had high rates of sexual side effects (91%), and weight gain was similar among the groups. Compared with cisgender men receiving the GnRH agonist, cisgender men treated with estrogen patches had a higher self-reported quality of life, lower rates of hot flushes (35% vs. 86%), and higher rates of gynecomastia (86% vs. 38%). Metabolically, cisgender men receiving estrogen patches had favorable changes with a lower mean fasting glucose, fasting total cholesterol, systolic and diastolic blood pressure. Conversely, cisgender men receiving the GnRH agonist experienced the opposite effects. Based on this study, eunuchs may consider a low dose of transdermal estrogen therapy to avoid adverse estrogen-depleting effects, which include hot flashes, fatigue, metabolic effects, and loss of bone mineral density (Hembree et al., 2017; Langley et al., 2021). For further information see Chapter 12—Hormone Therapy.

Statement 9.3.

We recommend health care professionals who are assessing eunuch individuals for treatment have demonstrated competency in assessing them.

A frequent topic on the discussion boards of the Eunuch Archive is the difficulty of finding practitioners who are able to understand their needs. Eunuchs and those seeking castration usually are less visible than other gender minorities (Wassersug & Lieberman, 2010). Due to stigma and fear of rejection by the medical community, they may not voluntarily disclose their identity and desires to their medical or mental health providers. In some environments, medical providers may not be aware eunuchs exist and may not even know they have treated eunuch-identified patients.

The SOC section on assessment is applicable to eunuch individuals. Like other gender diverse individuals, those seeking castration can engage in an informed consent process in which qualified providers conduct assessments to ensure individuals are capable of providing informed consent prior to medical interventions and to ensure a mental health problem is not the etiology of the desire. As with other sexual and gender minorities, working with eunuchs requires an understanding that they are a diverse population, and that each person is eunuch in their own way (Johnson et al., 2007). The person seeking services benefits from the professional's accepting stance, open inquiry, suspension of judgment, and flexible expectations, combined with professional competency and expertise.

To provide appropriate treatment, providers must establish trust and respect by creating an inclusive environment for eunuch-identified people. For eunuch-identified individuals, the ideal intake form would ask the assigned sex and identified gender and offer multiple gender options, including "eunuch" and "other." Individuals may identify with more than one option and should be able to select more than one.

HCPs may be involved in the assessment, psychotherapy (if desired), preparation, and follow-up for medical and surgical gender-affirming interventions. They may also provide support for partners and families. Eunuch-identified individuals who want the support of a qualified mental health provider will benefit from a therapist who meets the experience and criteria set out in Chapter 4—Education.

While some individuals seeking or considering castration come to counseling or therapy because they want emotional support or help with decision-making, many come to providers for an assessment in preparation for specific medical interventions (Vale et al., 2010).

Statement 9.4.

We suggest health care professionals providing care to eunuch individuals include sexuality education and counseling.

Several research studies have contributed to our knowledge of contemporary eunuch-identified people and have explored demographic characteristics and sexuality (Handy et al., 2015; Vale et al., 2013; Wibowo et al., 2012, 2016). Medical and MHPs should assume eunuchs are sexual people capable of sexual activity, pleasure, and relationships, unless they report otherwise (Wibowo et al., 2021). Research has shown there is great diversity among eunuchs regarding the level of desire, type of preferred physical or sexual contact, and nature of preferred relationships (Brett et al., 2007; Johnson et al., 2007; Roberts et al., 2008). While some enjoy active sex lives with or without romantic relationships, others identify as asexual or aromantic and are relieved by the loss of libido achieved through surgical or chemical castration (Brett et al., 2007). Each person is different, and one's genital status does not determine sexual or romantic attraction (Walton et al., 2016; Yule et al., 2015).

Regardless of the type of chemical suppression or surgery a person has undergone, they may be capable of sexual pleasure and sexual activity. Contrary to popular belief, eunuchs are not necessarily asexual or nonsexual (Aucoin & Wassersug, 2006). Safe sex education is necessary for all people who engage in sexual activity that could involve an exchange of body fluids. See Chapter 17—Sexual Health for information regarding sex education and safe sex options for people with diverse genders and sexualities. In addition, fertility preservation should be discussed when considering medical interventions that might impact the possibilities for future parenthood. For more considerations see Chapter 16—Reproductive Health.

CHAPTER 10 Intersex

The Standards of Care, Version 7 included a chapter on the applicability of the standards to people with physical intersexuality who become gender-dysphoric and/or change their gender because they differ from transgender individuals without intersexuality in phenomenological presentation, life trajectories, prevalence, etiology, and stigma risks. The current chapter provides an update and adds recommendations on the medically necessary clinical approach to the management of individuals with intersexuality in general (see medical necessity statement in Chapter 2—Global Applicability, Statement 2.1). Because a newborn with an atypical sexual differentiation may already present with clinical challenges, including the need for family education and support from early on, the decision-making on gender assignment, subsequent clinical gender management, components of which—especially genital surgery—may be controversial, and a later risk of gender dysphoria development and gender change that is markedly increased (Sandberg & Gardner, 2022).

Terminology

"Intersex" (from Latin, literal translation "between the sexes") is a term grounded in the binary system of sex underlying mammalian (including human) reproduction. In medicine, the term is colloquially applied to individuals with markedly atypical, congenital variations in the reproductive tract. Some variations, often labeled "genital ambiguity," preclude the simple recognition of somatic sex as male or female and, in resource-rich societies, may require a comprehensive physical, endocrine, and genetic work-up, before a sex/gender is "assigned." In recent years "intersex" has also become an identity label adopted by some individuals with intersex conditions and a subset of (non-intersex) individuals with a non-binary gender identity (Tamar-Mattis et al., 2018).

At a 2005 international consensus conference on intersex management, intersex conditions were subsumed under a new standard medical term, "Disorders of Sex Development" (DSD), defined as "congenital conditions in which development of chromosomal, gonadal, or anatomical sex is atypical" (Hughes et al., 2006). DSD covers a much wider range of conditions than those traditionally included under intersexuality and comprises conditions such as Turner syndrome and Klinefelter syndrome, which are much more prevalent. In addition, many affected individuals dislike the term "disorder," viewing it as inherently stigmatizing (Carpenter, 2018; Griffiths, 2018; Johnson et al., 2017; Lin-Su, et al., 2015; Lundberg et al., 2018; Tiryaki et al., 2018). Health care professionals (HCPs) also vary in their acceptance of the term (Miller et al., 2018). The wide-spread alternative reading of DSD as "Differences in Sex Development" can be seen as less pathologizing, but is semantically unsatisfactory as this term does not distinguish the typical genital differences between males and females from atypical sexual differentiation. Other recent attempts to come up with less obviously stigmatizing terms such as "Conditions Affecting Reproductive Development" (CARD; Delimata et al., 2018) or "Variations of/in Sex Characteristics" (VSC; Crocetti, et al., 2021) are also not specific to intersexuality.

Given these definitional issues, in this chapter we are using the term "intersexuality" (or "intersex") to refer to congenital physical manifestations only. This is done for both descriptive clarity and historical continuity. This choice is not meant to indicate an intention on our part to take sides in the ongoing discussion regarding the concept of sex/gender as a bipolar system or as a continuum, which may vary with considerations of context and utility (Meyer-Bahlburg, 2019). In 21st century societies, the concepts of sex and gender are in a process of evolution.

Prevalence

The prevalence of intersex conditions depends on the definition used. Obvious genital atypicality ("ambiguous genitalia") occurs with an estimated frequency ranging from approximately 1:2000—1:4500 people (Hughes et al., 2007). The most inclusive definitions of DSD estimate a prevalence of up to 1.7% (Blackless et al., 2000). Although these numbers are high in aggregate, the individual conditions associated with the intersex variations tend to be much rarer. For instance, androgen insensitivity syndrome (AIS) occurs in approximately 1 in 100,000 46,XY births (Mendoza & Motos, 2013), and classic congenital adrenal

hyperplasia (CAH) in approximately 1 in 15,000 46,XX births (Therrell, 2001). Prevalence figures for individual syndromes may vary dramatically between countries and ethnic groups.

Presentation

The presentation of individuals with intersex traits varies widely. Intersexuality can be recognized during prenatal ultrasound imaging, although most individuals will be identified during genital examinations at birth. In resource-rich societies, such children will undergo extensive medical diagnostic procedures within the first weeks of life. Taking into consideration the specific medical diagnosis, physical and hormonal findings, and information from long-term follow-up studies about gender outcome, joint decision-making between the health-care team and the parents generally leads to the newborn being assigned to the male or female sex/gender. Some individuals with intersexuality come to the attention of specialists only around the age of puberty, for instance, when female-raised adolescents are evaluated for primary amenorrhea.

HCPs assisting individuals with both intersexuality and gender uncertainty need to be aware that the medical context in which such individuals have grown up is typically very different from that of non-intersex TGD people. There are many different syndromes of intersexuality, and each syndrome can vary in its degree of severity. Thus, hormonal and surgical treatment approaches vary accordingly.

Some physical manifestations of intersexuality may require early urgent intervention, as in cases of urinary obstruction or of adrenal crisis in CAH. Most physical variations among individuals with intersexuality neither impair function, at least in the early years, nor risk safety for the individual. Yet, the psychosocial stigma associated with atypical genital appearance often motivates early genital surgery (commonly labeled 'corrective' or 'normalizing') long before the individual reaches the age of consent. This approach is highly controversial because it conflicts with ethical principles supporting a person's autonomy (Carpenter, 2021; Kon, 2015; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979). In addition, among the manifestations without immediate safety concerns, some individuals, when older, may opt for a range of medical interventions to optimize function and appearance. The specifics of medical treatments are far beyond the scope of what can be addressed in this chapter, and the interested reader should consult the respective endocrine and surgical literature.

Some intersex conditions are associated with a greater variability in long-term gender identity outcome than others (Dessens et al., 2005). For instance, the incidence of a non-cisgender gender identity in 46,XX individuals with CAH assigned female may be as high as 5–10% (Furtado et al., 2012). The substantial biological component underlying gender identity is a critical factor that must be considered when offering psychosocial, medical, and surgical interventions for individuals with intersex conditions.

There is also ample evidence people with intersexuality and their families may experience psychosocial distress (de Vries et al., 2019; Rosenwohl-Mack et al., 2020; Wolfe-Christensen et al., 2017), in part related to psychosocial stigma (Meyer-Bahlburg, Khuri et al., 2017; Meyer-Bahlburg, Reyes-Portillo et al., 2017; Meyer-Bahlburg et al., 2018).

Intersexuality in the psychiatric nomenclature

Since 1980, the American psychiatric nomenclature recognized individuals with intersexuality who meet the criteria for gender identity variants; however, their diagnostic categorization changed with successive DSM editions. For instance, in DSM-III (American Psychiatric Association, 1980), the Axis-I category of "transsexualism" could not be applied to such individuals in adulthood, but such children were labeled "gender identity disorder of childhood," with the medical intersex condition to be specified in Axis III. In DSM-IV-TR (American Psychiatric Association, 2000), individuals with intersexuality were excluded from the Axis-I category of "gender identity disorder" regardless of age and, instead, grouped with other conditions under the category "gender identity disorder not otherwise specified." In DSM-5 (American Psychiatric Association, 2013), which moved away from the multiaxial

Statements of Recommendations

10.1- We suggest a multidisciplinary team, knowledgeable in diversity of gender identity and expression as well as in intersexuality, provide care to individuals with intersexuality and their families.
10.2- We recommend health care professionals providing care for transgender youth and adults seek training and education in the aspects of intersex care relevant to their professional discipline.
10.3- We suggest health care professionals educate and counsel families of children with intersexuality from the time of diagnosis onward about the child's specific intersex condition and its psychosocial implications.
10.4- We suggest both providers and parents engage children/individuals with intersexuality in ongoing, developmentally appropriate communications about their intersex condition and its psychosocial implications.
10.5- We suggest health care professionals and parents support children/individuals with intersexuality in exploring their gender identity throughout their life.
10.6- We suggest health care professionals promote well-being and minimize the potential stigma of having an intersex condition by working collaboratively with both medical and non-medical individuals/organizations.
10.7- We suggest health care professionals refer children/individuals with intersexuality and their families to mental-health providers as well as peer and other psychosocial supports as indicated.
10.8- We recommend health care professionals counsel individuals with intersexuality and their families about puberty suppression and/or hormonal treatment options within the context of the individual's gender identity, age, and unique medical circumstances.
10.9- We suggest health care professionals counsel parents and children with intersexuality (when cognitively sufficiently developed) to delay gender-affirming genital surgery, gonadal surgery, or both, so as to optimize the children's self-determination and ability to participate in the decision based on informed consent.
10.10- We suggest only surgeons experienced in intersex genital or gonadal surgery operate on individuals with intersexuality.
10.11- We recommend health care professionals who are prescribing or referring for hormonal therapies/surgeries counsel individuals with intersexuality and fertility potential and their families about a) known effects of hormonal therapies/surgery on future fertility; b) potential effects of therapies that are not well studied and are of unknown reversibility; c) fertility preservation options; and d) psychosocial implications of infertility.
10.12- We suggest health care professionals caring for individuals with intersexuality and congenital infertility introduce them and their families, early and gradually, to the various alternative options of parenthood.

system, "gender identity disorder" was re-defined as "gender dysphoria" and applied regardless of age and intersex status, but individuals with intersexuality received the added specification "with a disorder of sex development" (Zucker et al., 2013). The just published text revision of DSM-5 (American Psychiatric Association, 2022) keeps the term gender dysphoria. Note, however, the recent revision of the International Classification of Diseases [ICD-11; World Health Organization, 2019a] has moved "gender incongruence" from the chapter "Mental, Behavioral, or Neurodevelopmental Disorders" to a new chapter "Conditions Related to Sexual Health."

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 10.1

We suggest a multidisciplinary team, knowledgeable in diversity of gender identity and expression as well as in intersexuality, provide care to individuals with intersexuality and their families.

Intersexuality, a subcategory of DSD, is a complex congenital condition that requires the involvement of experts from various medical and behavioral disciplines (Hughes et al., 2006). Team composition and function can vary depending on team location, local resources, diagnosis, and the needs of the individual with intersexuality and her/his/their family. The ideal team includes pediatric subspecialists in endocrinology, surgery and/or urology, psychology/psychiatry, gynecology, genetics, and, if available, personnel trained in social work, nursing, and medical ethics (Lee et al., 2006). The structure of the team can be in line with 1) the traditional multidisciplinary medical model; 2) the interprofessional model; or 3) the transdisciplinary model. Although these structures can appear similar, they are in fact very different and can exert varying influences on how the team functions (Sandberg & Mazur, 2014). The 2006 Consensus Statement makes no decision about which model is best—multidisciplinary, interdisciplinary, or transdisciplinary—and only states the models "imply different degrees of collaboration and professional

autonomy" (Lee, Nordenström et al., 2016). Since the publication of the Consensus Statement in 2006, such teams have been created both in Europe and in the US. A listing of teams in the US can be found on the DSD-Translational Network (DSD-TRN) website. There are also teams in a number of European countries (Thyen et al., 2018). While there are barriers to the creation of teams as noted by Sandberg and Mazur (2014), multidisciplinary teams help address a number of problems that have undermined the successful care of individuals with an intersex diagnosis and their families, such as the scattered nature of services, the limited or absent communication between professionals, and the resulting fragmented nature of the explanations individuals receive that cause more confusion than clarity.

Most individuals born with intersexuality will be identified at birth or shortly thereafter, while others will be identified at later times in the life cycle, for example at puberty (see Brain et al., 2010, Table 1). When this happens the team approach will be modified based on the diagnosis and the age of the person. In some circumstances, the composition of the team can be expanded to include other specialists as needed.

It has been reported children seen by a multidisciplinary team were significantly more likely to receive nearly the full range of services rather than only those services offered by a single provider (Crerand et al., 2019). Parents who received such care positively endorsed psychosocial services and the team approach and reported receiving more information than those who did not interact with such a team (Crerand et al., 2019).

Statement 10.2

We recommend health care professionals providing care for transgender youth and adults seek training and education in the aspects of intersex care relevant to their professional discipline.

Results from interviews with medical trainees (Liang et al., 2017; Zelin et al., 2018) and from programmatic self-audits and surveys (DeVita et al., 2018; Khalili et al., 2015) suggest medical training programs are not adequately preparing practitioners to provide competent care to individuals presenting with gender dysphoria and intersexuality. Professional and stakeholder attendees of intersex-specific events have identified ongoing education and collaboration as an important professional development need (Bertalan et al., 2018; Mazur et al., 2007). This may be especially true for adult care providers who may have less clinical guidance or support in assisting those individuals who are transitioning from pediatric to adult care (Crouch & Creighton, 2014).

However, there are few guidelines for training or assessing practitioner competency in managing these topics, and those that are available primarily apply to mental health professionals (MHPs) (Hollenbach et al., 2014), with the exception of a primary care guide (National LGBTQIA + Health Education Center, 2020).

For HCPs wanting to improve their competency, seeking consultation from experts may be an option when formal education or empirical guidelines are otherwise unavailable. Given the relative widespread adoption of multidisciplinary expert teams in the treatment of intersexuality (Pasterski et al., 2010), individuals serving on these teams are well positioned to consult with and educate other health care staff who may not have received adequate training (Hughes et al., 2006). Therefore, it is recommended the training of other professionals be a central component of team development (Auchus et al., 2010) and members of multidisciplinary teams receive training specific to team-based work, including strategies for engaging in interprofessional learning (Bisbey, et al., 2019; Interprofessional Education Collaborative Expert Panel, 2011).

Statement 10.3

We suggest health care professionals educate and counsel families of children with intersexuality from the time of diagnosis onward about the child's specific intersex condition and its psychosocial implications.

Full disclosure of medical information to families of children with intersex conditions through education and counseling should begin at the time of diagnosis and should be consistent with guidance from multiple international consensus guidelines. One of the most challenging issues presented by a newborn with intersexuality, particularly

when associated with noticeable genital ambiguity, is sex assignment and from the parents' perspective, the gender of rearing (Fisher, Ristori et al., 2016). Given this is a very stressful situation for most parents, it is generally recommended the decisions about sex/gender should be made as quickly as a thorough diagnostic evaluation permits (Houk & Lee, 2010). However, the criteria for sex/gender decisions have changed over time. In the second half of the 20th century, the decisions were biased towards female assignment, because feminizing genital surgery was seen as easier and less side-effect prone than masculinizing surgery. Yet, in certain intersex conditions, for instance 46,XY 5α-RD-2 deficiency, female sex/gender assignment was found to be associated with high rates of later gender dysphoria and gender change (Yang et al., 2010). Therefore, since the International Consensus Conference on Intersex Management in 2005, sex/gender assignment takes into consideration the gradually accumulating data on long-term gender outcome in the diverse conditions of intersexuality.

The practice of disclosure seeks to enable more fully informed decision-making about care. Additionally, while shame and stigma surrounding intersexuality is associated with poorer psychosocial outcomes, open and proactive communication of health information has been proposed as a strategy to reduce those risks (de Vries et al., 2019). Depending on the person's diagnosis and developmental stage, intersex conditions may differentially impact individuals and their health care needs. Intersex-health-related communication must therefore be continuous and tailored to the individual. Research on decision-making in intersex care suggests families are influenced by how clinical teams communicate (Timmermans et al., 2018). In keeping with the SOC, we encourage providers to adopt normalizing, affirming language and attitudes across education and counseling functions. For example, describing genital atypia as a "variation" or "difference" is more affirming than using the terms "birth defect" or "abnormality."

All HCPs involved in an individual's care can provide essential education and information to families. In multidisciplinary teams, the type of education may align with an HCP's area of expertise, for example, a surgeon educating the individual on their anatomy, an endocrinologist teaching the specifics of hormonal development, or an MHP conveying the spectrums of gender and sexual identity. Other HCPs may need to provide comprehensive education. Families should receive information that is pertinent to the individual's specific intersex variation, when known. All HCPs can supplement this information with patient-centered resources available from support groups. People with intersexuality have also been hired as team members to provide education using their lived experience.

Consensus guidelines also recommend families be offered ongoing peer and professional psychosocial support (Hughes et al., 2006) that may involve counseling with a focus on problem-solving and anticipatory guidance (Hughes et al., 2006). For example, families may seek guidance in educating other people—siblings, extended family, and caregivers—about the specific intersex condition of an individual. Other families may need support or mental health care to manage the stress of intersex treatment. Adolescents may benefit from guidance on how to disclose information to peers as well as from support when navigating dating and sex. Providing counseling may also involve guiding families and individuals of all ages through a shared decision-making process around medical or surgical care. Providers may employ decision aids to support this process (Sandberg et al., 2019; Weidler et al., 2019).

Statement 10.4

We suggest both providers and parents engage children/individuals with intersexuality in ongoing, developmentally appropriate communications about their intersex condition and its psychosocial implications.

Communicating health information is a multi-directional process that includes the transfer of information from providers to patients, from parents to patients, as well as from patients back to their providers (Weidler & Peterson, 2019). While much emphasis has been placed on communicating to parents around issues of diagnosis and surgical decision-making, youth with DSD have reported barriers to engaging with health care providers and may not always turn

to their parents for support (Callens et al., 2021). To prepare individuals to be fully engaged and autonomous in their treatment, it is critical both providers and parents communicate continuously with children/individuals.

Providers must set an expectation as soon as possible for ongoing, open communication between all parties, especially since parents may experience distress due to the uncertainty associated with DSD and may seek quick fixes (Crissman et al., 2011; Roberts et al., 2020). Models of shared decision-making as well as related decisional tools have been developed to support ongoing communication between HCPs and families/individuals (Karkazis et al., 2010; Sandberg et al., 2019; Siminoff & Sandberg, 2015; Weidler et al., 2019). In addition to setting an expectation for dialogue, providers can also set the tone of communication. Providers can help parents and individuals tolerate diagnostic uncertainty while simultaneously providing education on anatomic variations, modeling openness to gender and sexual identity, and welcoming the child's/individual's questions. As they age, children/individuals may have questions or need age-appropriate information on issues of sex, menstruation, fertility, the need for hormone treatment (adrenal/sex), bone health, and cancer risk.

Parents also play a critical role in educating their children and may be the first people to disclose health information to their child (Callens et al., 2021). As part of expectation-setting around communication, providers should prepare parents to educate their child and members of their support system about the intersex diagnosis and treatment history. Some parents report difficulties in knowing how much to disclose to others as well as to their own children (Crissman et al., 2011; Danon & Kramer, 2017). The stress parents experience while raising children with an intersex condition is increased when parents adopt an approach that minimizes disclosure/discussion of their child's diagnosis (Crissman et al., 2011). The level of stress also varies by developmental stage, with parents of adolescents reporting higher rates of stress (Hullman et al., 2011). Therefore, HCPs should assist parents in developing strategies specific to their child's developmental stage that address their psychosocial or cultural concerns and values (Danon & Kramer, 2017; Weidler & Peterson, 2019). Finally, broader research on sexuality and gender variance has found—counter to the associations between shame/stigma and negative health outcomes—supportive family behaviors (including talking with children about their identity and connecting them with peers) predicted greater self-esteem and better health outcomes in individuals (Ryan et al., 2010).

Statement 10.5

We suggest health care professionals and parents support children/individuals with intersexuality in exploring their gender identity throughout their life.

Psychological, social, and cultural constructs all intersect with biological factors to form an individual's gender identity. As a group, individuals with intersexuality show increased rates of gender nonconforming behavior, gender-questioning, and cross-gender wishes in childhood, dependent in part on the discrepancy between the prenatal sex-hormonal milieu in which the fetal brain has differentiated and the sex assigned at birth (Callens et al., 2016; Hines, et al., 2015; Meyer-Bahlburg et al., 2016; Pasterski et al., 2015). Gender identity problems are observed at different rates in individuals with different intersex conditions (de Vries et al., 2007). More recently, some individuals have been documented to develop a nonbinary identity, at least privately (Kreukels et al., 2018). Although the majority of people with intersexuality may not experience gender dysphoria or wishes for gender transition, they may still have feelings of uncertainty and unanswered questions regarding their gender (Kreukels et al., 2018). Questions about gender identity may arise from such factors as genital appearance, pubertal development, and knowledge of items such as the diagnostic term of the medical condition, gonadal status, sex chromosome status, and a history of genital surgery. Therefore, HCPs need to be accessible for clients to discuss such questions and feelings, openly converse about gender diversity, and adopt a less binary approach to gender. HCPs are advised to guide parents as well in supporting their children in exploring gender.

Furthermore, such support should not be confined to the childhood years. Rather, individuals should be given the opportunity to explore their gender identity throughout their lifetime, because different phases may come with new questions regarding gender (for example, puberty/adolescence, childbearing age). Children in general may have questions regarding their gender identity at salient points during their maturation and evolution. When faced with additional stressors, for example, genital ambiguity, genital examinations and procedures, as well as the intersectionality of cultural bias and influences, individuals with intersexuality may need support and should be encouraged to seek educated professional assistance and guidance when needed. Also, HCPs should inquire regularly to determine if their clients with intersexuality need such support. When people experience gender incongruence, gender-affirming interventions may be considered. Procedures that should be applied in such interventions are described in other chapters.

Statement 10.6

We suggest health care professionals promote well-being and minimize the potential stigma of having an intersex condition by working collaboratively with both medical and non-medical individuals/organizations.

Individuals with intersexuality are reported to experience stigma, feelings of shame, guilt, anger, sadness and depression (Carroll et al., 2020; Joseph et al., 2017; Schützmann et al., 2009). Higher levels of psychological problems are observed in this population than in the general population (Liao & Simmonds, 2014; de Vries et al., 2019). In addition, parental fear of stigmatization and adjustment to their child's diagnosis must not be overlooked by the clinical team. Parents may benefit from supportive counseling to assist them both in managing clinical decision-making (Fleming et al., 2017; Rolston et al., 2015; Timmermans et al., 2019) as well as understanding the impact of clinical decisions on their view of their child (Crissman et al., 2011; Fedele et al., 2010).

Thyen et al. (2005) found repeated genital examinations appear to be correlated with shame, fear and pain and may increase the likelihood of developing post-traumatic stress disorder (PTSD) later in life (Alexander et al., 1997; Money & Lamacz, 1987). Exposure to repeated genital examinations, fear of medical interventions, and parental and physician secrecy about being intersex ultimately undermine the self-empowerment and self-esteem of the person with intersexuality (Meyer-Bahlburg et al., 2018; Thyen et al., 2005; Tishelman et al., 2017; van de Grift, Cohen-Kettenis et al., 2018). For recommendations on how to conduct genital examinations to minimize adverse psychological side effects see Tishelman et al. (2017).

There is an active movement within the intersex community to alleviate stigma and to return human rights and dignity to intersex people rather than viewing them as medical anomalies and curiosities (Yogyakarta Principles, 2007, 2017). Chase (2003) summarizes the major reasons for the intersex advocacy movement and outlines how stigma and emotional trauma are the outcome of ignorance and the perceived need for secrecy. Public awareness of intersex conditions is very limited, and images and histories of individuals with intersexuality are still presented as "abnormalities of nature". We, therefore, advise HCPs to actively educate their colleagues, individuals with intersexuality, their families, and communities, raise public awareness, and increase knowledge about intersexuality. Societal awareness and knowledge regarding intersexuality may help reduce discrimination and stigmatization. Tools and education/information materials may also help individuals with intersexuality disclose their condition, if desired (Ernst et al., 2016).

HCPs should be able to recognize and address stigmatization in their clients (Meyer-Bahlburg et al., 2018) and should encourage people with intersexuality of various ages to connect via support groups. There is a need for developing specific techniques/methods for assisting clients to cope with stigma related to intersex.

Statement 10.7

We suggest health care professionals refer children/individuals with intersexuality and their families to mental health professionals as well as peer and other psychosocial supports as indicated.

For almost all parents, the birth of a child with intersexuality is entirely unexpected and comes as a shock. Their inability to respond immediately to the ubiquitous question, "Is your baby a boy or a girl?", their lack of knowledge about the child's condition, the uncertainty regarding the child's future, and the pervasive intersex stigma are likely to cause distress, sometimes to the level of PTSD and may lead to prolonged anxiety and depression (Pasterski et al., 2014; Roberts et al., 2020; Wisniewski & Sandberg, 2015). This situation may affect parental care and long-term outcome of their child with intersexuality (Schweizer et al., 2017). As these children grow up, they are also at risk of experiencing intersex stigma in its three major forms (enacted, anticipated, internalized) in all spheres of life (Meyer-Bahlburg et al., 2018), along with other potential difficulties such as body image problems, gender-atypical behavior, and gender identity questioning. Many may face the additional challenge presented by the awareness of the incongruence between their assigned gender and biological characteristics such as sexual karyotype, gonads, past and/or current sex-hormonal milieu, and reproductive tract configuration. This situation may also adversely affect the individuals' mental health (Godfrey, 2021; Meyer-Bahlburg, 2022). A recent online study of a very large sample of LGBTQ youth indicated that LGBTQ youth who categorized themselves as having a physical intersex variation had a rate of mental health problems that was higher than the rate in LGBTQ youth without intersexuality (Trevor Project, 2021). As intersex conditions are rare, parents of such children and later the individuals themselves may experience their situation as unique and very difficult for others to understand. Thus, based on clinical experience, there is a consensus among HCPs who are experienced in intersex care, that social support is a crucial component of intersex care, not only through professional support by MHPs (Pasterski et al., 2010), but also, importantly, through support groups of individuals with intersex conditions (Baratz et al., 2014; Cull & Simmonds, 2010; Hughes et al., 2006; Lampalzer et al., 2021). A detailed international listing of DSD and intersex peer support and advocacy groups with their websites has been provided by Lee, Nordenström et al. (2016). Given the heterogeneity of intersex conditions and treatment regimens, an individual with intersexuality may find it most helpful to associate with a support group that includes members with the same or similar condition as that of the individual. It is important HCPs specializing in intersex care also collaborate closely with such support groups so that occasional differences in opinions regarding specific aspects of care can be resolved through detailed discussions. Close contacts between HCPs and support groups also facilitate community-based participatory research that benefits both sides.

Statement 10.8

We recommend health care professionals counsel individuals with intersexuality and their families about puberty suppression and/or hormonal treatment options within the context of the individual's gender identity, age, and unique medical circumstances.

While many people with intersexuality have a gender identity in line with their XX or XY karyotype, there is sufficient heterogeneity that HCPs should be able to provide customized approaches. For example, among XX individuals with virilizing CAH, a larger than expected minority have a male gender identity (Dessens et al., 2005). Among XY individuals with partial androgen insensitivity syndrome, gender identity can vary significantly (Babu & Shah, 2021). Furthermore, among XY individuals with 5α-reductase-2 (5α-RD-2) deficiency and with 17-beta-hydroxysteroid dehydrogenase-3 deficiency who are assigned the female sex at birth, a large fraction (56–63% and 39–64%, respectively) change from a typical female gender role to a typical male gender role as they age (Cohen-Kettenis, 2005).

People with intersexuality have a wide range of medical options open to them depending on their gender identity and its alignment with anatomy. These options include puberty suppression medication, hormonal treatment, and surgeries, all customized to the unique circumstances of the individual (Weinand & Safer, 2015; Safer & Tangpricha, 2019) (for further information see Chapter 6—Adolescents and Chapter 12—Hormone Therapy). Specifically, when functional gonads are present, puberty may be temporarily suspended by using gonadotropin-releasing hormone (GnRH) analogues. Such intervention can

facilitate the necessary passage of time needed by the individual to explore gender identity and to actively participate in sex designation, especially for conditions in which sex role change is common (i.e., in female-raised individuals with 5α-RD-2 deficiency; Cocchetti, Ristori, Mazzoli et al., 2020; Fisher, Castellini et al., 2016).

HCPs can counsel individuals and their families directly if the providers have sufficient expertise and can leverage expertise needed to determine both a course of treatment appropriate for the individual and the logistics involved in implementing the chosen therapeutic option.

Statement 10.9

We suggest health care professionals counsel parents and children with intersexuality (when cognitively sufficiently developed) to delay gender-affirming genital surgery, gonadal surgery, or both, so as to optimize the children's self-determination and ability to participate in the decision based on informed consent.

International human rights organizations have increasingly expressed their concerns that surgeries performed before a child can participate meaningfully in decision-making may endanger the child's human rights to autonomy, self-determination, and an open future (e.g., Human Rights Watch, 2017). Numerous medical and intersex advocacy organizations as well as several countries have joined these international human rights groups in recommending the delay of surgery when medically feasible (Dalke et al., 2020; National Academies of Sciences, Engineering, and Medicine, 2020). However, it is important to note some anatomic variations, such as obstruction of urinary flow or exposure of pelvic organs, pose an imminent risk to physical health (Mouriquand et al., 2016). Others, such as menstrual obstruction or long-term malignancy risk in undescended testes, have eventual physical consequences. A third group of variations, i.e., variations in the appearance of external genitals or vaginal depth, pose no immediate or long-term physical risk. The above recommendation addresses only those anatomic variations that, if left untreated, have no immediate adverse physical consequences and where delaying surgical treatment poses no physical health risk.

Non-urgent surgical care for individuals with these variations is complex and often contested, particularly when an individual is an infant or a young child and cannot yet participate in the decision-making process. Older people with intersexuality have reported psychosocial and sexual health problems, including depression, anxiety, and sexual and social stigma (de Vries et al., 2019; Rosenwohl-Mack et al., 2020). Some studies have suggested individuals with a specific variation (e.g., 46,XX CAH) agree with surgery being performed before adolescence (Bennecke et al., 2021). Recent studies suggest some adolescents and adults are satisfied with the appearance and function of the genitals after childhood surgery (Rapp et al., 2021). A child's genital difference can also become a source of stress for parents, and there is research that reports a correlation of surgery to create binary genitals with a limited amount of reduction in parental distress (Wolfe-Christensen et al., 2017), although a minority of parents may report decisional regret (Ellens et al., 2017). Consequently, some organizations recommend surgery be offered to very young children (American Urological Association, 2019; Pediatric Endocrine Society, 2020).

This shows the division within the medical field regarding its management guidelines for early genital surgery. The authors of this chapter also did not reach complete consensus. Some intersex specialists consider it potentially harmful to insist on a universal deferral of early genital surgery for genital variations without immediate medical risks. Reasons supporting this view include 1) intersex conditions are highly heterogeneous with respect to type and severity as well as associated gonadal structure, function, and malignancy risk; 2) societies and families vary tremendously in gender norms and intersex stigma potential; 3) early surgery may present certain technical advantages; and 4) a review of surveys of individuals with intersexuality (most of whom had previously undergone genital surgery) show the majority endorse surgery before the age of consent, especially in the case of individuals with 46,XX CAH and less strongly for individuals with XY intersex conditions (Meyer-Bahlburg, 2022). Experts supporting this view call for an individualized approach to

decisions regarding genital surgery and its timing. This approach has been adopted by medical societies with high rates of intersex specialists (Bangalore Krishna et al., 2021; Pediatric Endocrine Society, 2020; Speiser et al., 2018; Stark et al., 2019) and by certain support organizations (CARES Foundation; Krege et al., 2019).

Nonetheless, long-term outcome studies are limited and most studies reporting positive outcomes lack a non-surgical comparison group (Dalke, et al., 2020; National Academies of Sciences, Engineering, and Medicine, 2020). There is also no evidence surgery protects children with intersex conditions from stigma (Roen, 2019). Adults with intersexuality do experience stigma, depression, and anxiety related to their genitalia, but can also experience stigma whether or not they have surgery (Ediati et al., 2017; Meyer-Bahlburg, Khuri et al., 2017; Meyer-Bahlburg et al., 2018). There is also evidence surgeries may lead to significant cosmetic, urinary, and sexual complications extending into adulthood (Gong & Cheng, 2017; National Academies of Sciences, Engineering, and Medicine, 2020). Recent studies suggest some groups of individuals may have particularly negative experiences with gonadectomy, although this risk has to be weighed against that of gonadal malignancy (Duranteau et al., 2020; Rapp et al., 2021). People with intersex conditions are also far more likely than the general population to be transgender, to be gender diverse, or to have gender dysphoria (Almasri et al., 2018; Pasterski et al., 2015). Genital surgeries of young children may therefore irreversibly reinforce a binary sex assignment that is not aligned with the persons' future. These findings, together with human rights perspectives, support the call for the delay in the decision for surgery until the individual can decide for him/her/themselves.

Systematic long-term follow-up studies are urgently needed to compare individuals with the same intersex conditions who differ in the age at surgery or have had no surgery with regard to gender identity, mental health, and general quality of life.

Statement 10.10

We suggest only surgeons experienced in intersex genital or gonadal surgery operate on individuals with intersexuality.

Intersex conditions are rare, and intersex genital and gonadal anatomy are heterogeneous. Surgeries have been associated with a risk of significant long-term complications (e.g., National Academies of Sciences, Engineering, and Medicine, 2020), and most surgical training programs do not prepare trainees to provide this specialized care (Grimstad, Kremen et al., 2021). In recognition of the complexity of surgical care across the lifespan, standards produced by expert and international consensus recommend this care be provided by multidisciplinary teams of experts (Krege et al, 2019; Lee, Nordenström et al., 2016; Pediatric Endocrine Society, 2020). Therefore, we advise surgical care be limited to intersex-specialized, multidisciplinary settings that include surgeons experienced in intersex care.

Statement 10.11

We recommend health care professionals who are prescribing or referring for hormonal therapies/surgeries counsel individuals with intersexuality and fertility potential and their families about a) known effects of hormonal therapies/surgery on future fertility; b) potential effects of therapies that are not well studied and are of unknown reversibility; c) fertility preservation options; and d) psychosocial implications of infertility.

Individuals with certain intersex conditions may have reproductively functional genitalia but experience infertility due to atypical gonadal development. Others may have functioning gonads with viable germ cells but an inability to achieve natural fertility secondary to incongruent internal or external genitalia (van Batavia & Kolon, 2016). Pubertal suppression, hormonal treatment with sex steroid hormones, and gender affirming surgeries may all have an adverse impact on future fertility. The potential consequences of the treatment and fertility preservation options should therefore be reviewed and discussed.

Individuals with functioning testes should be advised prolonged treatment with estrogen and suppression of testosterone, as studied in TGD people without intersexuality, may cause testicular atrophy and a reduction in sperm count (Mattawanon et al., 2018). Although interruption

of such gender affirming hormonal treatment may improve sperm quality, a complete reversal of semen impairment cannot be guaranteed (Sermondade et al., 2021). The principal fertility preservation option for individuals with functioning testes is cryopreservation of sperm collected through masturbation or vibratory stimulation (de Roo et al., 2016). Although there are no data for success in humans, there is a proposal to offer direct testicular extraction and cryopreservation of immature testicular tissue to adolescents who have not yet undergone spermarche (Mattawanon et al., 2018).

Individuals with functioning ovaries should be advised testosterone therapy usually results in cessation of both menses and ovulation, often within a few months of initiating therapy. There are major gaps in knowledge regarding the potential effects of testosterone on oocytes and subsequent fertility. In transgender people, one study reported testosterone treatment may be associated with the development of polycystic ovarian morphology (Grynberg et al., 2010). However, other researchers have not found evidence of polycystic ovarian syndrome (PCOS) among transgender men receiving gender affirming hormone therapy based on metabolic (Chan et al., 2018) or histologic parameters (de Roo et al., 2017). Individuals with an intact uterus and functioning ovaries may regain their fertility potential if testosterone therapy is discontinued.

Fertility preservation options in post-pubertal people with intersexuality and functioning ovaries include hormonal stimulation for mature oocyte cryopreservation or ovarian tissue cryopreservation. Alternatively, stimulated oocyte extraction has been reported even for a transgender man continuing testosterone therapy (Greenwald, 2021). Similarly, oocyte cryopreservation after ovarian stimulation has been reported in a transgender boy receiving GnRHa therapy (Rothenberg et al., 2019). It should be noted ovarian stimulation, temporary cessation of GnRHa, testosterone treatment, or both, as well as gynecological procedures, can all be psychologically distressing to individuals, with the stress reaction being influenced by mental health, gender identity, and other medical experience. Applicability of certain interventions may depend on the support of other people in the individual's social network, including potential partners.

Statement 10.12

We suggest health care professionals caring for individuals with intersexuality and congenital infertility introduce them and their families, early and gradually, to the various alternative options of parenthood.

For people with intersex characteristics, the likelihood of infertility may be recognized in infancy, childhood, adolescence as well as in adulthood, without first engaging in attempts to conceive. For many individuals, a diagnosis of infertility accompanies the intersex diagnosis (Jones, 2019). For some individuals, assisted heterologous fertilization (e.g., oocyte or sperm donation) may be an option. Multiple adoption pathways exist. Some may require commitment and a considerable investment of time. Individuals who are either not interested in engaging in the efforts to achieve fertility previously described or for whom fertility is not possible can benefit from early exposure to the options available for adoption and alternative parenthood. While uterus transplantation has had preliminary success in people with Mullerian agenesis (Richards et al., 2021), there is no protocol to date that avoids exposure of the developing fetus to the risks associated with the medications used to avoid transplant rejection.

CHAPTER 11 Institutional Environments

This chapter addresses care for transgender and gender diverse (TGD) individuals who reside in institutions. By definition, institutions are facilities or establishments in which people live and receive care in a congregate or large group setting, where individuals may or may not have freedom of movement, individual consent, or agency. Carceral facilities (correctional facilities, immigration detention centers, jails, juvenile detention centers) and noncarceral facilities (long-term care facilities, in-patient psychiatric facilities, domiciliaries, hospice/palliative care, assisted living facilities) are residential institutions where health care access for transgender persons may be provided. Much of the evidence in support of proper care of TGD persons comes from carceral settings. However, the recommendations put forth here apply to all institutions that house TGD individuals, both carceral and noncarceral (Porter et al., 2016). All of the recommendations of the Standards of Care apply equally to people living in both types of institutions. People should have access to these medically necessary treatments irrespective of their housing situation within an institution (Brown, 2009). Care for an institutionalized person must consider the individual does not have the access that non-institutionalized persons have to securing care on their own. For that reason, institutionalized persons must be supported in being able to receive the Standards of Care established by the World Professional Association for Transgender Health (WPATH).

TGD residents in carceral facilities report the lack of access to medically necessary transgender-specific health care (see Chapter 2—Global Applicability, Statement 2.1), which is ranked as their number one concern while incarcerated (Brown, 2014; Emmer et al., 2011). The systemic racial inequities inherent in many carceral environments (Sawyer, 2020), racial disparities in health outcomes (Nowotny et al., 2017), and the overrepresentation of TGD people of color in some facilities (Reisner et al., 2014) punctuate a need for facility leadership to attend to transitional care access issues. Controlled studies show clinically significant health and mental health disparities for justice-involved transgender people compared to matched groups of transgender people who have not been incarcerated or jailed (Brown and Jones, 2015). Too often the agencies, structures, and personnel that provide care are lacking in knowledge, training, and capacity to care for gender diverse people (Clark et al., 2017). Discrimination against TGD residents in palliative care settings, including hospice, is common, and the needs of TGD patients or their surrogates have been ignored in these settings (Stein et al., 2020). This is one reason why lesbian, gay, bisexual and transgender (LGBT)

Statements of Recommendations

11.1- We recommend health care professionals responsible for providing gender-affirming care to individuals residing in institutions (or associated with institutions or agencies) recognize the entire list of recommendations of the SOC-8 apply equally to people living in institutions.
11.2- We suggest institutions provide all staff with training on gender diversity.
11.3- We recommend medical professionals charged with prescribing and monitoring hormones for TGD individuals living in institutions who need gender-affirming hormone therapy do so without undue delay and in accordance with the SOC-8.
11.4- We recommend staff and professionals charged with providing health care to TGD individuals living in institutions recommend and support gender-affirming surgical treatments in accordance with the SOC-8 when sought by the individual, without undue delay.
11.5- We recommend administrators, health care professionals, and all others working in institutions charged with the responsibility of caring for TGD individuals allow those individuals who request appropriate clothing and grooming items to obtain such items concordant with their gender expression.
11.6- We recommend all institutional staff address TGD individuals by their chosen names and pronouns at all times.
11.7- We recommend institutional administrators, health care professionals, and other officials responsible for making housing decisions for TGD residents consider the individual's housing preference, gender identity and expression, and safety considerations rather than solely their anatomy or sex assignment at birth.
11.8- We recommend institutional personnel establish housing policies that ensure the safety of TGD residents without segregating or isolating these individuals.
11.9- We recommend institutional personnel allow TGD residents the private use of shower and toilet facilities upon request.

patients may choose to hide their sexual and/or gender identity when they enter a nursing home, despite the fact that prior to their admission to the facility they had been living publicly as a LGBT-identified person (Carroll, 2017; Serafin et al., 2013).

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable. The majority of the available literature related to institutions focuses on those who are incarcerated in jails, prisons, or other carceral environments. Literature about other institutional types were also considered and referenced where available. We hope future investigations will address this relative lack of data from noncarceral institutions. The recommendations summarized above are generalizable to a variety of institutional settings that have characteristics in common, including extended periods of stay, loss of or limited agency, and reliance on institutional staff for some or all of the basic necessities of life.

Statement 11.1

We recommend health care professionals responsible for providing gender-affirming care to individuals residing in institutions (or associated with institutions or agencies) recognize the entire list of recommendations of the SOC-8, apply equally to TGD people living in institutions.

Just as people living in institutions require and deserve mental and medical health care in general and in specialty areas, we recognize TGD people are in these institutions and thus need care specific to TGD concerns. We recommend the application of the Standards of Care (SOC) to people living in institutions as basic principles of health care and ethics (Beauchamp & Childress, 2019; Pope & Vasquez, 2016). Additionally, numerous courts have long upheld the need to provide TGD-informed care based in the WPATH SOC to people living in institutions as well (e.g., Koselik v. Massachusetts, 2002; Edmo v. Idaho Department of Corrections, 2020). Agencies that provide staffing for long-term, in-home services should also be aware of the applicability of the Standards of Care.

Statement 11.2

We suggest institutions provide all staff with training on gender diversity.

Because TGD care affects a small percentage of the population, it requires specialized training as outlined in this SOC Version 8. While the level of training will vary based on the staff member's role within the institutional setting, all staff will need training in addressing residents appropriately while other clinical staff may need more intensive training and/or consultation. These training recommendations also apply to agencies that supply staffing for in-home, long-term care. Misgendering institutionalized residents, not allowing for gender appropriate clothing, shower facilities, or housing, and not using chosen names communicates a lack of respect for TGD residents who may experience repeated indignities as emotionally traumatic, depressing, and anxiety-producing. By providing all institutional staff with training on gender diversity and basic competence in transgender-related health care issues, these harms can be prevented (Hafford-Letchfield et al., 2017). Surveys indicate individuals working with incarcerated individuals as well as in workers in noncarceral settings like palliative care have significant knowledge gaps (Stein et al., 2020; White et al., 2016). Hafford-Letchfied et al. (2017) showed benefit to training residential long-term care staff when such training began with "recognizing LBGT issues" and existed in "care homes". If the assigned health care providers lack the expertise to assess and/or treat gender diverse persons under their charge, outside consultation should be sought from professionals with expertise in the provision of gender-affirming health care (Brömdal et al., 2019; Sevelius and Jenness, 2017).

Statement 11.3

We recommend medical professionals charged with prescribing and monitoring hormones for TGD individuals living in institutions who need gender-affirming hormone therapy do so

without undue delay and in accordance with the SOC-8.

TGD persons may be admitted to institutions in need of evaluation for gender-affirming hormonal care or may develop this need after they have resided in an institutional setting for varying degrees of time. It is not uncommon for TGD persons to be denied access to hormonal care for months or years after making such needs known or to be undertreated and poorly monitored, delaying the necessary titration of medications for safety and efficacy (Keohane, 2018; Kosilek v. Massachusetts, 2002; Monroe v. Baldwin et al., 2019). This can result in significant negative mental health outcomes to include depression, anxiety, suicidality, and surgical self-treatment risks (Brown, 2010). As with all medically necessary health care, access to gender-affirming hormone therapies should be provided in a timely fashion when indicated for a TGD resident, in both carceral and noncarceral institutional environments. Medical professionals shall appropriately titrate hormones based on laboratory results and clinical outcomes to ensure results are within the range of recommended standards within the field of endocrinology. Such labs shall be taken at a frequency so as not to delay appropriate titration.

TGD elderly people living in long-term care facilities have unique needs (Boyd, 2019; Caroll, 2017; Porter, 2016). When elderly individuals request hormonal treatment, while physicians should assess pre-existing conditions, rarely do such conditions absolutely contraindicate administering hormones in this population (Ettner, 2013). People with gender incongruence in institutions may also have coexisting mental health conditions (Brown and Jones, 2015; Cole et al., 1997). These conditions should be evaluated and treated appropriately as part of the overall assessment. Persons receiving hormones must be closely medically monitored to avoid potential drug interactions and polypharmacy (Hembree et al., 2017).

TGD persons who enter an institution on an appropriate regimen of gender-affirming hormone therapy should be continued on the same or similar therapies and monitored according to the SOC Version 8. A "freeze frame" approach is inappropriate and dangerous (Kosilek v. Massachusetts, 2002). A "freeze frame" approach is the outmoded practice of denying hormones to people who are not already on them or keeping TGD persons on the same dose of hormones throughout their institutionalization that they were receiving upon admission, even if that dose was an initiation (low) dose. TGD persons who are deemed appropriate for de novo gender-affirming hormone therapy should be started on such therapy just as they would be outside of an institution (Adams v. Federal Bureau of Prisons, No. 09-10272 [D. MO June 7, 2010]; Brown 2009). The consequences of abrupt withdrawal of hormones or lack of initiation of hormone therapy when medically necessary include a significant likelihood of negative outcomes (Brown, 2010; Sundstrom and Fields v. Frank, 2011), such as surgical self-treatment by autocastration, depressed mood, increased gender dysphoria, and/or suicidality (Brown, 2010; Maruri, 2011).

If an individual in an institution does receive gender-affirming hormones and/or surgeries, decisions regarding housing in sex-segregated facilities may need to be reassessed for the safety and well-being of the TGD person (Ministry of Justice [UK], 2016).

Statement 11.4

We recommend staff and professionals charged with providing health care to TGD individuals living in institutions recommend and support gender-affirming surgical treatments in accordance with SOC-8, when sought by the individual, without undue delay.

TGD people with gender dysphoria should have an appropriate treatment plan to provide medically necessary surgical treatments that contain similar elements provided to persons who reside outside institutions (Adams v. Federal Bureau of Prisons, No. 09-10272 [D. MO June 7, 2010]; Brown 2009; Edmo v. Idaho Department of Corrections, 2020). The consequences of denial or lack of access to gender- affirming surgeries for residents of institutions who cannot access such care outside of their institutions may be serious, including substantial worsening of gender dysphoria symptoms, depression, anxiety, suicidality, and the possibility of surgical self-treatment

(e.g., autocastration or autopenectomy; Brown, 2010; Edmo v. Idaho Department of Corrections, 2020; Maruri, 2011). It is not uncommon for residents of institutions to be denied access to evaluation for gender-affirming surgery as well as denial of the treatment itself, even when medically necessary (Kosilek v. Massachusetts/Dennehy, 2012; Edmo v. Idaho Department of Corrections, 2020). The denial of medically necessary evaluations for and the provision of gender-affirming surgical treatments and necessary aftercare is inappropriate and inconsistent with these Standards of Care.

Statement 11.5

We recommend administrators, health care professionals, and all others working in institutions charged with the responsibility of caring for TGD individuals allow those individuals who request appropriate clothing and grooming items to obtain such items concordant with their gender expression.

Gender expression refers to people having hairstyles, grooming products, clothing, names, and pronouns associated with their gender identity in their culture and/or community (American Psychological Association, 2015; Hembree et al., 2017). Gender expression is the norm among most people within a culture or a community. Social transition is the process of TGD persons beginning and continuing to express their gender identity in ways that are authentic and socially perceptible. Often, social transition involves behavior and public presentation differing from what is usually expected for people assigned a given legal gender marker at birth. A gender marker is the legal label for a person's sex that is typically assigned or designated at birth on official documents (American Psychological Association, 2015). This is most commonly recorded as male or female but also intersex or "X" in some nations and jurisdictions. TGD individuals need the same rights to gender expression afforded cisgender people living both outside and inside institutional settings. Staff acceptance of social transition also sets a tone of respect and affirmation that may enhance respect and affirmation with others residing in the institution, thereby increasing safety and reducing some aspects of gender incongruence.

Research indicates social transition and congruent gender expression have a significant beneficial effect on the mental health of TGD people (Bockting & Coleman, 2007; Boedecker, 2018; Devor, 2004; Glynn et al., 2016; Russell et al., 2018). To allow for expressing gender identity, these recommendations include being allowed to wear gender congruent clothing and hairstyles, to obtain and use gender-appropriate hygiene and grooming products, to be addressed by a chosen name or legal last name (even if unable to change the assigned name legally yet), and to be addressed by a pronoun consistent with one's identity. These elements of gender expression and social transition, individually or collectively as indicated by the individual's needs, reduce gender dysphoria/incongruence, depression, anxiety, self-harm ideation and behavior, suicidal ideation and attempts (Russell et al., 2018). Furthermore, these elements of congruent gender expression enhance well-being and functioning (Glynn et al., 2016).

Statement 11.6

We recommend all institutional staff address TGD individuals by their chosen names and pronouns at all times.

Given that an increasing percentage of people openly identify as gender diverse, there is a need to develop and implement practices and policies that meet the needs of these people irrespective of where they live (McCauley et al., 2017). For example, institutions should utilize medical and administrative records systems for their residents that track gender markers consistent with gender identity and not solely sex assigned at birth. In developing these recommendations, there was recognition that gender expansiveness can challenge some institutional norms where TGD people live. However, all institutions have the responsibility to provide for the safety and well-being of all persons living therein (Australia, 2015; Corrective Services New South Wales, 2015; Edmo v. Idaho Department of Corrections, 2020; Kosilek v. Massachusetts, 2002; NCCHC, 2015). Sevelius and colleagues (2020) demonstrated correct pronoun usage is gender-affirming for

transgender women and correlates with positive mental health and HIV-related health outcomes. If a resident of an institution has legally changed names, the institutional records should be changed to reflect those changes.

Statement 11.7

We recommend institutional administrators, health care professionals, and other officials responsible for making housing decisions for TGD residents consider the individual's housing preference, gender identity and expression, and safety considerations, rather than solely their anatomy or sex assignment at birth.

The separation of people based on sex assigned at birth, a policy almost universally implemented in institutional settings (Brown and McDuffie, 2009; Routh et al., 2017), can create an inherently dangerous environment (Ledesma & Ford, 2020). Gender diverse people are extremely vulnerable to stigmatization, victimization, neglect, violence, and sexual abuse (Banbury, 2004; Beck, 2014; Jenness and Fenstermaker, 2016; Malkin & DeJong, 2018; Oparah, 2012; Stein et al., 2020). This systemic sex-segregated rigidity often fails to keep TGD people safe and may impede access to gender-affirming health care (Stohr, 2015). As a result, institutions should follow procedures that routinely evaluate the housing needs and preferences of TGD inmates (e.g., Federal Bureau of Prisons, 2016). Likewise, the Prison Rape Elimination Act specifically cites TGD individuals as a vulnerable population and directs prisons nationwide in the US to consider the housing preferences of these inmates (Bureau of Justice Assistance, 2017).

Statement 11.8

We recommend institutional personnel establish housing policies that ensure the safety of transgender and gender diverse residents without segregating or isolating these individuals.

Assigning placement for a TGD resident solely on the basis of their genital anatomy or sex assigned at birth is misguided and places people at risk for physical and/or psychological harm (Scott, 2013; Simopoulos & Khin, 2014; Yona & Katri, 2020). It is well established within carceral settings, transgender individuals are far more likely than other prisoners to be sexually harassed, assaulted, or both (James et al., 2016; Jenness & Fenstermaker, 2016; Malkin & DeJong, 2019). While placement decisions need to address security concerns, shared decision-making that includes the input of the individual should be made on a case-by-case basis (Federal Bureau of Prisons, 2016; Jenness and Smyth, 2011). Some transgender women prefer to reside in a male facility while others feel safer in a female facility. Given the range of gender identities, expression and transition status is so heterogeneous among gender diverse people, keeping residents safe requires flexible decision-making processes (Yona & Katri, 2020). One of the fears older LBGT individuals have living in long-term care is mistreatment by roommates (Jablonski et al., 2013). Consequently, housing in nursing homes and assisted living facilities should consider assigning rooms to elders based on their self-identified gender without regard to birth assignment or surgical history and in collaboration with the TGD patient.

Solitary confinement, sometimes referred to as administrative segregation in carceral facilities, refers to physical isolation of individuals during which they are confined in their cells for approximately twenty-three hours each day. The use of isolation is employed in some carceral facilities as a disciplinary measure as well as a means of protecting prisoners who are considered a risk to themselves or others or who are at risk of sexual assault by other inmates. However, isolating prisoners for safety concerns, if necessary, should be brief, as isolation can cause severe psychological harm and gross disturbances of functioning (Ahalt et al., 2017; Scharff Smith, 2006). National prison standards organizations as well as The United Nations consider isolation longer than 15 days to be torture (NCCHC, 2016; United Nations, 2015).

Statement 11.9

We recommend institutional personnel allow transgender and gender diverse residents the private use of shower and toilet facilities, upon request.

The necessity and importance of privacy is universal irrespective of gender identity. TGD

individuals report avoiding public restrooms, limiting the amount they eat and drink so as not to have to use a public facility, often leading to urinary tract infections and kidney-related problems (James et al., 2016). TGD individuals in institutions are often deprived of privacy in bathroom and shower use, which can result in psychological harm and/or physical and sexual abuse (Bartels and Lynch, 2017; Brown, 2014; Cook-Daniels, 2016; Mann, 2006). Similarly, in carceral environments, pat downs, strip searches and body cavity searches should be conducted by staff members of the same sex with the understanding this may not be possible in extreme emergencies. The incidental viewing of searches by other employees should be avoided (Bureau of Justice Assistance, 2017). Private use of shower and toilet facilities for incarcerated transgender people is also required by some laws, including for instance the United States' federal Prison Rape Elimination Act in the US.

The population of aging/older TGD persons who need to be served by institutions is increasing (Carroll, 2017; Witten & Eyler, 2016). Many long-term care and other facilities catering to the needs of the aging need to take into consideration the needs of their non-cisgender residents (Ettner, 2016; Ettner & Wiley, 2016). Surveys of HCPs working with elders in hospice and palliative care settings as well as other long-term care facilities report patients who identify as TGD often do not get their basic needs met, are discriminated against in their medical care access, or are physically and/or emotionally abused (Stein et al., 2020) A survey of retirement and residential care providers in Australia found little experience with or understanding of the issues facing this population. Indeed, many elderly TGD residents admitted to concealing their gender identity, bowing to the fear of insensitive treatment or frank discrimination (Cartwright et al., 2012; Cook-Daniels, 2016; Grant et al., 2012; Horner et al., 2012; Orel & Fruhauf, 2015).

CHAPTER 12 Hormone Therapy

Transgender and gender diverse (TGD) persons may require medically necessary gender-affirming hormone therapy (GAHT) to achieve changes consistent with their embodiment goals, gender identity, or both (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1). This chapter describes hormone therapy recommendations for TGD adults and adolescents. Please refer to Chapter 5—Assessment of Adults and Chapter 6—Adolescents for the assessment criteria related to initiation of hormone therapy for adults and adolescents, respectively. A summary of the recommendations and assessment criteria can be found in Appendix D.

Ever since the first World Professional Association for Transgender Health (WPATH) Standards of Care (SOC) was published in 1979 and in subsequent updates of the SOC, including SOC version 7, GAHT has been accepted as medically necessary (Coleman et al., 2012). WPATH endorsed the Endocrine Society's guidelines for GAHT for TGD persons in 2009 and 2017 (Hembree et al., 2009; Hembree et al., 2017). The European Society for Sexual Medicine has also published a position statement on hormone management in adolescent and adult TGD people (T'Sjoen et al., 2020). When provided under medical supervision, GAHT in adults is safe (Tangpricha & den Heijer, 2017; Safer & Tangpricha, 2019). However, there are some potential long-term risks, and careful monitoring and screening are required to reduce adverse events (Hembree et al., 2017; Rosenthal, 2021).

In general, the goal is to target serum levels of the sex steroids to match the levels associated with the individual's gender identity, although optimal target ranges have not been established (Hembree et al., 2017). Health care professionals (HCPs) can use serum testosterone and/or estradiol levels to monitor most sex steroid treatments. However, conjugated estrogens or synthetic estrogen use cannot be monitored. The assumption that the estrone/estradiol ratio should be monitored was not supported in a recent cohort study as there was no relationship between estrone concentration and change in body fat or breast development seen in a European cohort of 212 adult transgender women during a 1-year follow-up of hormone treatment (Tebbens et al., 2021). This study demonstrated higher estrone concentrations or higher estrone/estradiol ratios are not associated with antagonistic effects on feminization (fat percentage and breast development) (Tebbens et al., 2021). Thus, monitoring of the estrone to estradiol ratio is not supported by the current published evidence. Previously used conjugated estrogens have been abandoned in favor of bioidentical estrogens. Even if several studies have shown a significantly greater risk of thromboembolic and cardiovascular complications with the use of oral conjugated estrogens compared with oral estradiol in postmenopausal women, no randomized controlled trials have taken place, either in postmenopausal women or in transgender people undergoing estrogen treatment (Smith et al., 2014).

The approach to GAHT differs and depends on the developmental stage of the individual at the time of initiation of hormone therapy as well as their treatment goals. Hormone therapy is not recommended for children who have not begun endogenous puberty. In eligible youth (as per Chapter 6—Adolescents) who have reached the early stages of puberty, the focus is usually to delay further pubertal progression with gonadotropin releasing hormone agonists (GnRHas) until an appropriate time when GAHT can be introduced. In these cases, pubertal suppression is considered medically necessary. Eligible adults may initiate GAHT if they fulfill the criteria as per Chapter 5—Assessment for Adults. In addition, health care providers should discuss fertility goals and fertility preservation procedures prior to initiating GAHT. See Chapter 16—Reproductive Health.

GAHT with feminine embodiment goals typically consists of estrogen and an androgen-lowering medication (Hembree et al., 2017). Although there are anecdotal reports of progesterone use for breast development and mood management, there is currently insufficient evidence the potential benefits of progesterone administration outweigh the potential risks (Iwamoto, T'Sjoen et al., 2019). Masculinizing GAHT typically consists of testosterone. Both WPATH and the Endocrine Society recommend monitoring levels of sex

hormones. While GAHT is customized to meet the individual needs of the TGD person, typically hormone levels are maintained at a concentration sufficient to support good bone health and are not supraphysiologic (Hembree et al., 2017; Rosen et al., 2019).

Statements of Recommendations

12.1- We recommend health care professionals begin pubertal hormone suppression in eligible* transgender and gender diverse adolescents after they first exhibit physical changes of puberty (Tanner stage 2).
12.2- We recommend health care professionals use gonadotropin releasing hormone (GnRH) agonists to suppress endogenous sex hormones in eligible* transgender and gender diverse people for whom puberty blocking is indicated.
12.3- We suggest health care professionals prescribe progestins (oral or injectable depot) for pubertal suspension in eligible* transgender and gender diverse youth when GnRH agonists are either not available or are cost prohibitive.
12.4- We suggest health care professionals prescribe GnRH agonists for suppression of sex steroids without concomitant sex steroid hormone replacement in eligible* transgender and gender diverse adolescents seeking such intervention and who are well into or have completed pubertal development (past Tanner stage 3) but are either unsure about or do not want to begin sex steroid hormone therapy.
12.5- We recommend health care professionals prescribe sex hormone treatment regimens as part of gender-affirming treatment for eligible* transgender and gender diverse adolescents who are at least Tanner stage 2, with parental/guardian involvement unless their involvement is determined to be harmful or unnecessary to the adolescent.
12.6- We recommend health care professionals measure hormone levels during gender-affirming treatment to ensure endogenous sex steroids are lowered and administered sex steroids are maintained at levels appropriate for the treatment goals of transgender and gender diverse people according to the Tanner stage.
12.7- We recommend health care professionals prescribe progestogens or a GnRH agonist for eligible* transgender and gender diverse adolescents with a uterus to reduce dysphoria caused by their menstrual cycle when gender-affirming testosterone use is not yet indicated.
12.8- We recommend health care providers involve professionals from multiple disciplines who are experts in transgender health and in the management of the care required for transgender and gender diverse adolescents.
12.9- We recommend health care professionals institute regular clinical evaluations for physical changes and potential adverse reactions to sex steroid hormones, including laboratory monitoring of sex steroid hormones every 3 months during the first year of hormone therapy or with dose changes until stable adult dosing is reached followed by clinical and laboratory testing once or twice a year once an adult maintenance dose is attained.
12.10- We recommend health care professionals inform and counsel all individuals seeking gender-affirming medical treatment about the options available for fertility preservation prior to initiating puberty suppression and prior to treating with hormone therapy.
12.11- We recommend health care professionals evaluate and address medical conditions that can be exacerbated by lowered endogenous sex hormone concentrations and treatment with exogenous sex hormones before beginning treatment for transgender and gender diverse people.
12.12- We recommend health care professionals educate transgender and gender diverse people undergoing gender-affirming treatment about the onset and time course of the physical changes induced by sex hormonal treatment.
12.13- We recommend health care professionals not prescribe ethinyl estradiol for transgender and gender diverse people as part of a gender-affirming hormonal treatment.
12.14- We suggest health care professionals prescribe transdermal estrogen for eligible* transgender and gender diverse people at higher risk of developing venous thromboembolism based on age > 45 years or a previous history of venous thromboembolism, when gender-affirming estrogen treatment is recommended.
12.15- We suggest health care professionals not prescribe conjugated estrogens in transgender and gender diverse people when estradiol is available as a component of gender-affirming hormonal treatment.
12.16- We recommend health care professionals prescribe testosterone-lowering medications (either cyproterone acetate, spironolactone, or GnRH agonists) for eligible* transgender and gender diverse people with testes who are taking estrogen as part of a hormonal treatment plan if the individual's goal is to approximate circulating sex hormone concentrations in cisgender women.
12.17- We recommend health care professionals monitor hematocrit (or hemoglobin) in transgender and gender diverse people treated with testosterone.
12.18- We suggest health care professionals collaborate with surgeons regarding hormone use before and after gender-affirmation surgery.
12.19- We suggest health care professionals counsel transgender and gender diverse people about the various options available for gender-affirmation surgery unless surgery is not indicated or is medically contraindicated.
12.20- We recommend health care professionals initiate and continue gender-affirming hormone therapy for eligible* transgender and gender diverse people who require this treatment due to demonstrated improvement in psychosocial functioning and quality of life.
12.21- We recommend health care professionals maintain existing hormone therapy if the transgender and gender diverse individual's mental health deteriorates and assess the reason for the deterioration, unless contraindicated.

** For eligibility criteria for adolescents and adults, please refer to Chapter 5—Assessment for Adults and Chapter 6—Adolescents and Appendix D.*

In most cases, GAHT is maintained throughout life. It is not known if doses of GAHT should be reduced in older TGD people. Discontinuation of hormone therapy may result in bone loss in TGD individuals and will definitely do so in individuals whose gonads have been removed (Wiepjes et al., 2020). Routine primary care should also be performed (see Chapter 15—Primary Care). Epidemiology studies have reported an increased incidence of cardiovascular disease and venous thromboembolism (VTE) in TGD people receiving estrogen, most notably in older people and with different preparations of GAHT (Irwig, 2018; Maraka et al., 2017). TGD individuals treated with testosterone may also have increased adverse cardiovascular risks and events, such as increased myocardial infarction, blood pressure, decreased HDL-cholesterol, and excess weight (Alzahrani et al., 2019; Irwig, 2018; Kyinn et al., 2021). Health care professionals (HCPs) should discuss lifestyle and pharmacologic therapy with patients who are at the highest risk of developing cardiovascular disease (see Chapter 15—Primary Care). Polycythemia is another disorder that may present in TGD people taking testosterone (Antun et al., 2020). Therefore, it is important to continuously monitor for the development of conditions that can be exacerbated by GAHT throughout life (Hembree et al., 2017).

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Gender-Affirming Hormone Therapy in Youth

The following sections will discuss hormone therapy in TGD youth. Depending on the developmental stage of the youth, this hormone therapy generally comprises two phases, namely pubertal suppression followed by the addition of GAHT. During the first phase, pubertal development is halted to allow the youth to explore their gender identity and embodiment goals to prepare for the next phase, which may include GAHT. This section will discuss the recommendations for the use of gonadotropin releasing hormone agonists (GnRHas) as well as alternate approaches to pubertal suppression and will be followed by recommendations for GAHT. Sections that are applicable to youth and adults will follow in the next section.

Statement 12.1

We recommend health care professionals begin pubertal hormone suppression in eligible* transgender and gender diverse adolescents only after they first exhibit physical changes of puberty (Tanner stage 2).

In general, the goal of GnRHa administration in TGD adolescents is to prevent further development of the endogenous secondary sex characteristics corresponding to the sex designated at birth. Since this treatment is fully reversible, it is regarded as an extended time for adolescents to explore their gender identity by means of an early social transition (Ashley, 2019e). Treatment with GnRHas also has therapeutic benefit since it often results in a vast reduction in the level of distress stemming from physical changes that occur when endogenous puberty begins (Rosenthal, 2014; Turban, King et al., 2020).

For those prepubertal TGD children who have been persistent in their gender identity, any amount of permanent development of secondary sex characteristics could result in significant distress. While one might consider use of a GnRHa to prevent initiation of puberty in such individuals who remain at Tanner Stage 1, this use of GnRHa has not been recommended (Hembree et al., 2017). When a child reaches an age where pubertal development would normally begin (typically from 7-8 to 13 years for those with ovaries and from 9 to 14 years for those with testes), it would be appropriate to screen the child more frequently, perhaps at 4-month intervals, for signs of pubertal development (breast budding or testicular volume > 4 cc). Given the typical tempo of pubertal development (3.5–4 years for completion), it would be very unlikely for permanent pubertal changes to develop if one is only in puberty for 4 months or less. Thus, with frequent follow-up, the initiation of puberty can easily be detected before there are irreversible physical changes, and GnRHa can be started at that time with great efficacy. Of note, following initiation of a GnRHa, there is typically

a regression of one Tanner stage. Thus, if there is only Tanner stage 2 breast development, it typically fully regresses to the prepubertal Tanner stage 1; the same is typically true with Tanner stage 2 testes (often not even discernable to the patient and is not associated with development of secondary sex characteristics).

Given GnRHas work through GnRH receptor desensitization, if there's no uptick in endogenous GnRH stimulation of the pituitary (the first biochemical sign of puberty), there's no need for GnRH receptor desensitization. In addition, because of the wide variability in the timing of the start of puberty (as noted above), it is hard to justify using a GnRHa that might have some unknown risk if there's no physiological benefit before pubertal onset. Using a GnRHa with a child at Tanner stage 1 would only be indicated in cases of constitutional delay in growth and puberty, likely alongside the start of GAHT.

However, the use of a GnRHa could be considered in a child who, due to a constitutional delay in growth and puberty, starts GAHT while still in Tanner Stage 1. Initiating GAHT may activate the hypothalamic-pituitary gonadal axis in the beginning but may also mask the effects on the body of this activation. To avoid body changes with the potential to exacerbate an individual's gender incongruence, the GnRHa can be started as an adjunctive therapy to the GAHT shortly after the initiation of the GAHT to provide for pubertal development of the identified phenotype.

In addition, the suppression of the development of secondary sex characteristics is most effective when sex hormonal treatment is initiated in early to mid-puberty when compared with the initiation of sex hormonal treatment after puberty is completed (Bangalore-Krisha et al., 2019). Correspondingly, for adolescents who have already completed endogenous puberty and are considering starting GAHT, GnRHas can be used to inhibit physical functions, such as menses or erections, and can serve as a bridge until the adolescent, guardian(s) (if the adolescent is not able to consent independently), and treatment team reach a decision (Bangalore-Krishna et al., 2019; Rosenthal, 2021).

The onset of puberty occurs through reactivation of the hypothalamic-pituitary-gonadal axis. Clinical assessment of the stages of puberty is based on physical features that reflect that reactivation. In individuals with functioning ovaries, Tanner stage 2 is characterized by the budding of the mammary gland. The development of the mammary gland occurs from exposure to estrogen produced by the ovaries. In individuals with functioning testes, Tanner stage 2 is characterized by an increase in testicular volume (typically greater than 4 ml). The growth of the testes is mediated through the gonadotropins luteinizing hormone (LH) and follicle stimulating hormone (FSH). In the later stages, the testes produce enough testosterone to induce masculinization of the body.

Statement 12.2

We recommend health care professionals use GnRH agonists to suppress endogenous sex hormones in eligible* transgender and gender diverse people for whom puberty blocking is indicated. For supporting text, see Statement 12.4.

Statement 12.3

We suggest health care professionals prescribe progestins (oral or injectable depot) for pubertal suspension in eligible* transgender and gender diverse youth when GnRH agonists are not available or are cost prohibitive. For supporting text, see Statement 12.4.

Statement 12.4.

We suggest health care professionals prescribe GnRH agonists to suppress sex steroids without concomitant sex steroid hormone replacement in eligible transgender and gender diverse adolescents seeking such intervention who are well into or have completed pubertal development (past Tanner stage 3) but are unsure about or do not wish to begin sex steroid hormone therapy.

GnRHas reduce gonadotrophin and sex steroid concentrations in TGD adolescents and thus halt the further development of secondary sex characteristics (Schagen et al., 2016). Their use is generally safe with the development of hypertension being the only short-term adverse event reported in the literature (Delemarre-van de Waal & Cohen-Kettenis, 2006; Klink, Bokenkamp et al., 2015). GnRHas prevent the pituitary gland from

secreting LH and FSH (Gava et al., 2020). When the gonadotropins decrease, the gonad is no longer stimulated to produce sex hormones (estrogens or androgens), and the sex hormone levels in the blood decrease to prepubertal levels. GnRHa treatment leads to partial regression of the initial stages of the already developed secondary sex characteristics (Bangalore et al., 2019). TGD adolescents with functioning ovaries will experience diminished growth of breast tissue, and if treatment is started at Tanner stage 2, the breast tissue may disappear completely (Shumer et al., 2016). Menarche can be prevented or discontinued following the administration of GnRHas in adolescents with a uterus. In TGD adolescents with functioning testes, testicular volume will regress to a lower volume.

When GnRHa treatment is started in adolescents at the later phases of pubertal development, some physical changes of pubertal development, such as late-stage breast development in TGD adolescents with functioning ovaries and a lower voice and growth of facial hair in TGD adolescents with functioning testes, will not regress completely, although any further progression will be stopped (Delemarre-van de Waal & Cohen-Kettenis, 2006). GnRHas have been used since 1981 for the treatment of central precocious puberty (Comite et al., 1981; Laron et al., 1981), and their benefits are well established (please also see the statements in Chapter 6—Adolescents). The use of GnRHas in individuals with central precocious puberty is regarded as both safe and effective, with no known long-term adverse effects (Carel et al., 2009). However, the use of GnRHas in TGD adolescents is considered off-label because they were not initially developed for this purpose. Nonetheless, data from adolescents prescribed GnRHas in a similar dose and fashion demonstrate effectiveness in delaying the onset of puberty although the long-term effects on bone mass have not been well established (Klink, Caris et al., 2015). Although long-term data are more limited in TGD adolescents than in adolescents with precocious puberty, data collection specifically in this population are ongoing (Klaver et al., 2020; Lee, Finlayson et al., 2020; Millington et al., 2020; Olson-Kennedy, Garofalo et al., 2019).

We recognize even though GnRHas are a medically necessary treatment, they may not be available for eligible adolescents because it is not covered by health insurance plans in some countries or may be cost-prohibitive. Therefore, other approaches should be considered in these cases, such as oral or injectable progestin formulations. In addition, for adolescents older than 14 years, there are currently no data to inform HCPs whether GnRHas can be administered as monotherapy (and for what duration) without posing a significant risk to skeletal health. This is because the skeleton will not have any exposure to adequate levels of sex steroid hormones (Rosenthal, 2021).

A prolonged hypogonadal state in adolescence, whether due to medical conditions such as hypergonadotropic hypogonadism, iatrogenic causes such as GnRHa monotherapy or physiological conditions such as conditional delay of growth and development, is often associated with an increased risk of poor bone health later in life (Bertelloni et al., 1998; Finkelstein et al., 1996). However, bone mass accrual is a multifactorial process that involves a complex interplay between endocrine, genetic, and lifestyle factors (Anai et al., 2001). When deciding on the duration of GnRHa monotherapy, all contributing factors should be considered, including factors such as pretreatment bone mass, bone age, and pubertal stage from an endocrine perspective and height gain, as well as psychosocial factors such as mental maturity and developmental stage relative to one's adolescent cohort and the adolescent's individual treatment goals (Rosenthal, 2021). For these reasons, a multidisciplinary team and an ongoing clinical relationship with the adolescent and the family should be maintained when initiating GnRHa treatment (see Statements 6.8, 6.9, and 6.12 in Chapter 6—Adolescents). The clinical course of the treatment, e.g., the development of bone mass during GnRHa treatment and the adolescent's response to treatment, can help to determine the length of GnRHa monotherapy.

Statement 12.5

We recommend health care professionals prescribe sex hormone treatment regimens as part of gender-affirming treatment in eligible*

transgender and gender diverse adolescents who are at least Tanner stage 2, with parental/guardian involvement unless their involvement is determined to be harmful or unnecessary to the adolescent. For supporting text, see Statement 12.6.

Statement 12.6

We recommend health care professionals measure hormone levels during gender-affirming treatment to ensure endogenous sex steroids are lowered and administered sex steroids are maintained at a level appropriate for the treatment goals of transgender and gender diverse people according to the Tanner stage.

Sex steroid hormone therapy generally comprises two treatment regimens, depending on the timing of the GnRHa treatment. When GnRHa treatment is started in the early stages of endogenous pubertal development, puberty corresponding with gender identity or embodiment goals is induced with doses of sex steroid hormones similar to those used in peripubertal hypogonadal adolescents. In this context, adult doses of sex steroid hormones are typically reached over approximately a 2-year period (Chantrapanichkul et al., 2021). When GnRHa treatment is started in late- or postpubertal transgender adolescents, sex steroid hormones can be given at a higher starting dose and increased more rapidly until a maintenance dose is achieved, resembling treatment protocols used in transgender adults (Hembree et al., 2017). An additional advantage of GnRHa treatment is sex steroid hormones do not have to be administered in supraphysiological doses, which would otherwise be needed to suppress endogenous sex steroid production (Safer & Tangpricha, 2019). For TGD individuals with functioning testes, GnRHa treatment (or another testosterone-blocking medication) should be continued until such time as the TGD adolescent/young adult ultimately undergoes gonadectomy, if this surgical procedure is pursued as a medically necessary part of their gender-affirming care. Once adult levels of testosterone are reached in TGD individuals with functioning ovaries who have been initially suppressed with GnRHa's, testosterone alone at physiological doses is typically sufficient to lower ovarian estrogen secretion, and GnRHas can be discontinued as discussed below (Hembree et al., 2017). For TGD adolescents with functioning ovaries who are new to care, GAHT can be accomplished with physiological doses of testosterone alone without the need for concomitant GnRHa administration (Hembree et al., 2017).

Gender-affirming sex steroid hormone therapy induces the development of secondary sex characteristics of the gender identity. Also, the rate of bone mineralization, which decreases during treatment with GnRHa's, rapidly recovers (Klink, Caris et al., 2015). During GnRHa treatment in early-pubertal TGD adolescents, the bone epiphyseal plates are still unfused (Kvist et al., 2020; Schagen et al., 2020). Following the initiation of sex steroid hormone treatment, a growth spurt can occur, and bone maturation continues (Vlot et al., 2017). In postpubertal TGD adolescents, sex steroid hormone treatment will not affect height since the epiphyseal plates have fused, and bone maturation is complete (Vlot et al., 2017).

In TGD adolescents with functioning testes, the use of 17-ß-estradiol for pubertal induction is preferred over that of synthetic estrogens, such as the more thrombogenic ethinyl estradiol (see Appendix D (Asscheman et al., 2015). It is still necessary to either continue GnRHa's to suppress endogenous testosterone production or transition to another medication that suppresses endogenous testosterone production (Rosenthal et al., 2016). Breast development and a female-typical fat distribution are among a number of physical changes that occur in response to estrogen treatment. See Appendix C—Table 1.

For TGD adolescents seeking masculinizing treatment, androgens are available as injectable preparations, transdermal formulations, and subcutaneous pellets. For pubertal induction, the use of testosterone-ester injection is generally recommended by most experts initially because of cost, availability, and experience (Shumer et al., 2016). It is advised to continue GnRHas at least until a maintenance level of testosterone is reached. In response to androgen treatment, virilization of the body occurs, including a lowering of the voice, more muscular development particularly in the upper body, growth of facial and body hair, and clitoral enlargement (Rosenthal et al., 2016). See Appendix C—Table 1.

In almost all situations, parental/caregiver consent should be obtained. Exceptions to this recommendation, in particular when caregiver or parental involvement is determined to be harmful to the adolescent, are described in more detail in Chapter 6—Adolescents (see Statement 6.11) where the rationale for involving parents/caregivers in the consent process is also described.

Statement 12.7

We recommend health care professionals prescribe progestogens or a GnRH agonist for eligible* transgender and gender diverse adolescents with a uterus to reduce dysphoria caused by their menstrual cycle when gender-affirming testosterone use is not yet indicated.

Menstrual suppression is a treatment option commonly needed by TGD individuals who experience distress related to menses or the anticipation of menarche. Statement 6.7 in Chapter 6—Adolescents describes this in more detail. To achieve amenorrhea, menstrual suppression can be initiated as a solo option before initiating testosterone or alongside testosterone therapy (Carswell & Roberts, 2017). Some youth, who are not ready for testosterone therapy or are not yet at an appropriate pubertal/developmental stage to begin such treatment, will benefit from the induction of amenorrhea (Olson-Kennedy, Rosenthal et al., 2018). Adolescents who experience an exacerbation of dysphoria related to the onset of puberty may elect to be treated with GnRHas for pubertal suppression (also see the Adolescents chapter).

Progestogens may be effective in adolescents whose goal is solely menstrual suppression. Continuous administration of progestin-only oral pills (including the contraceptive and noncontraceptive options), medroxyprogesterone injections, or levonorgestrel intrauterine device can be used for induction of amenorrhea (Pradhan & Gomez-Lobo, 2019). TGD individuals with functioning ovaries who start testosterone therapy may have 1–5 menstrual cycles before amenorrhea is achieved (Taub et al., 2020). Once amenorrhea is achieved, some TGD individuals with functioning ovaries may also choose to continue progestin treatment for birth control if relevant to their sexual practices.

TGD individuals with functioning ovaries and a uterus should be counseled about the potential for breakthrough menstrual bleeding in the first few months after initiating menstrual suppression. With GnRHa therapy, breakthrough bleeding may occur 2–3 weeks after initiation of the medication. For individuals seeking contraception or for those who continue to experience menstrual bleeding on progestin therapy, an estrogen combination with progestin may be considered for the maintenance of amenorrhea, yet they should be counseled on the possible side effect of breast development (Schwartz et al., 2019).

Statement 12.8

We recommend health care providers involve professionals from multiple disciplines who are experts in transgender health and in the management of the care of transgender and gender diverse adolescents.

As with the care of adolescents, we suggest where possible a multidisciplinary expert team of medical and mental health professionals (MHPs) be assembled to manage this treatment. In adolescents who pursue GAHT (given this is a partly irreversible treatment), we suggest initiating treatment using a schedule of gradually increasing doses after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and has established the individual possesses the mental capacity to give informed consent (Hembree et al., 2017). Specific aspects concerning the assessment of adolescents and the involvement of their caregivers and a multidisciplinary team are described in more detail in Chapter 6—Adolescents.

If possible, TGD adolescents should have access to experts in pediatric transgender health from multiple disciplines including primary care, endocrinology, fertility, mental health, voice, social work, spiritual support, and surgery (Chen, Hidalgo et al., 2016; Eisenberg et al., 2020; Keo-Meier & Ehrensaft, 2018). Individual providers are encouraged to form collaborative working relationships with providers from other disciplines to facilitate referrals as needed for the individual youth and their family (Tishelman et al., 2015). However, the lack of available

experts and resources should not constitute a barrier to care (Rider, McMorris et al., 2019). Helpful support for adolescents includes access to accurate, culturally informed information related to gender and sexual identities, transition options, the impact of family support, and connections to others with similar experiences and with TGD adults through online and in person support groups for adolescents and their family members (Rider, McMorris et al., 2019).

Many TGD adolescents have been found to experience mental health disparities and initial mental health screening (e.g., PHQ-2, GAD) can be employed as indicated (Rider, McMorris et al., 2019). Providers should keep in mind being transgender or questioning one's gender does not constitute pathology or a disorder. Therefore, individuals should not be referred for mental health treatment exclusively on the basis of a transgender identity. HCPs and MHPs who treat these youths and make referrals should, at a minimum, be familiar with the impact of trauma, gender dysphoria, and gender minority stressors on any potential mental health symptomatology, such as disordered eating, suicidal ideation, social anxiety. These health care providers should also be knowledgeable about the level of readiness of inpatient mental health services in their region to provide competent, gender-affirming care to TGD youth (Barrow & Apostle, 2018; Kuper, Wright et al., 2018; Kuper, Mathews et al., 2019; Tishelman & Neumann-Mascis, 2018). Statements 6.3, 6.4, and 6.12d in Chapter 6—Adolescents address this in more detail. Because parents of these youth commonly experience high levels of anxiety immediately after learning their youth is TGD, and their response to their child predicts that child's long-term physical and mental health outcomes, appropriate referrals for mental health support of the parents can be of great utility (Coolhart et al., 2017; Pullen Sansfaçon et al., 2015; Taliaferro et al., 2019).

Statement 12.9

We recommend health care professionals organize regular clinical evaluations for physical changes and potential adverse reactions to sex steroid hormones, including laboratory monitoring of sex steroid hormones every 3 months during the first year of hormone therapy or with dose changes until a stable adult dosing is reached followed by clinical and laboratory testing once or twice a year once an adult maintenance dose is attained.

Sex steroid hormone therapy is associated with a broad array of physical and psychological changes (Irwig, 2017; Tangpricha & den Heijer, 2017) (see Appendix C—Table 1). After sex steroid hormone therapy has been initiated, the HCP should regularly assess the progress and response of the individual to the treatment (also see Chapter 6—Adolescents). This evaluation should assess the presence of any physical changes as well as the impact of treatment on gender dysphoria (if present) and psychological well-being (see Appendix C—Table 1). Clinical visits provide important opportunities for HCPs to educate patients about the typical time course required for physical changes to manifest and encourage realistic expectations. During the first year of hormone therapy, sex steroid hormone doses are often increased. A major factor guiding the dose is the serum level of the corresponding sex steroid hormone. In general, the goal is to target serum levels of the sex steroids to match the levels associated with the individual's gender identity, although optimal target ranges have not been established (Hembree et al., 2017).

In addition to assessing the positive changes associated with sex steroid hormone therapy, the HCP should regularly assess whether the treatment has caused any adverse effects (see Appendix C—Table 2**).** Examples of adverse signs and symptoms include androgenic acne or bothersome sexual dysfunction (Braun et al., 2021; Kerckhof et al., 2019). GAHT also has the potential to adversely influence several laboratory tests. For example, spironolactone may cause hyperkalemia, although it is an uncommon and transient phenomenon (Millington et al., 2019). Testosterone increases the red blood cell count (hematocrit), which may occasionally cause erythrocytosis (Antun et al., 2020) (see Statement 12.17) (Hembree et al., 2017). Both estrogen and testosterone can alter lipid parameters, such as high-density protein lipoprotein (HDL) cholesterol and triglycerides (Maraka et al., 2017). See Appendix C—Tables 3 and 4.

The frequency of clinical evaluations should be individualized and guided by the individual's response to treatment. We suggest clinical assessments be performed approximately every 3 months during the first year of hormone therapy in patients who are stable and are not experiencing significant adverse effects (Appendix C—Table 5). We suggest rather than recommend testing be carried out every 3 months in the first year to allow some flexibility on the timing of these tests as there is no strong evidence or evidence from published studies supporting specific testing intervals. If an individual does experience an adverse effect, more frequent laboratory testing and/or clinical visits are often needed. Given the potential harm associated with sex hormone levels that exceed expected ranges in humans, we strongly recommend regular testing be performed as a standard practice when initiating GAHT in TGD individuals. Once a person has reached a stable adult dose of sex steroid hormone with no significant adverse effects, the frequency of clinic visits can be reduced to one to two per year (Hembree et al., 2017).

Statement 12.10

We recommend health care professionals inform and counsel all individuals seeking gender-affirming medical treatment about options for fertility preservation prior to initiating puberty suppression and prior to administering hormone therapy.

Pubertal suppression and hormone treatment with sex steroid hormones may have potential adverse effects on a person's future fertility (Cheng et al., 2019) (see also Chapter 6—Adolescents and Chapter 16—Reproductive Health). Although some TGD people may not have given much thought to their future reproductive potential at the time of their initial assessment to begin medical therapy, the potential implications of the treatment and fertility preservation options should be reviewed by the hormone prescriber and discussed with the person seeking these therapies (Ethics Committee of the American Society for Reproductive Medicine et al., 2015; De Roo et al., 2016).

Individuals with testes should be advised prolonged treatment with estrogen often causes testicular atrophy and a reduction in sperm count and other semen parameters (Adeleye et al., 2018). Nonetheless, there are major gaps in knowledge, and findings regarding the fertility of trans feminine people who take estrogen and antiandrogens are inconsistent (Cheng et al., 2019). In one study, heterogeneity in testicular histology was evident whether patients discontinued or continued therapy prior to orchiectomies (Schneider et al., 2015). For example, the discontinuation of estrogen and antiandrogens for six weeks resulted in complete spermatogenesis in 45% of individuals with the remainder showing meiotic arrest or spermatogonial arrest (Schneider et al., 2015). However, serum testosterone levels confirmed to be within female reference ranges leads to complete suppression of spermatogenesis in most transgender women (Vereecke et al., 2020). The principal fertility preservation option for patients with functioning testes is sperm cryopreservation, also known as sperm banking (Mattawanon et al., 2018). For prepubertal patients, suppression of puberty with GnRHs pauses the maturation of sperm (Finlayson et al., 2016).

Individuals with functioning ovaries should be advised testosterone therapy usually results in the cessation of menses and ovulation, often within a few months of initiation (Taub et al., 2020). There are also major gaps in knowledge regarding the potential effects of testosterone on oocytes and subsequent fertility of TGD patients (Eisenberg et al., 2020; Stuyver et al., 2020). One study found testosterone treatment may be associated with polycystic ovarian morphology, whereas other studies reported no metabolic (Chan et al., 2018) or histologic (De Roo et al., 2017; Grynberg et al., 2010) evidence of polycystic ovary syndrome (PCOS) following treatment with testosterone, and some studies have found a pre-existing higher prevalence of PCOS in transgender patients with ovaries (Baba, 2007; Gezer et al., 2021). TGD patients with an intact uterus and ovaries often regain their fertility potential if testosterone therapy is discontinued (Light et al., 2014). Indeed, a live birth after assisted reproductive technology has been reported following hormone-stimulated egg retrieval from a TGD

individual who did not discontinue testosterone therapy (Greenwald et al., 2021; Safer and Tangpricha, 2019). Other fertility preservation options for TGD patients with ovaries are oocyte cryopreservation and embryo cryopreservation with sperm from a partner or donor. The above options require hormonal stimulation for egg retrieval and the use of assisted reproductive technology.

For early pubertal transgender youth, suppression of puberty with GnRHa's pauses the maturation of germ cells, although a recent report noted ovarian stimulation of a TGD adolescent treated with a GnRHa's in early puberty (and continued during ovarian stimulation) resulted in a small number of mature oocytes that were cryopreserved (Rothenberg et al., 2019). Treating an TGD adolescent with functioning testes in the early stages of puberty with a GnRHa not only pauses maturation of germ cells but will also maintains the penis in a prepubertal size. This will likely impact surgical considerations if that person eventually undergoes a penile-inversion vaginoplasty as there will be less penile tissue to work with. In these cases, there is an increased likelihood a vaginoplasty will require a more complex surgical procedure, e.g., intestinal vaginoplasty (Dy et al., 2021; van de Grift et al., 2020). Such considerations should be included in any discussions with patients and families considering use of pubertal blockers in early pubertal adolescents with functioning testes.

Statement 12.11

We recommend health care professionals evaluate and address medical conditions that can be exacerbated by lowered endogenous sex hormone concentrations and treatment with exogenous sex hormones before beginning treatment in transgender and gender diverse people.

TGD people seeking masculinization must be informed about the possibilities, consequences, limitations, and risks associated with testosterone treatment. Testosterone therapy is contraindicated during pregnancy or while attempting to become pregnant given its potential iatrogenic effects on the fetus. Relative contraindications to testosterone therapy include severe hypertension, sleep apnea, and polycythemia since these conditions can be exacerbated by testosterone. Monitoring blood pressure and lipid profiles should be performed before and after the onset of testosterone therapy. The increase in blood pressure typically occurs within 2 to 4 months following the initiation of testosterone therapy (Banks et al., 2021). Patients who develop hypercholesterolemia and/or hypertriglyceridemia may require treatment with dietary modifications, medication, or both.

TGD people seeking feminizing treatment with a history of thromboembolic events, such as deep vein thrombosis and pulmonary embolism, should undergo evaluation and treatment prior to the initiation of hormone therapy. This is because estrogen therapy is strongly associated with an increased risk of thromboembolism, a potentially life-threatening complication. In addition, risk factors that can increase the risk of thromboembolic conditions, such as smoking, obesity, and sedentary lifestyle, should be modified. In patients with nonmodifiable risk factors, such as a known history of thrombophilia, a past history of thrombosis, or a strong family history of thromboembolism, treatment with transdermal estrogen concomitant with anticoagulants may decrease the risk of thromboembolism. However, there are limited data to guide treatment decisions. The presence of a disease at baseline such as a hormone sensitive cancer, coronary artery disease, cerebrovascular disease, hyperprolactinemia, hypertriglyceridemia, and cholelithiasis should be evaluated prior to the initiation of gender-affirming hormone therapy as relative risks may be shifted in association with exogenous hormone treatment (Hembree et al., 2017).

Statement 12.12

We recommend health care professionals educate transgender and gender diverse people undergoing gender-affirming treatment about the onset and time course of physical changes induced by sex hormone treatment.

The effects of testosterone treatment are multiple and may include the appearance of increased body and facial hair, male pattern baldness, increased muscle mass and strength, decreased fat mass, deepening of the voice, interruption of

menses (if still present), increased prevalence and severity of acne, clitoral enlargement, and increased sexual desire (Defreyne, Elaut et al., 2020; Fisher, Castellini et al., 2016; Giltay & Gooren, 2000; T'Sjoen et al., 2019; Yeung et al., 2020). Other testosterone-associated changes include increased lean body mass, skin oiliness, (de Blok et al., 2020; Hembree et al., 2017; Kuper, Mathews et al., 2019; Taliaferro et al., 2019; Tishelman & Neumann-Mascis, 2018) (see Appendix C—Table 1).

Estrogen treatment induces breast development. However, fewer than 20% of individuals reach Tanner breast stages 4–5 after 2 years of treatment (de Blok et al., 2021). Additional changes include decreases in testicular volume, lean body mass, skin oiliness, sexual desire, spontaneous erections, facial hair, and body hair along with increased subcutaneous body fat) (see Appendix C—Table 1). In adult patients, estrogen does not alter a person's voice or height (Iwamoto, Defreyne et al., 2019; Wiepjes et al., 2019).

The time course and extent of physical changes vary among individuals and are related to factors such as genetics, age of initiation, and overall state of health (Deutsch, Bhakri et al., 2015; van Dijk et al., 2019). Knowledge of the extent and timing of sex hormone–induced changes, if available, may prevent the potential harm and expense of unnecessary treatment changes, dosage increases, and premature surgical procedures (Dekker et al., 2016).

Statement 12.13

We recommend health care professionals not prescribe ethinyl estradiol for transgender and gender diverse people as part of a gender-affirming hormonal treatment. For supporting text, see Statement 12.15.

Statement 12.14

We suggest health care professionals prescribe transdermal estrogen for eligible* transgender and gender diverse people at higher risk of developing venous thromboembolism based on age >45 years or a previous history of venous thromboembolism, when gender-affirming estrogen treatment is recommended. For supporting text, see Statement 12.15).

Statement 12.15

We suggest health care professionals not prescribe conjugated estrogens in transgender and gender diverse people when estradiol is available as part of a gender- affirming hormonal treatment.

Determining the safest and most efficacious estrogen compound and route of administration for TGD people is an important topic. The recommended estrogen-based regimens are presented in Appendix C—Table 4. The Amsterdam Medical Center (AMC) first reported 45 events of VTE occurring in 816 transgender women, notably an expected incidence ratio of VTE 20-fold higher than that reported in a reference population (van Kesteren et al., 1997). Following this report, the AMC clinic recommended the use of transdermal estradiol for transgender women older than 40 years of age, which subsequently lowered the incidence of VTE (Nota et al., 2019; Toorians et al., 2003). Other studies suggested ethinyl estradiol is associated with a higher risk of blood clotting due to an increased resistance to the anticoagulating effects of activated protein C (APC) and elevated concentrations of the clotting factors protein C and protein S (Toorians et al., 2013). Other studies published within the past 15 years from other clinics reported transgender women taking other forms of estrogen had lower rates of VTE than transgender women taking ethinyl estradiol (Asscheman et al., 2013). Furthermore, a 2019 systematic review concluded ethinyl estradiol administration was associated with the highest risk of VTE in transgender women, while an association between progesterone use and VTE was also identified (Goldstein et al., 2019).

The 2017 Endocrine Society guidelines did not recommend conjugated equine estrogens (CEEs) as a treatment option because blood levels of conjugated estrogens cannot be measured in transgender women making it difficult to prevent supraphysiologic dosing of estrogen and thereby increasing the potential risk of VTE (Hembree et al., 2017). A retrospective study from the UK examined the risks of oral CEE versus oral estradiol valerate versus oral ethinyl estradiol and found up to a 7-fold increase in the percentage of transgender women in the oral CEE group

who developed VTE compared with transgender women using other forms of estrogen (Seal et al., 2012). In a nested, case-control study, over 80,000 cisgender women aged 40–79 who developed a VTE were matched to approximately 390,000 cisgender women without VTE; the results showed oral estradiol use had a lower risk of VTE than conjugated estrogens, and transdermal estrogen was not associated with an increased risk of VTE (Vinogradova et al., 2019).

A systematic review evaluated several formulations of estrogen and identified a retrospective and a cross-sectional study that made head-to-head comparisons of the risks associated with different formulations (Wierckx, Mueller et al., 2012; Wierckx et al., 2013). No identified studies evaluating the risk of different formulations of estrogen employed a prospective interventional design. The retrospective study examined 214 transgender women taking transdermal estradiol (17β-estradiol gel 1.5 mg/d or estradiol patch 50 mcg/d) or a daily intake of oral estrogens (estradiol 2 mg/d, estriol 2 mg/d, ethinyl estradiol 50 mcg/day, or ethinyl estradiol 30–50 mcg in an oral contraceptive) (Wierckx et al., 2013). Within a 10-year observation period, 5% of the cohort developed a VTE, 1.4% (3 of 214) experienced a myocardial infarction (MI), and 2.3% (5 of 214) a transient ischemic attack or cerebrovascular accident (TIA/CVA). The prevalence of VTE, MI and TIA/CVA was increased following the initiation of estrogen therapy. However, the authors did not report differences between regimens of estrogen in terms of these endpoints.

The same group of investigators conducted a cross-sectional study that examined 50 transgender women (mean age 43 ± 10) taking oral estrogen (estradiol valerate 2 mg/d, estriol 2 mg/d or ethinyl estradiol 50–120 mcg/day) or using transdermal estradiol (17β-estradiol 1.5 mg/day or estradiol 50 mcg/day) over a follow-up duration of 9.2 years (Wierckx, Mueller et al., 2012). Twelve percent (n = 6) developed either a VTE, MI, or a TIA/CVA. Two of the participants were taking conjugated estrogen 0.625 mg/d (one person in combination with cyproterone acetate), 2 participants were taking ethinyl estradiol 20–50 mcg/d, 1 was taking cyproterone acetate 50 mg/d, while the estrogen regimen used by the sixth participant was not defined. None of the subjects taking oral estradiol or transdermal estradiol developed a VTE, MI, or TIA/CVA.

One prospective study examined the route of estrogen administration in 53 transgender women in a multicenter study carried out throughout Europe. Transgender women younger than 45 years of age (n = 40) received estradiol valerate 4 mg/d in combination with cyproterone acetate (CPA) 50 mg/d and transgender women older than 45 years of age (n = 13) received transdermal 17β-estradiol, also with CPA. No VTE, MI, or TIA/CVA was reported after a 1-year follow-up in either the oral or transdermal estrogen group. An additional retrospective study from Vienna found no occurrences of VTE among 162 transgender women using transdermal estradiol who were followed for a mean of 5 years (Ott et al., 2010).

We are strongly confident in our recommendation against the use of ethinyl estradiol based on historical data from the Amsterdam clinic demonstrating a reduction in the incidence of VTE after discontinuing the use of ethinyl estradiol and the recent systematic review demonstrating an increased risk of VTE in transgender women taking ethinyl estradiol (Weinand & Safer, 2015). We are confident in our recommendation against the use of CEE based on the 2012 study by Seal et al. demonstrating an increased risk of VTE in transgender women taking CEE compared with other formulations of estrogen and with data from cisgender women on hormone replacement therapy (Canonico et al., 2007; Seal et al., 2012). Prospective and retrospective studies in transgender women have reported occurrences of VTE/MI/CVA only in those taking CEE or ethinyl estradiol. Since estradiol is inexpensive, more widely available, and appears safer than CEE in limited studies, the committee recommends against using CEE when estradiol is an available treatment option. The quality of studies may be limited to prospective, cohort or cross-sectional study designs; however, the stronger level of recommendation is based on the consistent evidence supporting the association between the use of ethinyl estradiol and CEE and a greater risk of VTE/MI/CVA in transgender women.

We are also confident in our recommendation for the administration of transdermal preparations of estrogen in older transgender women

(age > 45 years) or those with a previous history of VTE. The confidence in our recommendation is based on the decreased incidence of VTE reported from the Amsterdam clinic when transgender women are switched to using transdermal preparations after age 40 (van Kesteren et al., 1997). Furthermore, the prospective, multicenter cohort study ENIGI found no incidence of VTE/MI/CVA in transgender women who are routinely switched to transdermal estrogen at age 45 (Dekker et al., 2016). In addition, a study by Ott et al. demonstrated no incidence of VTE in 162 transgender women treated with estradiol patches (Ott et al., 2010).

With the exception of cyproterone acetate (note this is not approved for use in the US because of concerns of potential hepatotoxicity), the use of progestins in hormone therapy regimens remains controversial. To date, there have been no quality studies evaluating the role of progesterones in hormone therapy for transgender patients.

We are aware some practitioners who prescribe progestins, including micronized progesterone, are under the impression there may be improvements in breast and/or areolar development, mood, libido, and overall shape for those seeking it along with other benefits yet to be demonstrated (Deutsch, 2016a; Wierckx, van Caenegem et al., 2014). However, these improvements remain anecdotal, and there are no quality data to support such progestin use. An attempted systematic review we commissioned for this version of the SOC failed to identify enough data to make a recommendation in favor of any progestins. Instead, existing data suggest harm is associated with extended progestin exposure (Safer, 2021).

For cisgender women who have a uterus, progestins in combination with estrogens are necessary to avoid the endometrial cancer risk associated with the administration of unopposed estrogen. For cisgender women who do not have a uterus, progestins are not used. The best data for the concerns related to progestin use come from comparisons between the above two cisgender populations, which we acknowledge is not necessarily generalizable to this population. Although not definitive of a class effect for all progestins, medroxyprogesterone added to combined equine estrogens is associated with greater breast cancer and cardiac risks (Chlebowski 2020; Manson, 2013). It is important to note data from the Women's Health Initiative (WHI) studies may not be generalizable to transgender populations. Compared with the cisgender women in the studies, transgender populations seeking hormone therapy tend to be younger, do not use equine estrogen, and hormone therapy in these cases address current mental health and quality of life and not solely risk prevention (Deutsch, 2016a).

Potential adverse effects of progestins include weight gain, depression, and lipid changes. Micronized progesterone may be better tolerated and may have a more favorable impact on the lipid profile than medroxyprogesterone (Fitzpatrick et al., 2000). When paired with estrogens for transgender women, the progestin cyproterone acetate is associated with elevated prolactin, decreased HDL cholesterol, and rare meningiomas—none of which are seen when estrogens are paired with GnRH agonists or spironolactone (Bisson, 2018; Borghei-Razavi, 2014; Defreyne, Nota et al., 2017; Sofer et al., 2020).

Thus, data to date do not include quality evidence supporting a benefit of progestin therapy for transgender women. However, the literature does suggest a potential harm of some progestins, at least in the setting of multi-year exposure. If, after a discussion of the risks and benefits of progesterone treatment, there is a collaborative decision to begin a trial of progesterone therapy, the prescriber should evaluate the patient within a year to review the patient's response to this treatment.

Statement 12.16

We recommend health care professionals prescribe testosterone-lowering medications (either cyproterone acetate, spironolactone, or GnRH agonists) for eligible* transgender and gendered diverse people with testes taking estrogen as part of a hormonal treatment plan if their individual goal is to approximate levels of circulating sex hormone in cisgender women.

Most gender clinics in the US and Europe prescribe estrogen combined with a testosterone-lowering medication (Mamoojee et al., 2017) (see Appendix C—Table 5). In the

US, spironolactone is the most commonly prescribed testosterone-lowering medication, while GnRHas are commonly used in the UK, and cyproterone acetate are most often prescribed in the rest of Europe (Angus et al., 2021; Kuijpers et al., 2021). The rationale for adding a testosterone-lowering medication is two-fold 1) to lower testosterone levels to within the reference range of cisgender women; and 2) to reduce the amount of estrogen needed to achieve adequate physical effects. Each testosterone-lowering medication has a different side effect profile. Spironolactone is an antihypertensive and potassium-sparing diuretic, and thus may lead to hyperkalemia, increased frequency of urination, and a reduction in blood pressure (Lin et al., 2021). Cyproterone acetate has been associated with the development of meningioma and hyperprolactinemia (Nota et al., 2018). GnRHa's, while very effective in lowering testosterone levels, can result in osteoporosis if doses of estrogen given concurrently are insufficient (Klink, Caris et al., 2015).

One systematic review identified one study that reported findings from a head-to-head comparison of the testosterone-lowering medications cyproterone acetate and leuprolide (Gava et al., 2016). Two studies compared a group of transgender women taking estrogen plus testosterone-lowering medications with a group who received only estrogen. The systematic review did not provide sufficient evidence to suggest any of the three testosterone-lowering medications had a better safety profile in terms of improved outcomes in bone health, testosterone levels, potassium levels, or in the incidence of hyperprolactinemia or meningiomas (Wilson et al., 2020). Therefore, no recommendation can be given. The review did report spironolactone-based regimens were associated with a 45% increase in prolactin levels, whereas cyproterone-based regimens increased prolactin levels by more than 100%. However, the clinical significance of elevated prolactin levels is not clear because the rates of prolactinomas were not significantly elevated in either the spironolactone- or CPA-treated groups (Wilson et al., 2020). One retrospective, cohort study from a single center in the US reported no clinically significant increases in prolactin levels in 100 transgender women treated with estrogen plus spironolactone (Bisson et al., 2018). A retrospective study from the Netherlands of 2,555 transgender women taking primarily CPA with various formulations of estrogen reported an increased standardized incidence ratio of meningiomas in patients who used cyproterone acetate after gonadectomy for many years when compared with the general Dutch population (Nota et al., 2018). Furthermore, in a shorter study in Belgium, 107 transgender women had transient elevations in prolactin levels following treatment with cyproterone acetate, which declined to normal after discontinuation (Defreyne, Nota et al., 2017). A recent publication, not included in the systematic review, examined 126 transgender women taking spironolactone, GnRHas, or cyproterone and concluded cyproterone was associated with higher prolactin levels and a worse lipid profile than spironolactone or GnRHas (Sofer et al., 2020). After balancing the costs and accessibility of measuring prolactin levels against the clinical significance of an elevated level, a decision was made not to make a recommendation for or against monitoring prolactin levels at this time. HCPs should therefore make individualized clinical decisions about the necessity to measure prolactin levels based on the type of hormone regimen and/or the presence of symptoms of hyperprolactinemia or a pituitary tumor (e.g., galactorrhea, visual field changes).

Cyproterone has also been linked to meningiomas. Nine cases of meningioma have been reported in the literature among transgender women primarily taking cyproterone acetate (Mancini et al., 2018). This increased risk has also been identified in cisgender populations. In 2020, the European Medicines Agency published a report recommending cyproterone products with daily doses of 10 mg or more should be restricted because of the risk of developing meningioma (European Medicines Agency, 2020). Most likely this association is a specific effect of cyproterone acetate and has not been extrapolated to include other testosterone-lowering drugs. In the US, where cyproterone acetate is not available, the North American Association of Central Cancer Registries (NAACCRs) database did not identify an increased risk of brain tumors (not specific to

meningiomas) among transgender women (Nash et al., 2018). Furthermore, there was not an increase in the hazard ratio of brain tumors in the Kaiser cohort of 2,791 transgender women compared with cisgender controls (Silverberg et al., 2017). No long-term studies have reported on the risk of meningiomas and prolactinomas in transgender women taking GnRHas.

Our strong recommendation for the use of testosterone-lowering medications as part of a hormone regimen for transgender individuals with testes is based on the global practice of using these medications in addition to estrogen therapies as well as the relatively minimal risk associated with these therapies. However, we are not able to make a recommendation favoring one testosterone-lowering medication over another at this time. The published data thus far raises some concerns about the risk of meningiomas with the prolonged use (>2 years) and higher doses (>10mg daily) of cyproterone acetate (Nota et al., 2018; Ter Wengel et al., 2016; Weill et al., 2021).

Bicalutamide is an antiandrogen that has been used in the treatment of prostate cancer. It competitively binds to the androgen receptor to block the binding of androgens. Data on the use of bicalutamide in trans feminine populations is very sparse and safety data is lacking. One small study looked at the use of bicalutamide 50 mg daily as a puberty blocker in 23 trans feminine adolescents who could not obtain treatment with a GnRH analogue (Neyman et al., 2019). All adolescents experienced breast development which is also commonly seen in men with prostate cancer who are treated with bicalutamide. Although rare, fulminant hepatotoxicity resulting in death has been described with bicalutamide (O'Bryant et al., 2008). Given that bicalutamide has not been adequately studied in trans feminine populations, we do not recommend its routine use.

The administration of 5α-reductase inhibitors block the conversion of testosterone to the more potent androgen dihydrotestosterone. The Food & Drug Administration (FDA) approved indications of finasteride administration include benign prostatic hypertrophy and androgenetic alopecia. Data on the use of 5α-reductase inhibitors in trans feminine populations is very sparse (Irwig, 2021). It is unclear whether this class of medication could have any clinical benefit in trans feminine individuals whose testosterone and dihydrotestosterone levels have already been lowered with estrogen and an antiandrogen. We therefore do not recommend their routine use in trans feminine populations. Finasteride may be an appropriate treatment option in trans masculine individuals experiencing bothersome alopecia resulting from higher dihydrotestosterone levels. Nonetheless, treatment with a 5α-reductase inhibitor may impair clitoral growth and the development of facial and body hair in trans masculine individuals. Studies are needed to assess the efficacy and safety of 5α-reductase inhibitors in transgender populations.

Statement 12.17

We recommend health care professionals monitor hematocrit (or hemoglobin) levels in transgender and gender diverse people treated with testosterone.

There are good quality data suggesting a rise in hematocrit (or hemoglobin) is associated with TGD persons treated with testosterone (Defreyne et al., 2018). The testosterone regimens in the systematic review included testosterone esters ranging from the equivalent of 25–250 mg SC/IM weekly, testosterone undecanoate 1000 mg every 12 weeks, or testosterone gel 50 mg applied daily to the skin (Defreyne et al., 2018; Gava et al., 2018; Giltay et al., 2000; Meriggiola et al., 2008; Pelusi et al., 2014; T'Sjoen et al., 2005; Wierckx, van Caenegem et al., 2014; Wierckx, van de Peer et al., 2014). The expected rise should be consistent with reference ranges in cisgender males.

Statement 12.18

We suggest health care professionals collaborate with surgeons regarding hormone use before and after gender-affirmation surgery. For supporting text, see Statement 12.19.

Statement 12.19

We suggest health care professionals counsel eligible* transgender and gender diverse people about the various options for gender-affirmation surgery unless surgery is either not indicated or is medically contraindicated.

Despite the absence of evidence, perioperative clinical standards for gender-affirmation surgeries have included cessation of hormone therapy for 1–4 weeks before and after surgery, most commonly genital surgeries (Hembree et al., 2009). Such practice was meant to mitigate the risk of VTE associated with exogenous estrogen administration (Hembree et al., 2009). Estrogen and testosterone could then be resumed at some point postoperatively.

After careful examination, investigators have found no perioperative increase in the rate of VTE among transgender individuals undergoing surgery, while being maintained on sex steroid treatment throughout when compared with that among patients whose sex steroid treatment was discontinued preoperatively (Gaither et al., 2018; Hembree et al., 2009; Kozato et al., 2021; Prince & Safer, 2020). Sex steroid treatment is especially important after gonadectomy to avoid the sequelae of hypogonadism, the risk of developing osteoporosis, and for the maintenance of mental health and quality of life (Fisher, Castellini et al., 2016; Rosen et al., 2019). Thus, hormone providers and surgeons should educate patients about the necessity for continuous exogenous hormone therapy after gonadectomy.

To be able to educate patients and serve as clinical advocates, HCPs should be knowledgeable about the risks and benefits of gender-affirmation surgeries and should also be cognizant of the performance measures and surgical outcomes of the surgeons to whom they might refer patients (Beek, Kreukels et al., 2015; Colebunders et al., 2017; Wiepjes et al., 2018). In general, most medically necessary surgeries can be thought of as involving three regions: the face, chest/breasts, and genitalia (internal and external). Additional medically necessary procedures include body contouring and voice surgery. See medical necessity statement in Chapter 2—Global Applicability, Statement 2.1).

Multiple procedures are available for facial gender-affirming surgeries including, but not limited to chondrolanryngoplasty, rhinoplasty, contouring or augmentation of the jaw, chin, and forehead, facelift, hair removal and hair transplantation (see Chapter 13—Surgery and Postoperative Care). Procedures available for chest/breast surgery include breast augmentation, double mastectomy with nipple grafts, periareolar mastectomy, and liposuction. The most common gender-affirmation surgery for TGD individuals with endogenous breast development is masculinizing chest surgery (mastectomy) (Horbach et al., 2015; Kailas et al., 2017).

Internal genital surgery procedures include but are not limited to orchiectomy, hysterectomy, salpingo-oophorectomy, vaginoplasty, and colpectomy/vaginectomy (Horbach et al., 2015; Jiang et al., 2018). The inner lining in vaginoplasty is typically constructed from penile skin, skin grafts, a combination of both, or a bowel segment. Removal of the uterus/ovaries can be performed individually or all at once (hysterectomy, salpingo-oophorectomy, and colpectomy). If colpectomy is performed, a hysterectomy must also be performed. The ovaries may remain in situ, upon patient request. A potential benefit of leaving one or both ovaries is fertility preservation, while the downside is the potential for the development of ovarian pathology, including cancer (De Roo et al., 2017).

External genital surgery procedures include but are not limited to vulvoplasty, metoidioplasty, and phalloplasty (Djordjevic et al., 2008; Frey et al., 2016). Hair removal is generally necessary before performing external genital procedures (Marks et al., 2019). Vulvoplasty can include the creation of the mons, labia, clitoris, and urethral opening. Urethral lengthening is an option for both metoidioplasty and phalloplasty, but is associated with a greatly increased complication rate (Schechter & Safa, 2018). Wound care and physical therapy are necessary for managing wounds resulting from the donor sites for phalloplasty (van Caenegem, Verhaeghe et al., 2013). Pelvic physical therapy can also be an important adjunct intervention after surgery for managing voiding and sexual function (Jiang et al., 2019). Dialogue, mutual understanding, and clear communication in a common language between patients, HCPs, and surgeons will contribute to well-considered decisions about the available surgical procedures.

Statement 12.20

We recommend health care professionals initiate and continue gender-affirming hormone

therapy for eligible* transgender and gender diverse people who wish this treatment due to demonstrated improvement in psychosocial functioning and quality of life. For supporting text, see Statement 12.21.

Statement 12.21

We recommend health care professionals maintain existing hormone therapy if the transgender and gender diverse individual's mental health deteriorates and assess the reason for the deterioration, unless contraindicated.

Several mental health disparities have been documented in the transgender population including depression, suicidality, anxiety, decreased self-esteem, and post-traumatic stress disorder (Arcelus et al., 2016; Becerra-Culqui et al, 2018; Bouman et al., 2017; Eisenberg et al., 2017; Heylens, Elaut et al., 2014; Witcomb et al., 2018). The gender minority stress model provides evidence of several mediators and moderators of these disparities (Hendricks & Testa, 2012; Meyer, 2003). Mediators and moderators of mental health disparities unique to transgender people include experiences of discrimination, victimization, misgendering, family rejection, and internalized transphobia (Hendricks & Testa, 2012). Factors that have a positive effect on mental health include family acceptance, supportive social and romantic relationships, transgender community connectedness, protection by affirming and inclusive policies, policies of affirmation and inclusion, possession of updated legal name/gender documentation, and achievement of physical gender transition based on individualized embodiment goals (Bauer et al., 2015; Bockting et al., 2013; Bouman et al., 2016; Davey et al., 2014; de Vries et al., 2014; Du Bois et al., 2018; Gower, Rider, Brown et al., 2018; Hendricks & Testa, 2012; Keo-Meier et al., 2015; Meier et al., 2013; Pflum et al., 2015; Ryan et al., 2010; Smith et al., 2018).

Hormone therapy has been found to positively impact the mental health and quality of life of TGD youth and adults who embark on this treatment (Aldridge et al., 2020; Allen et al., 2019; Bauer et al., 2015; Nobili et al., 2018; Russell et al., 2018; Ryan, 2009). In many cases, hormone therapy is considered a lifesaving intervention (Allen et al., 2019; Grossman & D'Augelli, 2006; Moody et al., 2015). Several studies have found associations between the initiation of hormone therapy and improved mental health in youth and adults (Aldridge et al., 2020; Costa et al., 2016; de Vries et al., 2014; Kuper et al., 2020; Nguyen et al., 2018; White Hughto & Reisner, 2016), including improvements in quality of life (Gorin-Lazard et al., 2012; Gorin-Lazard et al., 2013; Murad et al., 2010; Newfield et al., 2006; Nobili et al., 2018; White Hughto & Reisner, 2016), a reduction in anxiety and depression (Aldridge et al., 2020; Colizzi et al., 2014; Davis & Meier, 2014; de Vries, Steensma et al., 2011; Gómez-Gil et al., 2012; Rowniak et al., 2019), decreased stress, and decreased paranoia (Keo-Meier & Fitzgerald, 2017). A prospective, controlled trial using the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) demonstrated significant improvement in multiple domains of psychological functioning in transgender men after only 3 months of testosterone treatment (Keo-Meier et al., 2015). Although there are higher rates of autism symptoms in the transgender population, these symptoms have not been found to increase after the initiation of hormone therapy (Nobili et al., 2020).

As a reduction in depressive symptoms may correlate with a decrease in the risk of suicide, withholding hormone therapy based on the presence of depression or suicidality may cause harm (Keo-Meier et al., 2015; Levy et al., 2003). Turban, King et al. (2020) found a decrease in the odds of lifetime suicidal ideation in adolescents who required pubertal suppression and had access to this treatment compared with those with a similar desire with no such access (Turban, King et al., 2020). A recent systematic review found pubertal suppression in TGD adolescents was associated with an improved social life, decreased suicidality in adulthood, improved psychological functioning and quality of life (Rew et al., 2020). Because evidence suggests hormone therapy is directly linked to decreased symptoms of depression and anxiety, the practice of withholding hormone therapy until these symptoms are treated with traditional psychiatry is considered to have iatrogenic effects

(Keo-Meier et al., 2015). If psychiatric treatment is indicated, it can be started or adjusted concurrently without discontinuing hormone therapy.

**For eligibility criteria for adolescents and adults, please refer to Chapter 5—Assessment for Adults and Chapter 6—Adolescents as well as Appendix D.*

CHAPTER 13 Surgery and Postoperative Care

Medically necessary gender-affirmation surgery (GAS) refers to a constellation of procedures designed to align a person's body with their gender identity (see Chapter 2—Global Applicability for medical necessity, Statement 2.1). This chapter describes surgery and postoperative care recommendations for TGD adults and adolescents. Please refer to Chapter 5—Assessment of Adults and Chapter 6—Adolescents for the assessment criteria related to surgery for adults and adolescents, respectively. A summary of the recommendations and assessment criteria can be found in Appendix D.

Recognizing the diverse and heterogeneous community of individuals who identify as transgender and gender diverse (TGD), gender-affirming surgical interventions may be categorized along a spectrum of procedures for individuals assigned male at birth (AMAB) and assigned female at birth (AFAB).

In appropriately selected TGD individuals, the current literature supports the benefits of GAS. While complications following GAS occur, many are either minor or can be treated with local care on an outpatient basis (Canner et al., 2018; Gaither et al., 2018; Morrison et al., 2016). In addition, complication rates are consistent with those of similar procedures performed for different diagnoses (i.e., non-gender-affirming procedures).

In individuals AFAB, gender-affirming chest surgery or "top surgery" (i.e. "subcutaneous mastectomy") has been studied in prospective (Agarwal et al., 2018; Frederick et al., 2017; Top & Balta, 2017; van de Grift, Elaut et al., 2017; van de Grift et al., 2016), retrospective (Bertrand et al., 2017; Claes et al., 2018; Esmonde et al., 2019; Lo Russo et al., 2017; Marinkovic & Newfield, 2017; Poudrier et al., 2019; Wolter et al., 2015; Wolter et al., 2018), and cross-sectional cohort studies (Olson-Kennedy, Warus et al., 2018; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018; van de Grift, Elfering et al., 2018). The efficacy of top surgery has been demonstrated in multiple domains, including a consistent and direct increase in health-related quality of life, a significant decrease in gender dysphoria, and a consistent increase in satisfaction with body and appearance. Additionally, rates of regret remain very low, varying from 0 to 4%. While the effect of top surgery on additional outcome measures such as depression, anxiety, and sexual function also demonstrated a benefit, the studies were of insufficient strength to draw definitive conclusions. Although further investigation is needed to draw more robust conclusions, the evidence demonstrates top surgery to be a safe and effective intervention.

In individuals AMAB, fewer studies have been published regarding gender-affirming breast surgery ("breast augmentation") and include 2 prospective (Weigert et al., 2013; Zavlin et al., 2018), 1 retrospective cohort (Fakin et al., 2019), and 3 cross-sectional cohort studies (Kanhai et al., 2000; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018). All the studies reported a consistent and direct improvement in patient satisfaction, including general satisfaction, body image satisfaction, and body image following surgery. Owen-Smith et al. (2018) demonstrated a positive trend toward improvement in both depression and anxiety scores with increasing levels of gender-affirming interventions. However, there was no statistical comparison between individuals who underwent top surgery and any other group.

Gender-affirming vaginoplasty is one of the most frequently reported gender-affirming surgical interventions; 8 prospective (Buncamper et al., 2017; Cardoso da Silva et al., 2016; Kanhai, 2016; Manero Vazquez et al., 2018; Papadopulos, Zavlin et al., 2017; Tavakkoli Tabassi et al., 2015; Wei et al., 2018; Zavlin et al., 2018), 15 retrospective cohort (Bouman, van der Sluis et al., 2016; Buncamper et al., 2015; Hess et al., 2016; Jiang et al., 2018; LeBreton et al., 2017; Manrique et al., 2018; Massie et al., 2018; Morrison et al., 2015; Papadopulos, Lelle et al., 2017; Raigosa et al., 2015; Salgado et al., 2018; Seyed-Forootan et al., 2018; Sigurjonsson et al., 2017; Simonsen et al., 2016; Thalaivirithan et al., 2018), and 3 cross-sectional cohort studies have recently been reported (Castellano et al., 2015; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018).

Although different assessment measurements were used, the results from all studies consistently reported both a high level of patient satisfaction (78–100%) as well as satisfaction with sexual function (75–100%). This was especially evident

Statements of Recommendations

13.1- We recommend surgeons who perform gender-affirming surgical procedures have the following credentials:
13.1.a- Training and documented supervision in gender-affirming procedures;
13.1.b- Maintenance of an active practice in gender-affirming surgical procedures;
13.1.c- Knowledge about gender diverse identities and expressions;
13.1.d- Continuing education in the field of gender-affirmation surgery
13.1.e- Tracking of surgical outcomes.
13.2- We recommend surgeons assess transgender and gender diverse people for risk factors associated with breast cancer prior to breast augmentation or mastectomy.
13.3- We recommend surgeons inform transgender and gender diverse people undergoing gender-affirming surgical procedures about aftercare requirements, travel and accommodations, and the importance of postoperative follow-up during the preoperative process.
13.4- We recommend surgeons confirm reproductive options have been discussed prior to gonadectomy in transgender and gender diverse people.
13.5- We suggest surgeons consider offering gonadectomy to eligible* transgender and gender diverse adults when there is evidence they have tolerated a minimum of 6 months of hormone therapy (unless hormone replacement therapy or gonadal suppression is not clinically indicated or the procedure is inconsistent with the patient's desires, goals, or expressions of individual gender identity).
13.6- We suggest health care professionals consider gender-affirming genital procedures for eligible* transgender and gender diverse adults seeking these interventions when there is evidence the individual has been stable on their current treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).
13.7- We recommend surgeons consider gender-affirming surgical interventions for eligible* transgender and gender diverse adolescents when there is evidence a multidisciplinary approach that includes mental health and medical professionals has been involved in the decision-making process.
13.8- We recommend surgeons consult a comprehensive, multidisciplinary team of professionals in the field of transgender health when eligible* transgender and gender diverse people request individually customized (previously termed "non-standard") surgeries as part of a gender-affirming surgical intervention.
13.9- We suggest surgeons caring for transgender men and gender diverse people who have undergone metoidioplasty/phalloplasty encourage lifelong urological follow-up.
13.10- We recommend surgeons caring for transgender women and gender diverse people who have undergone vaginoplasty encourage follow-up with their primary surgeon, primary care physician, or gynecologist.
13.11- We recommend patients who regret their gender-related surgical intervention be managed by an expert multidisciplinary team.

** For eligibility criteria for adolescents and adults, please refer to the Assessment for Adults and Adolescents chapters and Appendix D.*

when using more recent surgical techniques. Gender-affirming vaginoplasty was also associated with a low rate of complications and a low incidence of regret (0–8%).

Recent literature reflects the increased clinical interest in metoidioplasty and phalloplasty as reflected by 3 prospective cohort (Garaffa et al., 2010; Stojanovic et al., 2017; Vukadinovic et al., 2014), 6 retrospective cohort (Cohanzad, 2016; Garcia et al., 2014; Simonsen et al., 2016; van de Grift, Pigot et al., 2017; van der Sluis et al., 2017; Zhang et al., 2015), and 4 cross-sectional studies (Castellano et al., 2015; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018; Wierckx, Van Caenegem et al., 2011), which reviewed the risks and benefits of these procedures.

In terms of urinary function, between 75 and 100% of study participants were able to void while standing. In terms of sexual function, between 77 and 95% of study participants reported satisfaction with their sexual function. Most of these studies report high overall levels of postoperative satisfaction (range 83–100%), with higher rates of satisfaction in studies involving newer surgical techniques. Two prospective and two retrospective cohort studies specifically assessed regret following surgery and found no transgender men experienced regret. While study limitations were identified, the reported results were consistent and direct.

In recent years, facial GAS (FGAS) has received increased attention, and current literature supports its benefits. Eight recent publications include 1 prospective cohort (Morrison et al., 2020), 5 retrospective cohort (Bellinga et al., 2017; Capitán et al., 2014; Noureai et al., 2007; Raffaini et al., 2016; Simon et al., 2022), and 2 cross-sectional studies (Ainsworth & Spiegel, 2010; van de Grift, Elaut

et al., 2018). All 8 studies clearly demonstrated individuals were very satisfied with their surgical results (between 72% and 100% of individuals). Additionally, individuals were significantly more satisfied with the appearance of their face compared with individuals who had not undergone surgery. One prospective, international, multicenter, cohort study found facial GAS significantly improves both mid- and long-term quality of life (Morrison et al., 2020). The results were direct and consistent, but somewhat imprecise because of certain study limitations. While gender-affirming facial surgery for AFAB individuals is an emerging field, current limited data points toward equal benefits in select patients. Future studies are recommended.

Additional procedures and/or interventions such as hair removal (prior to facial and/or genital surgery) may be required as part of the preoperative process. See Chapter 15—Primary Care. Furthermore, consultation with pelvic floor physical therapy may be important (or required) both before and after surgery.

Representative surgical interventions include (for complete list, see appendix E and the end of this chapter):

AMAB: facial feminization surgery (including chondrolaryngoplasty/vocal cord surgery), gender-affirming breast surgery, body contouring procedures, orchiectomy, vagino/vulvoplasty (with/without depth), aesthetic procedures, and procedures designed to prepare individuals for surgery (i.e., hair removal).

AFAB: facial masculinization surgery, gender-affirming chest surgery, hysterectomy/oophorectomy, metoidioplasty (including placement of testicular prosthesis), phalloplasty (including placement of testicular/penile prostheses), body contouring procedures, aesthetic procedures, and procedures designed to prepare individuals for surgery (i.e., hair removal).

It is important surgeons understand the indication(s) and the timing for GAS. This is especially important when caring for adolescents (see Chapter 6—Adolescents).

It is important the surgeon and the patient participate in a shared decision-making approach that includes 1) a multidisciplinary approach; 2) an understanding of the patient's goals and expectations; 3) a discussion regarding the surgical options and associated risks and benefits; and 4) an informed plan for aftercare (see Chapter 5—Assessment for Adults). These recommendations are designed to facilitate an individualized approach to care.

Appropriate aftercare is essential for optimizing outcomes (Buncamper et al., 2015; Lawrence, 2003), and it is important patients are informed about postoperative needs (including local wound care, activity restrictions, time off from work or school, etc.). In addition, it is important the surgeon is available to provide and facilitate postoperative care, refer to specialty services, or both as needed. This may include the need for ongoing support (i.e., both from the caregiver as well as the primary care provider, mental health professionals (MHPs), or both), as well as the need for routine primary care (i.e., breast/chest cancer screening, urologic/gynecologic care, etc.).

With the increase both in public interest and in the number of gender-affirming surgical procedures (Canner et al., 2018; Ross, 2017; Shen et al., 2019), additional training, tracking of outcomes, and continuing medical education for surgeons are necessary (Schechter et al., 2017).

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 13.1

We recommend surgeons who perform gender-affirming surgical procedures have the following credentials:

a. **Training and documented supervision in gender-affirming procedures;**
b. **Maintenance of an active practice in gender-affirming surgical procedures;**
c. **Knowledge about gender diverse identities and expressions;**
d. **Continuing education in the field of gender-affirmation surgery;**
e. **Tracking of surgical outcomes.**

Surgeons offering GAS may have a variety of surgical specialty training and backgrounds. The most common surgical specialties include plastic surgery, urology, gynecology, otolaryngology and oro-maxillofacial surgery (Jazayeri et al., 2021). Consistent with other surgical domains, we recommend only surgeons who are certified or eligible to be certified by their respective national professional boards offer GAS. Furthermore, it is recommended surgeons offering care for TGD people have received documented training in gender-affirming procedures and principles of gender-affirming care (Schechter et al., 2017; Schechter & Schechter, 2019). The latter includes, but is not limited, to knowledge about gender diverse identities and expressions, and how those affect patient goals, expectations, and outcomes. It is important surgeons offering GAS be familiar with the available procedures and can provide informed consent. If surgeons do not offer a requested procedure, they may offer a referral for a second opinion. Surgeons offering GAS are expected to participate in continuing education activities in the field of GAS (i.e., meetings, conferences, seminars, etc.) to maintain current knowledge. We further recommend surgical outcomes be tracked and communicated to the patients as part of the informed consent (Schechter et al., 2017).

In addition, hospitals, institutions, and physician offices that offer GAS need to be knowledgeable regarding cultural competencies (i.e., language, terminology, etc.). This may require ongoing and regular staff education.

Statement 13.2

We recommend surgeons assess transgender and gender diverse people for risk factors associated with breast cancer prior to breast augmentation or mastectomy.

Prior to breast augmentation or mastectomy, individuals need to be informed about and assessed for breast cancer risk factors, including genetic mutations (i.e., BRCA1, BRCA2), family history, age, radiation, exposure to estrogen, and the amount of breast tissue anticipated to remain after surgery (Brown, Lourenco et al., 2021; Brown & Jones, 2015; Colebunders et al., 2014; Gooren et al., 2013; Salibian et al., 2021; Weyers et al., 2010). Breast cancer screening balances the identification of cancer with the selection of appropriate imaging, tests, and procedures. Currently, evidence-based screening guidelines specific for TGD individuals do not exist (Salibian et al., 2021), however, recent guidelines have been proposed by the American College of Radiology (Brown, Lourenco et al., 2021). Because the risk of cancer in individuals seeking gender-affirming breast augmentation or mastectomy is similar to that in the general population (even in the setting of hormone use), existing cancer screening guidelines need to be followed (Brown & Jones, 2015; Gooren et al., 2013; Salibian et al., 2021; Weyers et al., 2010). Professionals need to be familiar with updates to these guidelines as they are subject to change. Individuals who undergo gender-affirming surgery of the chest should have ongoing breast cancer surveillance, which should be overseen by their primary care providers.

Statement 13.3

We recommend surgeons inform transgender and gender diverse people undergoing gender-affirming surgical procedures about aftercare requirements, travel and accommodations, and the importance of postoperative follow-up during the preoperative process.

Details about the timing, technique, and duration of the aftercare requirements are shared with patients in the preoperative period such that appropriate planning may be undertaken. This includes a discussion regarding the anticipated staging of surgical procedures (and associated travel requirements). Given the small number of surgeons who specialize in GAS, it is common for patients to travel for their procedures. Prior to surgery, surgeons should provide patients with a postoperative follow-up schedule. The surgeon should discuss the duration of the patient's travel dates, the anticipated inpatient versus outpatient stay, and the potential need for flexibility in travel arrangements (especially if complications occur). Given the complexity and cost of travel and lodging, changes in the care plan should be shared with the patient as early as possible. Surgeons should facilitate continuity of care with a local provider upon returning home.

Aftercare and postsurgical follow-up are important. Gender-affirming surgical procedures

often have specific aftercare requirements, such as postsurgery resources (stable, safe housing; resources for travel and follow-up care), instructions in health-positive habits (e.g., personal hygiene, healthy living, prevention of urinary tract infections (UTIs) and sexually-transmitted infections (STIs) (Wierckx, Van Caenegem et al., 2011)), postsurgery precautions or limitations on activities of daily life (e.g., bathing, physical activity, exercise, nutritional guidance, resumption of sexual activity) (Capitán et al., 2020), postsurgery resumption of medications (i.e., anticoagulants, hormones, etc.), and detailed postsurgery self-care activities (e.g., postvaginoplasty dilation and douching regimens, activation of a penile prosthesis, strategies to optimize postphalloplasty urination, recommendations for hair transplant care) (Capitán et al., 2017; Falcone et al., 2018; Garcia, 2018; Hoebeke et al., 2005). Some aspects of postsurgery self-care activities may be introduced prior to surgery and are reinforced after surgery (Falcone et al., 2018). As issues such as wound disruptions, difficulty with dilation, and UTIs may occur (Dy et al., 2019), the follow-up period provides an opportunity to intervene, mitigate, and prevent complications (Buncamper et al., 2016; Garcia, 2021).

Statement 13.4

We recommend surgeons confirm reproductive options have been discussed prior to gonadectomy in transgender and gender diverse people.

Infertility is often a consequence of both gender-affirming hormone therapy (temporary) and GAS (permanent), and fertility preservation is discussed prior to medical interventions, surgical interventions, or both (Defreyne, van Schuylenbergh et al., 2020; Jahromi et al., 2021; Jones et al., 2021). Surgical interventions that alter reproductive anatomy or function may limit future reproductive options to varying degrees (Nahata et al., 2019). It is thus critical to discuss infertility risk and fertility preservation (FP) options with transgender individuals and their families prior to initiating any of these interventions and on an ongoing basis thereafter (Hembree et al., 2017).

For specific recommendations regarding reproductive options, see Chapter 16—Reproductive Health.

Statement 13.5

We suggest surgeons consider offering gonadectomy to eligible* transgender and gender diverse adults when there is evidence they have tolerated a minimum of 6 months of hormone therapy (unless hormone replacement therapy or gonadal suppression is not clinically indicated or the procedure is inconsistent with the patient's desires, goals, or expressions of individual gender identity). For supporting text, see Statement 13.6.

Statement 13.6

We suggest health care professionals consider gender-affirming genital procedures in eligible* transgender and gender diverse adults seeking these interventions when there is evidence the individual has been stable on their current treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result unless hormone therapy is either not desired or is medically contraindicated).

GAHT leads to anatomical, physiological, and psychological changes. The onset of the anatomic effects (e.g., clitoral growth, vaginal mucosal atrophy) may begin early after the initiation of therapy, and the peak effect is expected at 1–2 years (T'Sjoen et al., 2019). Depending upon the surgical result required, a period of hormone treatment may be required (e.g., sufficient clitoral virilization prior to metoidioplasty/phalloplasty) or preferred for psychological reasons, anatomical reasons, or both (breast growth and skin expansion prior to breast augmentation, softening of skin and changes in facial fat distribution prior to facial GAS) (de Blok et al., 2021).

For individuals who are not taking hormones prior to surgical interventions, it is important surgeons review the impact of this on the proposed surgery.

For individuals undergoing gonadectomy who are not taking hormones, a plan for hormone replacement can be developed with their prescribing professional prior to surgery.

Statement 13.7

We recommend surgeons consider gender-affirming surgical interventions for eligible* transgender and gender diverse adolescents when there is evidence a multidisciplinary approach that includes mental health and medical professionals has been involved in the decision-making process.

Substantial evidence (i.e., observational studies (Monstrey et al., 2001; Stojanovic et al., 2017), literature reviews and expert opinions (Esteva de Antonio et al., 2013; Frey et al., 2017; Hadj-Moussa et al., 2019; Pan & Honig, 2018), established guidelines (Byne et al., 2018; Chen, Fuqua et al., 2016; Hembree et al., 2017; Karasic & Fraser, 2018; Klein, Paradise et al., 2018; Weissler et al., 2018), and a thematic content analysis (Gerritse et al., 2018), support the importance of a multidisciplinary (i.e., medical, mental health, and surgery) approach to transgender health care.

A multidisciplinary approach is especially important in managing mental health issues if these are experienced by a TGD person undergoing GAS (de Freitas et al., 2020; Dhejne et al., 2016; van der Miesen et al., 2016). In addition, primary care providers and medical specialists can help support decisions regarding the timing of surgery, surgical outcomes and expectations, perioperative hormone management, and optimization of medical conditions (Elamin et al., 2010; Hembree et al., 2017).

For specific recommendations regarding presurgical assessment in adolescents, see Chapter 6—Adolescents.

Statement 13.8

We recommend surgeons consult a comprehensive, multidisciplinary team of professionals in the field of transgender health when eligible* transgender and gender diverse people request individually customized (previously termed "non-standard") surgeries as part of a gender-affirming surgical intervention.

Gender identities may present along a spectrum, and the expression of a person's identity may vary quite widely amongst individuals (Beek et al., 2015; Koehler et al., 2018). While the overall goal of a particular procedure usually includes reduction of gender dysphoria (van de Grift, Elaut et al., 2017) or achieving gender congruence, gender diverse presentations may lead to individually customized surgical requests some may consider "non-standard" (Beek et al., 2015; Bizic et al., 2018). Individually customized surgical requests can be defined as 1) a procedure that alters an individual's gender expression without necessarily aiming to express an alternative, binary gender; 2) the "non-standard" combination of well-established procedures; or 3) both.

This is designed to help counsel and inform the patient as well as to ensure their goals can be achieved. The patient and their surgeon need to work together to ensure the patient's expectations are realistic and achievable, and the proposed interventions are safe and technically feasible. The patient and their surgical team need to engage in a shared decision-making process (Cavanaugh et al., 2016). This informed consent process needs to address the irreversibility of some procedures, the newer nature of some procedures, and the limited information available about the long-term outcomes of some procedures.

Statement 13.9

We suggest surgeons caring for transgender men and gender diverse people who have undergone metoidioplasty/phalloplasty encourage lifelong urological follow-up.

Postoperative complications following metoidioplasty/phalloplasty comprise the urinary tract and sexual function (Kang et al., 2019; Monstrey et al., 2009; Santucci, 2018; Schardein et al., 2019). Reported urethral complications (related to urethral lengthening) include urethral strictures 35–58%, urethral fistulae 15–70% (Monstrey et al., 2009; Santucci, 2018; Schardein et al., 2019), diverticulae, mucocele due to vaginal remnant, and hair growth within the neourethra (Berli et al., 2021; Veerman et al., 2020). Complications related to sexual function include limited to absent tactile and/or erogenous sensation, difficulties with orgasm function, and complications with penile prosthetics (Kang et al., 2019; Santucci, 2018). Penile prosthesis-related complications are estimated to involve infection (incidence 8–12%),

malfunction, urethral erosion, skin extrusion, and dislocation of its bone fixation (Falcone et al., 2018; Kang et al., 2019; Morrison et al., 2016). Although most urethral and prosthetic complications occur in the immediate and intermediate postoperative period, complications can occur at any time. Early detection may reduce morbidity (e.g., urethral strictures resulting in fistulae, pending erosion of a penile prosthetic leading to infection and requiring total explant) (Blecher et al., 2019).

Routine follow-up to assess for early evidence of urethral stricture (or other urinary issues) includes bladder ultrasound measurement of postvoid residual volume (to screen for and stage neourethral stricture), fluoroscopic urethrography (to identify and stage neourethral strictures, fistulae, and diverticulae), and cystourethroscopy to examine the urethra and bladder. TGD men may also have routine urologic issues that need not be related to gender transition (urinary calculi, hematuria, and genitourinary malignancies; fertility preservation) (Sterling & Garcia, 2020a, 2020b).

Statement 13.10

We recommend surgeons caring for transgender women and gender diverse people who have undergone vaginoplasty encourage follow-up with their primary surgeon, primary care physician, or gynecologist.

Vaginoplasty is a safe procedure (Hontscharuk, Alba, Hamidian Jahromi et al., 2021). While complications may occur, most are self-limited or can be treated with minor interventions (Hontscharuk, Alba, Hamidian Jahromi et al., 2021). Minor complications include issues such as the formation of granulation tissue, intravaginal hair growth, delayed wound healing or wound disruption (or both), aesthetic concerns, and introital stenosis (Ferrando, 2020; Kloer et al., 2021). While these complications are usually self-limited, they may impact patient well-being after surgery. Additionally, these issues may go either undiagnosed or may be misdiagnosed if patients are not able to access care provided by professionals with expertise in the field of transgender health. We recommend patients be followed by their primary surgeon in person and at regular intervals—for example at two weeks, three months, six months, and one year after surgery—although more follow-up may be indicated for some individuals.

Additional gynecologic care is conducted throughout the TGD person's lifetime and can be managed in many settings. A speculum exam to check for granulation tissue, hair, and lesions can be performed by the primary care provider, gynecologist, or GAS surgeon and may be necessary outside of the immediate postoperative period (Grimstad, McLaren et al., 2021; Suchak et al., 2015; van der Sluis et al., 2020). After confirmation by laboratory testing, UTIs, STIs, and other fluctuations in the vaginal microbiome may be treated following relevant guidelines formulated for cisgender populations (Hooton, 2012; Sherrard et al., 2018). Manual prostate checks are performed based on relevant guidelines formulated for cisgender populations via the vaginal canal, as the prostate is located on the anterior wall of the vagina (Carter et al., 2013).

Other complications include issues such as stenosis of the neovaginal canal, rectovaginal fistulae, and inflammation (intestinal vaginoplasty) (Bustos et al., 2021). These require a combination of nonsurgical and surgical treatment with consultation and possible referral back to the primary surgeon with other surgical consultants (i.e., colorectal surgeon), if required. In addition, as pelvic floor dysfunction may affect 30–40% of patients both prior to and following vaginoplasty, the availability of pelvic floor physical therapists is an important adjunct in the postoperative period (Jiang et al., 2019).

Statement 13.11

We recommend patients who regret their gender-related surgical intervention be managed by an expert multidisciplinary team.

The percentage of individuals who regret their GAS is very low (between 0.3% and 3.8%) (De Cuypere & Vercruysse, 2009; Defreyne, Motmans et al., 2017; Hadj-Moussa et al., 2019; Hadj-Moussa, Agarwal et al., 2018; Hadj-Moussa, Ohl et al., 2018; Landén et al., 1998; Narayan et al., 2021; van de Grift, Elaut et al., 2018; Wiepjes et al., 2018). The highest incidence of

regret was reported at a time when surgical techniques were less refined, the role of multidisciplinary care was less established, and the *Standards of Care* did not exist or were not widely known (Landén et al., 1998). Regret can be temporarily or permanent and may be classified as (Narayan et al., 2021) social regret (caused by difficulties in familial, religious, social, or professional life), medical regret (due to long-term medical complications, disappointment in surgical results or inadequate preoperative decision-making), and true gender-related regret (mostly based on patient experienced misdiagnosis, insufficient exploration of gender identity, or both). This classification is in accordance with previously discussed positive and negative predictive factors (De Cuypere & Vercruysse, 2009; Gils & Brewaeys, 2007; Pfäfflin & Junge, 1998).

A multidisciplinary team can help identify the etiology of regret as well as the temporal stability of the surgical request (Narayan et al., 2021). Following this evaluation and in consideration of the individual's circumstances, medical and/or surgical interventions with the intent of either continuing transition or performing surgical procedures to return anatomy to that of the sex assigned at birth may be indicated. For further information see Chapter 5—Assessment of Adults.

**For eligibility criteria for adolescents and adults, please refer to the Assessment for Adults and Adolescent chapters and Appendix D*

GENDER-AFFIRMING SURGICAL PROCEDURES

As the field's understanding of the many facets of gender incongruence expands, and as technology develops which allows for additional treatments, it is imperative to understand this list is not intended to be exhaustive. This is particularly important given the often lengthy time periods between updates to the SOC, during which evolutions in understanding and treatment modalities may occur.

FACIAL SURGERY	
Brow	• Brow reduction • Brow augmentation • Brow lift
Hair line advancement and/or hair transplant	
Facelift/mid-face lift (following alteration of the underlying skeletal structures)	
Facelift/mid-face lift (following alteration of the underlying skeletal structures)	• Platysmaplasty
Blepharoplasty	• Lipofilling
Rhinoplasty (+/- fillers)	
Cheek	• Implant • Lipofilling
Lip	• Upper lip shortening • Lip augmentation (includes autologous and non-autologous)
Lower jaw	• Reduction of mandibular angle • Augmentation
Chin reshaping	• Osteoplastic • Alloplastic (implant-based)
Chondrolaryngoplasty	• Vocal cord surgery (see voice chapter)
BREAST/CHEST SURGERY	
Mastectomy	• Mastectomy with nipple-areola preservation/reconstruction as determined medically necessary for the specific patient • Mastectomy without nipple-areola preservation/reconstruction as determined medically necessary for the specific patient
Liposuction	
Breast reconstruction (augmentation)	• Implant and/or tissue expander • Autologous (includes flap-based and lipofilling)
GENITAL SURGERY	
Phalloplasty (with/without scrotoplasty)	• With/without urethral lengthening • With/without prosthesis (penile and/or testicular) • With/without colpectomy/colpocleisis
Metoidioplasty (with/without scrotoplasty)	• With/without urethral lengthening • With/without prosthesis (penile and/or testicular) • With/without colpectomy/colpocleisis
Vaginoplasty (inversion, peritoneal, intestinal)	• May include retention of penis and/or testicle
Vulvoplasty	• May include procedures described as "flat front"
GONADECTOMY	
Orchiectomy	
Hysterectomy and/or salpingo-oophorectomy	
BODY CONTOURING	
Liposuction	
Lipofilling	
Implants	• Pectoral, hip, gluteal, calf
Monsplasty/mons reduction	
ADDITIONAL PROCEDURES	
Hair removal: Hair removal from the face, body, and genital areas for gender affirmation or as part of a preoperative preparation process. (see Statement 15.14 regarding hair removal)	• Electrolysis • Laser epilation
Tattoo (i.e., nipple-areola)	
Uterine transplantation	
Penile transplantation	

CHAPTER 14 Voice and Communication

Human beings engage in communication practices not only to exchange ideas about the outside world, but also to present themselves as sociocultural beings and to negotiate forms of address, referral and treatment by others that allow them to feel safe and respected (Azul et al., 2022). The human voice is widely regarded as one of the key modalities that contributes to the communication of gender as one of the dimensions of human diversity. However, other aspects and ways of communicating (e.g., articulation, word choice, gesture, listener perceptions and attributions) need to be considered as well (Azul, 2015; Azul & Hancock, 2020). Throughout this chapter "voice and communication" is used as a phrase encompassing the meaning-making practices in which each of the participants of a social encounter engage according to their own needs, wishes, identifications, and capacities.

While a binary understanding of gender has dominated the research literature in this area, the approach recommended in this chapter implies a broadly inclusive view of gender identification (e.g., trans feminine, trans masculine, gender fluid, nonbinary, genderqueer, agender) and the understanding that gender does not exist in isolation, but intersects with other aspects of human diversity (e.g., First Nation status, ethnicity/race, sexuality, dis/ability, faith/religion/spirituality). The recommendations in this chapter apply to all transgender and gender diverse (TGD) people who are seeking professional voice and communication support, including children, adolescents, younger and older adults, and people who wish to transition or detransition, irrespective of their intervention choices.

Not every TGD person experiences challenges with or wants professional support for their voice and communication, but those who do often encounter barriers in accessing care. Although the percentages vary by country and TGD subpopulation, the statistics support the concern TGD people are not able to access voice and communication services when and how they desire (Eyssel et al., 2017; James et al., 2016; Oğuz et al., 2021; Södersten et al., 2015; Veale et al., 2019). In these studies, the percentage of TGD people wishing to receive voice and communication training or voice surgery is generally higher than the percentage of people who have undergone these interventions. With few exceptions, access to voice training is usually greater than access to voice surgery. Groups of TGD people who are further marginalized in their societies, such as TGD people of marginalized race/ethnicity, experience discrimination and limited access to care at even greater rates (James et al., 2016; Xavier et al., 2005).

Cost, not knowing where to access services, and services not being available are amongst the most common barriers cited by research participants. According to studies in the US (Hancock & Downs, 2021; Kennedy & Thibeault, 2020), Turkey (Oğuz et al., 2021), and Aotearoa/New Zealand (Veale et al., 2019), lack of accurate information about options for voice and communication services among TGD people is a significant and ubiquitous barrier to care. Notably, in Sweden, all TGD people are offered support for their voice and communication when a diagnosis of gender incongruence is made (Södersten et al., 2015). Additionally, cultural responsiveness of providers is only slowly improving (Hancock & Haskin, 2015; Jakomin et al., 2020; Matthews et al., 2020; Sawyer et al., 2014). Hancock and Downs (2021) have conducted preliminary work to identify specific barriers to voice and communication services and develop effective means for eliminating them.

This chapter is intended to provide guidance for health care professionals (HCPs) to support and foster well-being in all TGD people who are experiencing challenges or distress regarding their own voice and communication practices and/or regarding responses and attributions they receive from others (Azul et al., 2022).

A number of different approaches TGD people can use to modify their voice and communication, either individually or in combination include self-initiated change, which may be supported by resources TGD people use to guide their voice use and communication practice; behavioral change supported by voice and communication specialists (hereafter referred to as "voice and communication training"); and change as a result of androgen hormonal treatment and/or laryngeal surgery. The currently existing research evidence

does not include self-initiated change, but is focused on the latter three approaches.

A "voice and communication specialist" is someone who has knowledge regarding the ongoing and dynamic agency of speaker and listener practices, relevant professional interventions including behavioral, hormonal, and surgical, and relevant processes related to biophysiology, sociocultural meaning-making, and external material forces (Azul & Hancock, 2020). This specialist is capable of conducting appropriate assessments to inform the TGD person's choice and support the exploration of goals and intervention options by providing guidance in a culturally responsive, person-centered approach. This specialist has knowledge and skills in behavioral voice and communication intervention approaches.

Practices amenable to behavioral change include: speaking and singing voice, mindfulness, relaxation, respiration, pitch and pitch range, voice quality, resonance/timbre, loudness, projection, facial expression, gesture, posture, movement, introducing self to others, describing identifications and requesting culturally responsive treatment and forms of address by others, assertive and resilient responses to misattributions, practicing implementation of voice use and communication practices with different people and in different everyday settings (e.g., Hancock & Siegfriedt, 2020; Mills & Stoneham, 2017).

Voice and communication services are offered as part of a complete and coordinated approach to health, including support for medical, psychological, and social needs (Södersten et al., 2015); however, there are no prerequisites (e.g., hormone use, pursuit of surgeries, or duration living in a gender role). The overall purposes of voice and communication support for TGD people are:

- To educate clients about the factors that influence functional voice and communication practices and the communication of the speaker's identity (speaker, listener, professional practices, external material, biophysiological, and sociocultural factors);
- To enable clients to communicate their sense of sociocultural belonging (e.g., in terms of gender) in everyday encounters in a manner that matches the client's desired self-presentation and to develop, maintain and habituate voices, vocal qualities, and communication practices that support the clients' goals in a manner that does not harm the voice production mechanism;
- To provide training in functional voice production for clients who present with restrictions of voice function (e.g., as a result of overextending their voice production mechanism);
- To support clients with developing the capacity to assertively negotiate desired forms of address and referral from others (e.g., names, pronouns, titles) and to respond to misattributions in a skillful manner that contributes to increasing and maintaining the client's well-being;
- To support clients to develop the problem-solving skills needed to manage anxiety, stress, and dysphoria in collaboration with mental health providers; and to navigate barriers to practice or real-life use of one's preferred voice and communication.
- To provide, or refer clients to, supportive resources that facilitate developing voice and communication skills, vocal awareness, and well-being.
- To refer clients to, or collaborate with, other specialists such as mental health practitioners, laryngeal surgeons, and endocrinologists, who may be more equipped to meet the specific needs of that client. This may be especially relevant in cases where clients face unique challenges due to multiple barriers to their health and well-being or when the client wishes to pursue laryngeal surgery or hormone therapy.

Two types of laryngeal surgeries are relevant for TGD populations: those for raising voice pitch (e.g., glottoplasty with retro-displacement of the anterior commissure, cricothyroid approximation (CTA), feminization laryngoplasty, laser-assisted voice adjustment (LAVA)) (Anderson, 2007; Anderson, 2014; Brown, 2000; Casado, 2017; Geneid, 2015; Gross, 1999; Kelly et al., 2018; Kanagalingam, 2005; Kim, 2017; Kim, 2020; Kocak, 2010; Kunachak, 2000; Mastronikolis, 2013; Mastronikolis et al., 2013; Matai, 2003; Meister,

Statements of Recommendations

14.1- We recommend voice and communication specialists assess current and desired vocal and communication function of transgender and gender diverse people and develop appropriate intervention plans for those dissatisfied with their voice and communication.
14.2- We recommend voice and communication specialists working with transgender and gender diverse people receive specific education to develop expertise in supporting vocal functioning, communication, and well-being in this population.
14.3- We recommend health care professionals in transgender health working with transgender and gender diverse people who are dissatisfied with their voice or communication consider offering a referral to voice and communication specialists for voice-related support, assessment, and training.
14.4- We recommend health care professionals consider working with transgender and gender diverse people who are considering undergoing voice surgery consider offering a referral to a voice and communication specialist who can provide pre- and/or postoperative support.
14.5- We recommend health care professionals in transgender health inform transgender and gender diverse people commencing testosterone therapy of the potential and variable effects of this treatment on voice and communication.

2017; Mora, 2018; Neumann, 2004; Nuyen et al., 2022; Orloff, 2006; Pickuth, 2000; Remacle, 2011; Thomas & MacMillan, 2013; Tschan, 2016; Van Borsel, 2008; Wagner, 2003; Wendler, 1990; Yang, 2002) and for lowering voice pitch (e.g., thyroplasty type III, vocal fold injection augmentation) (Bultynck et al, 2020; Isshiki et al., 1983; Kojima, et al. 2008; Webb et al., 2021). Reported acoustic benefits of pitch-raising surgery include increased voice pitch (average frequency (f_o)) and increased Min f_o(the lowest frequency in physiological voice range). TGD people's self-rating ratings show general satisfaction with voice postsurgery, although individuals who are interested in more comprehensive changes to vocal self-presentation may need to engage in behavioral interventions with a voice and communication specialist in addition to laryngeal surgery (Brown, Chang et al. 2021; Kelly et al., 2018; Nuyen et al., 2022). Potential harms of pitch-raising surgery can be assessed and addressed in voice training by a voice and communication specialist. Reported harms of pitch-raising surgery include voice problems such as dysphonia, weak voice, restricted speaking voice range especially upper range (lowered Max f_o, in the physiological voice range), hoarseness, vocal instability, and lowering of frequency values over time (Kelly et al., 2018; Song & Jiang, 2017), although the rate of these outcomes is inconsistent.

Research on pitch-lowering surgeries is limited. However, studies including eight TGD people who elected to undergo thyroplasty type III after continued dissatisfaction with hormonal treatment (Bultynck et al., 2020) and one person who received injection augmentation after testosterone therapy and voice training (Webb et al., 2020), reported statistically significant lowering of fundamental frequency, perceived as pitch.

Estrogen treatment in TGD people has not been associated with measurable voice changes (Mészáros et al., 2005), while testosterone treatment in TGD people has been found to result in both desired and undesired changes in gender- and function-related aspects of voice production (Azul, 2015; Azul et al., 2017, 2018, 2020; Azul & Neuschaefer-Rube, 2019; Cosyns et al., 2014; Damrose, 2008; Deuster, Di Vicenzo et al., 2016; Deuster, Matulat et al. 2016; Hancock et al., 2017; Irwig et al., 2017; Nygren et al., 2016; Van Borsel et al., 2000; Yanagi et al., 2015; Ziegler et al., 2018). Desired changes associated with testosterone treatment include lowered voice pitch, increased male attributions to voice, and increased satisfaction with voice. Reported dissatisfaction with testosterone treatment include lack of or insufficient lowering of voice pitch, dysphonia, weak voice, restricted singing pitch range, and vocal instability. These areas can be assessed and addressed in voice training by a voice and communication specialist.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 14.1.

We recommend voice and communication specialists assess current and desired vocal and

communication function of transgender and gender diverse people and develop appropriate intervention plans for those dissatisfied with their voice and communication.

Voice and communication specialists may assess satisfaction with the presentation of sociocultural positionings in communicative encounters, including gender and other intersecting identifications, taking into consideration that these may or may not be static over time; attributions received from others, and how these relate to the individual's identifications, wishes, and well-being; ratings of voice and speech naturalness; and voice and communication function in relation to vocal demands. Assessments may vary in nature (e.g., client-reported outcome measures, perceptual, acoustic, aerodynamic, endoscopic) according to their purpose (Davies et al., 2015; Leyns et al., 2021; Oates & Dacakis, 1983). For example, laryngeal visualization is used when individuals present with a concomitant voice problem, (e.g., muscle tension dysphonia) (Palmer et al., 2011) or experience voice difficulties, which may or may not be secondary to medical gender-affirming interventions of androgen therapy or laryngeal surgery (Azul et al., 2017).

Voice and communication specialists inform intervention-seeking TGD people who are dissatisfied with their voice and communication about available interventions that support TGD people with their voice, communication, and well-being. The nature of each option, including potential outcomes and permanence, is presented objectively to provide the TGD person respect and autonomy in decision-making. Appropriate intervention plans are individualized and feasible and should be inclusive of any professional services available. Goals may evolve over the course of the support period as the TGD person explores modifications to voice and communication, assesses their satisfaction with achieved change and refines their goals.

Statement 14.2.

We recommend voice and communication specialists working with transgender and gender diverse people receive specific education to develop expertise in supporting vocal functioning, communication, and well-being in this population.

Academic and licensing credentials of voice and communication specialists (e.g., speech-language pathologists, speech therapists, singing voice teachers, voice coaches) vary by location but typically do not specify criteria for working with specific populations. Standard curricula in formal education for these professions often do not include specific or adequate training for working with TGD populations (Jakomin et al., 2020; Matthews et al., 2020). General knowledge and skills related to the vocal mechanism and interpersonal communication are foundational but insufficient for conducting culturally responsive, person-centered care for TGD people that is effective, efficient, inclusive, and accessible (Hancock, 2017; Russell & Abrams, 2019).

Professionals in this area should receive comprehensive education that invites them to develop self-awareness, cultural humility, and cultural responsiveness in order to be respectful of and attentive to gender diversity and other aspects of a client's identifications that can take a variety of forms and imply a range of different support needs (Azul, 2015; Azul et al., 2022). Client preferences for use of names, formal forms of address, gender entry, and pronouns need to be respected in all communication with and about the client (including medical records, reports, emails). Education also needs to inform the setting up of a training space or clinic and administrative practices that are designed to be welcoming to TGD people and allow TGD people to feel safe and respected when raising concerns or issues with the voice and communication support team.

Voice and communication specialists working with TGD people will need working knowledge of applicable intervention principles, mechanisms, and effectiveness, competence in teaching and modeling voice and communication modification skills, and a basic understanding of transgender health, including hormonal and surgical treatments and trans-specific psychosocial issues. Education needs to include methodologies and practices that have been developed within TGD communities and shown to be effective and should ideally be presented by or in collaboration with TGD people with lived experience of voice and communication support.

Statement 14.3.

We recommend health care professionals in transgender health working with transgender and gender diverse people who are dissatisfied with their voice or communication consider offering a referral to voice and communication specialists for voice-related support, assessment, and training.

A voice and communication specialist is well positioned to provide information and guidance to the TGD person expressing dissatisfaction with their voice or communication when available. There is evidence voice and communication specialists provide support in such a way that a client's satisfaction with voice and communication can be achieved, thereby reducing gender dysphoria and improving communication-related quality of life (Azul, 2016; Block, 2017; Deuster, Di Vincenzo et al., 2016; Hancock, 2017; Hancock et al., 2011; Hardy et al., 2013; Kelly et al., 2018; McNamara, 2007; McNeill et al., 2008; Owen & Hancock, 2010; Pasricha et al., 2008; Söderpalm et al., 2004; Watt et al., 2018).

There is empirical evidence that behavioral voice support for TGD AMAB people is effective with regard to achieving the targeted voice changes (Oates, 2019). Seven studies prior to 2020 provide empirical evidence for the effectiveness of voice training, although it is somewhat weak (Carew et al., 2007; Dacakis, 2000; Gelfer & Tice, 2013; Hancock et al., 2011;Hancock & Garabedian, 2013; McNeill et al., 2008; Mészáros et al., 2005). Voice training methods across these seven studies were similar and indicated voice training can be effective at increasing average fundamental frequency (average pitch), fundamental frequency range (pitch range), satisfaction with voice, self-perception and listener perception of vocal femininity, voice-related quality of life, and social and vocational participation. Weaknesses of the identified studies include lack of randomized controlled trials evaluating voice training, small sample sizes, inadequate long-term follow-up, and lack of control of confounding variables. In 2021, another systematic review of the effects of behavioral speech training for AMAB people reached similar conclusions (Leyns et al., 2021).

Until recently, there was almost no research exploring the effectiveness of voice training with TGD AFAB people. There is, however, some promising, although weak evidence of effectiveness from a case study (Buckley et al., 2020) and one uncontrolled prospective study of group voice training (Mills et al., 2019).

Statement 14.4.

We recommend health care professionals working with transgender and gender diverse people who are considering undergoing voice surgery consider offering a referral to a voice and communication specialist who can provide pre- and/or postoperative support.

This statement does not intend to require TGD people receive presurgical voice training. Rather, it is recommended that every available support be offered to provide individualized informational counseling critical to person-centered care. The recommendation is for the TGD person's consideration to be informed as necessary by individualized informational counseling based on voice assessment, trial voice training, and discussion of expected voice outcomes and risks of surgery with a voice and communication specialist.

For most types of laryngeal surgery, voice training is recommended both prior to surgery to ensure preparation of the vocal mechanism for the surgical intervention and postsurgery to ensure a return to functional voice production (Branski et al., 2006; Park et al., 2021). For pitch-raising surgery in particular, another reason a trial of voice training is recommended is because there are indications certain measures improve with training but not with pitch-raising surgery (e.g., factors relevant to intonation and naturalness, such as maximum *f0* pitch in speech range; Kelly et al., 2018).

The number and quality of research studies evaluating pitch-lowering surgeries are currently insufficient, particularly with regard to comparing outcomes with and without other interventions (i.e., testosterone) (Bultynck et al., 2020). There are more techniques and studies of pitch-raising surgeries, but the quality of the evidence is still low. Outcomes from pitch-raising surgeries have been compared to outcomes from having no surgery (Anderson, 2007, 2014; Brown et al., 2000;

Geneid et al., 2015; Gross, 1999; Kim, 2017; Kocak et al., 2010; Kunachak et al., 2000; Matai et al., 2003; Meister et al., 2017; Neumann & Welzel, 2004; Orloff et al., 2006; Pickuth et al., 2000; Remacle et al., 2011; Thomas & Macmillan, 2013; Tschan et al., 2016; Van Borsel et al., 2008; Yang et al., 2002), another type of surgical technique (Mora, 2018), voice training alone (Kanagalingam, 2005; Mastronikolis, 2013; Wagner, 2003) and surgery in conjunction with voice training (Casado, 2017; Kelly et al., 2018).

In the 11 studies reporting whether participants had voice training prior to pitch-raising surgery, most participants had prior voice training, but remained dissatisfied with voice and sought surgical intervention. Thus, most studies of surgical outcomes reflect the combined effects of voice training and surgical intervention. Attributes predicting which clients will pursue surgery after training are unknown.

Statement 14.5.

We recommend health care professionals in transgender health inform transgender and gender diverse people commencing testosterone therapy of the potential and variable effects of this treatment on voice and communication.

The research on the effects of androgen treatment on voice and communication of TGD people points to diverse and unpredictable effects on individual clients. While a number of studies have revealed effects on voice that matched TGD people's expectations and wishes, there is high quality evidence demonstrating TGD people are not always satisfied with the vocal outcomes of testosterone therapy, and many experience difficulties such as inadequate pitch lowering, compromised voice quality, vocal loudness, vocal endurance, pitch range, and flexibility (Azul, 2015, 2016, 2017, 2018; Cosyns et al., 2014; Nygren et al., 2016; Ziegler et al., 2018). A recent meta-analysis of 19 studies examining the effects of at least 1 year of testosterone therapy estimated 21% of participants did not achieve cisgender male normative frequencies, 21% of participants reported incomplete voice-gender congruence and voice problems, and 16% were not completely satisfied with their voice (Ziegler, 2018).

For people who wish to be treated with androgens, accurate informational counseling prior to commencing treatment should enable the development of realistic expectations to avoid disappointment regarding the permanent impact of hormone treatment on voice and communication. In addition, TGD people who do not have access to or do not wish to be treated with testosterone, but want to change their voice and those who are dissatisfied with the outcomes of testosterone treatment can be advised by a voice and communication specialist of alternative and additional support options (e.g., behavioral voice and communication training; pitch-lowering surgery).

CHAPTER 15 Primary Care

Primary care is the broadest of health care disciplines and is defined as the "provision of integrated, accessible health care services by health care professionals who are accountable for addressing a large majority of personal health care needs, developing a sustained partnership with patients, and practicing in the context of family and community." (Institute of Medicine, 1996).

Primary care providers (PCPs) encompass a wide range of health care professionals (HCPs) who deliver this care, including general and family medical practitioners, nurse practitioners, advanced practice nurses, physician associates/assistants, and internists. PCPs are represented by a variety of educational backgrounds, training, and specialties. Given the type of degree and the nature of the specialty, the scope of practice varies, and not all providers may be trained or qualified to directly provide the full breadth of transgender health care, such as mental health, genital/pelvic care, or postoperative care, following gender-affirming procedures. Physicians and other providers receive little education in transgender and gender-diverse (TGD) health at any time during their training (Dubin et al., 2018), and thus most skills are currently acquired in practice, either informally or through brief continuing education opportunities, see also Chapter 4—Education. However, if providers are competent to deliver similar care for cisgender patients, they should develop competency in caring for TGD patients. The competencies outlined below are all to be understood as being within the provider's scope of licensure and practice. However, all PCPs should be able to manage the comprehensive health of TGD patients either directly or by appropriate referral to other HCPs, including other specialists, for evaluation and treatment. There is no evidence competency in caring for TGD patients can only be achieved through a formal or certification process. In explicitly stating recommended competencies, however, PCP's and TGD persons across all settings can share a standard set of expectations of the knowledge, skills, and cultural competence required for the care of TGD persons.

Due to the unique medical, surgical, and social conditions faced by TGD people, PCPs need distinct competencies in the care of TGD persons, apart from what is expected of all PCP's who may otherwise care for a diverse population that includes ethnic, racial, or sexual minorities. Professional bodies from a range of generalist disciplines have issued position statements and guidelines specific to the care of TGD people (American College of Obstetricians and Gynecology, 2021; Italian Society of Gender, Identity and Health (SIGIS); the Italian Society of Andrology and Sexual Medicine (SIAMS); the Italian Society of Endocrinology (SIE), 2021; Polish Sexological Society, 2021; the Southern African HIV Clinicians' Society, 2021). Wylie et al. (2016) state "For the most part, the general health and well-being of transgender people should be attended to within the primary care setting, without differentiation from services offered to cisgender (non-transgender) people for physical, psychological, and sexual health issues. Specific care for gender transition is also possible in primary care." There are many examples of these services being provided safely and effectively outside of specialist care in diverse cities such as Toronto and Vancouver in Canada, New York and Boston in the US, and in Sydney, Australia, (Radix & Eisfeld, 2014; Reisner, Radix et al., 2016; Spanos et al., 2021).

Hormone therapy

Whether TGD patients receive medically necessary gender-affirming hormone therapy (GAHT) from a specialist, e.g., an endocrinologist, or a PCP may depend on the availability of knowledgeable and welcoming providers and country-level factors, such as health care regulations and health services funding (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1). In much of the world, specialty services for TGD people are partly or wholly unavailable, which reinforces the need for all health providers to undertake

training in the provision of gender-affirming care. In some countries, PCPs may be required to refer TGD patients to specialist services (e.g., gender identity clinics) resulting in unacceptable delays to access GAHT (Royal College of General Practitioners, 2019).

Hormone-related therapy encompasses a range of interventions, such as puberty suppression and hormone initiation or hormone maintenance. With training, gender-affirming hormone therapy can be managed by most PCPs. Regardless of whether they serve as the primary hormone prescriber, all PCPs should be familiar with the medications, suggested monitoring, and potential side effects associated with GAHT (see Chapter 12—Hormone Therapy). PCPs should be able to make appropriate referrals to appropriate providers for all transition-related services they do not themselves provide.

This chapter supports the argument GAHT can be prescribed by PCPs or other non-specialists—"Considering barriers to health care access and the importance of GAHT to this population, it is imperative that PCPs are able and willing to provide GAHT for TGD patients." (Shires, 2017).

PCPs are commonly called upon to provide care for a broad range of conditions and needs, including those with which they may have had limited or no prior experience. Often this involves accessing commonly used and readily available reference sources, such as professional society guidelines or obtaining a subscription to online knowledge bases. PCPs are advised to use a similar approach when asked to provide basic GAHT care by using the Standards of Care as well as other readily accessed resources (Cheung et al., 2019; Hembree et al., 2017; Oliphant et al., 2018; T'Sjoen et al., 2020). It should be noted most of the commonly used medications in gender-affirming regimens are familiar to everyday primary care practice, including, but not limited to, testosterone, estradiol, progesterone and other progestagens, and spironolactone.

Mental health

PCPs should be able and willing to assess and provide mental health support for TGD people and GAHT that can alleviate gender dysphoria and allow gender expression. At the very least, they should be aware of these needs and consult additional specialty support if needed.

Preventive care

General practitioners are versed to provide comprehensive primary and secondary cancer prevention as a part of routine primary care. Evidence-based cancer prevention guidelines vary globally due to differences in national guidelines and levels of access to screening modalities at the local level. To date, research on the long-term impact of GAHT on cancer risk is limited (Blondeel et al., 2016; Braun et al., 2017). We have insufficient evidence to estimate the prevalence of cancer of the breast or reproductive organs among TGD populations (Joint et al., 2018). However, cancer screening should commence, in general, according to local guidelines. Several modifications are discussed in detail, below, depending on the type and duration of hormone use, surgical intervention, or both. In caring for transgender patients, the PCP should maintain an updated record of which organs are present in TGD patients so that appropriate, routine screening can be offered.

This organ inventory should be updated based on the surgical history or any development that has occurred due to taking gender-affirming hormones. Not all PCP's provide care across the lifespan. However, if providers routinely care for children, adolescents, or elder cisgender persons, they should develop competency in transgender care that is applicable to these age groups. If they are unable to do so, then PCPs should be able to make appropriate referrals to other HCPs who care for these populations.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statements of Recommendations

15.1- We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people that includes past and present use of hormones, gonadal surgeries, as well as the presence of traditional cardiovascular and cerebrovascular risk factors with the aim of providing regular cardiovascular risk assessment according to established, locally used guidelines.
15.2- We recommend health care professionals assess and manage cardiovascular health in transgender and gender diverse people using a tailored risk factor assessment and cardiovascular/cerebrovascular management methods.
15.3- We recommend health care professionals tailor sex-based risk calculators used for assessing medical conditions to the needs of transgender and gender diverse people, taking into consideration the length of hormone use, dosing, serum hormone levels, current age, and the age at which hormone therapy was initiated.
15.4- We recommend health care professionals counsel transgender and gender diverse people about their tobacco use and advise tobacco/nicotine abstinence prior to gender-affirming surgery.
15.5- We recommend health care professionals discuss and address aging-related psychological, medical, and social concerns with transgender and gender diverse people.
15.6- We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people who have received estrogens, taking into consideration the length of time of hormone use, dosing, current age, and the age at which hormones were initiated.
15.7- We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people with breasts from natal puberty who have not had gender-affirming chest surgery.
15.8- We recommend health care professionals apply the same respective local screening guidelines (including the recommendation not to screen) developed for cisgender women at average and elevated risk for developing ovarian or endometrial cancer in their care of transgender and gender diverse people who have the same risks.
15.9- We recommend against routine oophorectomy or hysterectomy solely for the purpose of preventing ovarian or uterine cancer for transgender and gender diverse people undergoing testosterone treatment and who have an otherwise average risk of malignancy.
15.10- We recommend health care professionals offer cervical cancer screening to transgender and gender diverse people who currently have or previously had a cervix following local guidelines for cisgender women.
15.11- We recommend health care professionals counsel transgender and gender diverse people that the use of antiretroviral medications is not a contraindication to gender-affirming hormone therapy.
15.12- We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people that includes past and present use of hormones, gonadal surgeries as well as the presence of traditional osteoporosis risk factors to assess the optimal age and necessity for osteoporosis screening.
15.13- We recommend health care professionals discuss bone health with transgender and gender diverse people including the need for active weight bearing exercise, healthy diet, calcium, and vitamin D supplementation.
15.14- We recommend health care professionals offer transgender and gender diverse people referrals for hair removal from the face, body, and genital areas for gender-affirmation or as part of a preoperative preparation process.

Statement 15.1

We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people, that includes past and present use of hormones, gonadal surgeries, as well as the presence of traditional cardiovascular and cerebrovascular risk factors with the aim of providing regular cardiovascular risk assessment according to established, locally used guidelines. For supporting text, see Statement 15.3.

Statement 15.2

We recommend health care professionals assess and manage cardiovascular health in transgender and gender diverse people using a tailored risk factor assessment and cardiovascular/cerebrovascular management methods. For supporting text, see Statement 15.3.

Statement 15.3

We recommend health care professionals tailor sex-based risk calculators used for assessing medical conditions to the needs of transgender and gender diverse people, taking into consideration the length of hormone use, dosing, serum hormone levels, current age, and the age at which hormone therapy was initiated.

Cardiovascular disease (CVD) and stroke are the leading causes of mortality worldwide (World Health Organization, 2018). Extensive data among racial, ethnic, and sexual minorities in multiple settings demonstrate significant disparities in the prevalence of CVD and its risk factors as well as in the outcomes to medical interventions. Structural factors such as access to care, socioeconomic status, and allostatic load related to minority stress contribute to these disparities (Flentje et al., 2020; Havranek et al., 2015; Streed et al., 2021). TGD people often experience social, economic, and discriminatory conditions similar to other minority populations with known increased cardiovascular risk (Carpenter et al., 2020; James et al., 2016; Reisner, Radix et al., 2016). TGD persons of racial, ethnic, and sexual

minorities have been shown to experience increased impact related to intersectional stress. Conversely, access to gender-affirming care, including GAHT, may buffer against the elevation of CVD risk due to the improvement in quality of life and reduction in gender dysphoria and incongruence (Defreyne et al., 2019; Martinez et al., 2018). PCPs can significantly improve TGD health through screening and prevention of CVD and its associated risk conditions—such as tobacco use, diabetes mellitus, hypertension, dyslipidemia, and obesity.

The few, primarily US based, studies evaluating the prevalence of CVD, stroke, or CVD risk in TGD persons independent of GAHT indicate an elevated CV risk, including high rates of undiagnosed and untreated CV risk factors with inadequate CV prevention when compared with cisgender populations (Denby et al., 2021; Malhotra et al., 2022; Nokoff et al., 2018). In one population-based study, TGD people had greater odds of discrimination, psychological distress, and adverse childhood experience, and these were associated with increased odds of having a cardiovascular condition (Poteat et al., 2021).

In US studies that are based on data from the Behavioral Risk Factor Surveillance System, both transgender men and transgender women show a higher prevalence of myocardial infarction (MI), stroke, or any CVD compared with cisgender men, cisgender women or both. Results vary based on the adjustment of data for additional variables, including race, income, or cardiovascular risk factors (Alzahrani et al., 2019; Caceres et al., 2020; Nokoff et al., 2018). Gender nonbinary persons also have higher odds of CVD (Downing & Przedworski, 2018). Data on hormone use was not collected in these studies, which are also limited by the use of self-reported health histories. In the US, TGD individuals presenting for GAHT may have higher rates of undiagnosed and untreated CVD risk factors compared with the cisgender population (Denby et al., 2021), although this may not be applicable globally.

A large 2018 case control study from several US centers that used 10:1 cisgender matched controls found no statistically significant difference in rates of MI or stroke between transgender women and cisgender men, and no difference in rates of MI, stroke, or venous thromboembolism (VTE) between transgender men and cisgender men or women. There was a statistically significant hazard ratio of 1.9 for VTE among transgender women when compared with cisgender men. A subcohort of transgender women who initiated GAHT during (versus prior to) the 6-year study window did show an increased risk of stroke. Increases in rates of VTE in the overall cohort of transgender women and in rates of stroke in the initiation subcohort of transgender women demonstrated calculated numbers-needed-to-harm (not reported in the paper) between 71-123 (Getahun et al., 2018). Other studies have demonstrated no increase in CV events or stroke among transgender men undergoing testosterone therapy, although studies are limited by their small sample size, relatively short follow-up, and the younger age of the sample population (Martinez et al., 2020; Nota et al., 2019).

European and US studies in transgender women who have accessed feminizing GAHT increasingly indicate a higher risk of CVD, stroke, or both, compared with cisgender women and, in some studies, cisgender men (Getahun et al., 2018; Nota et al., 2019; Wierckx et al., 2013). Many of these studies had significant limitations, such as variably adjusting for CV-related risk factors, small sample sizes—especially involving older transgender women—and variable duration and types of GAHT (Connelly et al., 2019; Defreyne et al., 2019, Martinez et al., 2020). Furthermore, the overall increased risk was small. In many of these studies, the majority of transgender women who experienced cardiac events or stroke were over 50 years old, had one or more CVD risk factors, and were taking a variety of hormone regimens, including, but not limited, to ethinyl estradiol, a synthetic estrogen that confers significant elevations in thrombotic risk and is not recommended for use in feminizing regimens (Gooren et al., 2014; Martinez et al., 2020). Current limited evidence suggests estrogen-based GAHT is associated with an increased risk of myocardial infarction and stroke, but whether this small risk is a result of GAHT or an effect of pre-existing CV risk is unclear. There are no known studies that specifically address CVD and

related conditions in nonbinary individuals, individuals who use subphysiologic doses of gender-affirming hormones, or in adults previously treated with puberty suppression.

PCPs can best address CVD risk during GAHT by assessing TGD people for CVD and modifiable CVD risk factors, such as diabetes mellitus, hypertension, hyperlipidemia, obesity, and smoking, as well as by addressing the impact of minority stress on cardiovascular risk (Streed et al., 2021). In addition, PCPs can mitigate transgender cardiovascular health disparities by providing a timely diagnosis and treatment of risk conditions and by tailoring their management in a way that supports ongoing gender-affirming interventions.

Risk assessment guidelines vary based on the national or international context and scientific affiliation of guideline developers. CVD prevention guidelines also vary in terms of the nature and frequency of the risk assessment for otherwise healthy adults under age 40 (Arnett et al., 2019; Piepoli et al., 2020; Précoma et al., 2019; Streed et al., 2021; WHO, 2007). Over age 40, when cardiovascular risk increases, guidelines clearly recommend scheduled risk assessments using a calculated prediction of ten-year total CVD risk based on risk prediction equations from large population samples. Examples of risk calculators include SCORE (recommended by the European Guidelines on CVD Prevention), Pooled Cohort Studies Equations (2013 AHA ACC Guideline on the Assessment of CVD risk), Framingham Risk scores, and the World Health Organization (WHO) Risk Prediction Charts. The WHO charts were developed based on information from the countries in each WHO subregion. In many low resource settings, facilities are not available to measure cholesterol or serum glucose, and alternative predication charts are available without these measures.

Of note, all current cardiovascular risk calculators are gendered, using sex as a significant risk variable. There is currently insufficient data on cardiovascular risk interventions across the lifespan in TGD persons with medical and surgical interventions to adjust these predictive equations. Nonetheless, it is clear both sex assigned at birth and medical transition can affect the parameters used to calculate cardiovascular risk (Connelly et al., 2019; Defreyne et al., 2019; Maraka et al., 2017; Martinez et al., 2020). Providers can take a variety of approaches to using cardiovascular risk calculators in TGD persons, including employing the risk calculator for the sex assigned at birth, affirmed gender, or a weighted average of the two, taking into consideration total lifetime exposure to GAHT. Although data are lacking, using the affirmed gender for transgender adults with a history of pubertal-age GAHT initiations is likely to be most appropriate. Patients with a history of submaximal GAHT use or prolonged periods of time postgonadectomy without hormone replacement before roughly age 50 may require an even more nuanced approach. Providers should be aware of the characteristics and limitations of the risk calculator in use and should engage patients in shared decision-making regarding these specific considerations.

There are currently no studies comparing the prevalence of dyslipidemia between transgender and cisgender samples, while controlling for hormone use. As noted previously, data in other populations demonstrate the presence of psychosocial stress during childhood and remote adulthood favor adiposity and abnormal lipid metabolism. Both testosterone- and estrogen-based GAHT affect lipid metabolism, although evidence is limited by the variety of hormone regimens and additional variables (Connelly et al., 2019; Defreyne et al., 2019; Deutsch, Glidden et al., 2015; Maraka et al., 2017; Martinez et al., 2020;). On balance, estrogen tends to increase high-density lipoprotein (HDL) cholesterol and triglycerides with variable effects on low density lipoprotein (LDL) cholesterol, while testosterone variably affects triglycerides, decreases HDL cholesterol and increases LDL cholesterol. The method of administration may also affect this pattern, particularly in relation to oral versus transdermal estrogen and their impact on triglycerides (Maraka et al., 2017). In general, the effect sizes of these differences are minimal, and the overall impact on cardio- and cerebrovascular outcomes is unclear. There are no studies examining hormone effects in TGD people with pre-existing dyslipidemia with hormone use starting over age 50, or investigating effects beyond 2-5 years of therapy.

Studies comparing the prevalence of hypertension between TGD and cisgender samples that controlled for hormone use are lacking. Data in other populations demonstrate chronic and acute psychosocial stress, including experiences of discrimination can mediate hypertension (Din-Dzietham et al., 2004; Spruill, 2010). In US studies that were based on the Behavioral Risk Factor Surveillance System, a large national US health survey, there were no differences in reported hypertension between transgender men or women compared with cisgender samples (Alzahrani et al., 2019; Nokoff et al., 2018).

Studies of testosterone—and estrogen-based GAHT have shown inconsistent effects on systolic and diastolic blood pressure. A retrospective study of the effects of estrogen- and testosterone-based GAHT regimens on blood pressure found a slight reduction in systolic blood pressure with the initiation of estrogen-based regimens; while there was a slight elevation (4 mm Hg) in mean systolic blood pressure on long term follow-up of testosterone-based regimens, this difference was at the margin of statistical significance and of limited clinical relevance (Banks et al., 2021). A systematic review concluded, given the limited quality of the studies, there is insufficient data to reach conclusions on the effects of gender-affirming hormone therapy on blood pressure (Connelly et al., 2021). Spironolactone, often used as an androgen blocker in feminizing GAHT, is a potassium sparing diuretic and may increase potassium when used in conjunction with ACE inhibitors or angiotensin receptor blocker medications, as well as salt substitutes. There are no studies examining hormone effects in TGD people with pre-existing hypertension with hormone use starting over age 50, or investigating effects beyond 2–5 years of therapy. Transgender persons receiving GAHT should undergo any additional blood pressure screening or monitoring indicated by WPATH guidelines for GAHT.

There are limited data comparing the prevalence of diabetes mellitus between TGD and cisgender samples independent of hormone use. Recent data from the STRONG cohort study (Islam et al., 2021) found the prevalence and incidence of type 2 diabetes was more common in the trans feminine cohort compared with cisgender females but not cisgender male controls. No significant differences in the prevalence or incidence of type 2 diabetes were observed in the trans masculine cohort and in TGD persons overall after starting hormone therapy. However, the mean follow-up for both cohorts was 2.8 and 3.1 years, respectively (Islam et al., 2021). Data in other populations, including sexual minorities, indicates chronic and acute psychosocial stress can mediate the development and control of type 2 diabetes (Beach et al., 2018; Kelly & Mubarak, 2015).

US studies based on the Behavioral Risk Factor Surveillance System found no differences in reported diabetes between transgender men, transgender women and nonbinary persons compared with cisgender persons (Alzahrani et al., 2019; Caceres et al., 2020; Nokoff et al., 2018). Several small studies have shown a higher-than-expected prevalence of polycystic ovarian syndrome or hyperandrogenemia among transgender men (Feldman et al., 2016), conditions associated with insulin resistance and diabetes risk. While studies of both testosterone- and estrogen-based GAHT show varying effects on weight/body fat, glucose metabolism, and insulin resistance (Defreyne et al., 2019), most do not demonstrate any increase in prediabetes or diabetes (Chan et al., 2018; Connelly et al., 2019). There are no studies examining hormone effects in TGD people with pre-existing diabetes, with hormone use starting over age 50, or investigating effects beyond 2–5 years of therapy. There are currently no studies specifically addressing diabetes in adults previously treated with puberty suppression.

While intermediate-outcome studies of the effects of GAHT on blood pressure and lipids are helpful for hypothesis generation and for studying etiology, future studies should focus on cardiovascular outcomes of interest, with a specific focus on individual predictors such as age, route and dose of hormones used, and total lifetime exposure to GAHT. Interpretation of data should always consider whether cisgender controls were of the same natal sex or identified gender.

Statement 15.4

We recommend health care professionals counsel transgender and gender diverse people about

their tobacco use and advise tobacco/nicotine abstinence prior to gender-affirming surgery.

Tobacco use is a leading contributor to cardiovascular disease, pulmonary disease, and cancer worldwide (World Health Organization, 2020). TGD persons have a higher prevalence of tobacco use compared with cisgender individuals, which varies across the gender spectrum (Azagba et al., 2019; Buchting et al., 2017). This pattern is consistent with other populations experiencing minority stress (Gordon et al., 2021). PCPs can promote protective factors against tobacco use, including reducing exposure to personal or structural discrimination, having gender-affirming identification, and having health insurance (Kidd et al., 2018; Shires & Jafee, 2016).

The health risks of tobacco use affect TGD persons disproportionately, primarily due to decreased access to culturally competent, affordable screening, and treatment of tobacco-related diseases (Shires & Jafee, 2016). Smoking may further increase cardiovascular and VTE risk for TGD individuals taking feminizing GAHT (Hontscharuk, Alba, Manno et al., 2021). Smoking also doubles or triples the risk of general surgery complications, such as wound healing, scarring, and infection (Yoong et al., 2020) and increases these risks for those accessing gender-affirming surgeries. Data in cisgender populations show quitting smoking prior to surgery and maintaining abstinence for six weeks postoperatively significantly reduces complications (Yoong et al., 2020).

There are currently few studies of smoking cessation programs specifically focused on TGD persons (Berger & Mooney-Somers, 2017). However, limited evidence suggests PCPs can enhance smoking cessation efforts by addressing the effects of minority stress (Gamarel et al., 2015) and incorporating gender-affirming interventions, such as GAHT (Myers & Safer, 2016).

HCPs should take into consideration the significant barriers people habituated to nicotine encounter when attempting cessation. Nicotine replacement therapy and/or other cessation adjuncts should be made available, with an emphasis on individual preferences and a recognition of underlying behavioral health factors that contribute to continued nicotine use. Decision-making regarding approaches to GAHT or surgery should include consideration of the "first do no harm" principle of medical practice, with the realities of an individual patient's abilities and needs.

Statement 15.5

We recommend health care professionals discuss and address aging-related psychological, medical, and social concerns with transgender and gender diverse people.

Aging presents specific social, physical, and mental health challenges for TGD persons. While the literature on aging and transgender elders is limited, many older TGD adults have experienced a lifetime of stigma, discrimination, and repression of identified gender (Fabbre & Gaveras, 2020; Witten, 2017). This experience affects TGD elders' interactions with health care systems (Fredriksen-Goldsen et al., 2014; Kattari & Hasche, 2016; Walker et al., 2017). Transgender elders are more likely than cisgender LGB peers to report poor physical health, even when controlling for socio-demographic factors (Fredriksen-Goldsen 2011; Fredriksen-Goldsen et al., 2014). Reduced access to culturally competent care and the sequelae of minority stress often result in delayed care, potentially exacerbating chronic conditions common with aging (Bakko & Kattari, 2021; Fredriksen-Goldsen et al., 2014).

Although there are few studies on gender-affirming medical interventions among TGD elders, evidence suggests older adults experience a significantly higher quality of life with medical transition even when compared with younger TGD adults (Cai et al., 2019). Although age itself is not an absolute contraindication or limitation to gender-affirming medical or surgical interventions, TGD elders may not be aware of the current range of social, medical or surgical options available that can help them meet their individual needs (Hardacker et al., 2019; Houlberg, 2019).

While studies on mental health among TGD elders are limited, those over age fifty experience significantly higher rates of depressive symptoms and perceived stress compared with cisgender LGB and heterosexual older adults (Fredriksen-Goldsen 2011, Fredriksen-

Goldsen et al., 2014). Risk factors specific to TGD elders include gender- and age-related discrimination, general stress, identity concealment, victimization, and internalized stigma, while social support and community belonging appear protective (Fredriksen-Goldsen et al., 2014; Hoy-Ellis & Fredriksen-Goldsen, 2017; White Hughto & Reisner, 2018). PCPs can assist patients by encouraging spirituality, self-acceptance and self-advocacy, and an active healthy lifestyle, all of which are associated with resilience and successful aging (McFadden et al., 2013; Witten, 2014).

TGD elders often face social isolation, loss of support systems, and disconnection from close friends and children (Fredriksen-Goldsen 2011; Witten, 2017). The most common aging concerns among TGD persons are losing the ability to care for themselves followed by having to go into a nursing home or assisted living facility (Henry et al., 2020). While long-term care settings offer the helpful needed assistance, they also have the potential for physical or emotional abuse, for denial of GAHT and routine care, for being "outed," and being prevented from living and dressing according to one's affirmed gender (Auldridge et al., 2012; Pang et al., 2019; Porter et al., 2016). TGD elders identify senior housing, transportation, social events, support groups as being the most needed services (Auldridge et al., 2012; Witten, 2014).

Despite barriers, most TGD persons engage in successful aging strengthened by self-acceptance, caring relationships, and advocacy (Fredriksen-Goldsen 2011; Witten, 2014). PCPs should address core health issues facing TGD elders, including mental health, gender-affirming medical interventions, social support, and end of life/long-term care.

Beyond the independent impact of factors such as minority stress and social determinants of health in later years, data are lacking on specific health issues facing transgender people who use GAHT later in life, individuals who began GAHT at a younger age, and those seeking to continue or begin GAHT in their sixth, seventh, eighth, or later decades. With an increasing proportion of transgender people beginning GAHT at younger ages, including some who begin at the time of puberty, studies to examine the impact of decades of such treatment on long-term health are ever more important.

Statement 15.6

We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people who have received estrogens, taking into consideration length of time of hormone use, dosing, current age, and the age at which hormones were initiated.

TGD individuals taking estrogen-based GAHT will develop breasts, and therefore warrant consideration for breast cancer screening. Exogenous estrogen may be one of multiple factors that contribute to breast cancer risk in cisgender people. Two cohort studies have been published evaluating breast cancer prevalence among transgender women in the Netherlands (Gooren et al., 2013) and the US (Brown & Jones, 2015). Both were retrospective cohorts of clinical samples using a diagnosis of breast cancer as the outcome of interest and cisgender controls as a comparison group. Neither study involved prospective screening for breast cancer, and both had significant methodological limitations. Numerous guidelines have been published (Deutsch, 2016a) recommending some combination of "age plus length of estrogen exposure" as the determinant of need to commence screening. These recommendations are based on expert consensus only and are evidentiarily weak.

BRCA1 and 2 mutations increase the risk of breast cancer, however the role sex hormone exposure plays, if any, in this increased risk is unclear (Rebbeck et al., 2005) The degree of increase in risk, if any, from gender-affirming estrogen therapy is unknown. Patients with a known BRCA1 mutation should be counseled about the unknowns and shared decision-making with informed consent should occur between the patient and provider, recognizing the numerous benefits of GAHT.

Breast cancer screening among transgender women should also take into consideration the likelihood that a transgender woman's breasts may be denser on mammography. Dense breasts, a history of injecting breasts with fillers such as silicone, and breast implants may complicate the interpretation of mammographic findings (Sonnenblick et al., 2018). Therefore, special

techniques should be used accordingly. People who have injected particles such as silicone or other fillers for breast augmentation may also develop complications, such as sclerosing lipogranulomas, which obscure normal tissue on mammography or ultrasound.

Statement 15.7

We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people with breasts from natal puberty who have not had gender-affirming chest surgery.

For TGD people assigned female at birth and who developed breasts via natal puberty, there are theoretical concerns about whether direct exposure to testosterone and exposure to aromatized estrogen resulting from testosterone therapy are risk factors for the development of breast cancer. Limited retrospective data has not demonstrated increased risk for breast cancer among transgender men (Gooren et al., 2013; Grynberg et al., 2010), however prospective and comparison data are lacking. Most people in this group will have some breast tissue remaining, and therefore it is important for providers to be aware breast cancer risk is not zero in this population. The timing and approach to breast cancer screening in this group who have had chest surgery is currently not established, and, similar to cisgender men with significant family history or BRCA gene mutation, screening via MRI or ultrasound may be appropriate. Because the utility and performance of these approaches have not been studied and because self- and HCP-led chest/breast screening exams are not recommended in cisgender women due to potential harms of both false-positive results and over-detection (detection of a cancer which would have regressed on its own with no need for intervention), any approach to screening in this group should occur in the context of shared decision-making between patients and providers regarding the potential harms, benefits, and unknowns of these approaches.

Statement 15.8

We recommend health care professionals apply the same respective local screening guidelines (including the recommendation not to screen) developed for cisgender women at average and elevated risk for developing ovarian or endometrial cancer in their care of transgender and gender diverse people who have the same risks.

Current consensus guidelines do not recommend routine ovarian cancer screening for cisgender women. Case reports of ovarian cancer among transgender men have been reported (Dizon et al., 2006; Hage et al., 2000). There is currently no evidence testosterone therapy leads to an increased risk of ovarian cancer, although long-term prospective studies are lacking (Joint et al., 2018).

Statement 15.9

We recommend against routine oophorectomy or hysterectomy solely for the purpose of preventing ovarian or uterine cancer for transgender and gender diverse people undergoing testosterone treatment and who have an otherwise average risk of malignancy.

TGD people with ovaries who are taking testosterone-based GAHT are often in an oligo- or anovulatory state, or otherwise experience shifts in luteal phase function and progesterone production. This condition combined with the possible increased estrogen exposure from aromatization of exogenous testosterone raises the concern for excessive or unopposed endometrial estrogen exposure, although the clinical significance is unknown. Histologic studies of the endometrium in TGD people taking testosterone have found atrophy rather than hyperplasia (Grimstad et al., 2018; Grynberg et al., 2010; Perrone et al., 2009). In a large cohort of trans masculine people who underwent a hysterectomy with oophorectomy, benign ovarian histopathology was noted in all cases (n = 85) (Grimstad et al., 2020). While prospective outcome data are lacking, there is insufficient evidence at this time to support a recommendation transgender men undergo routine hysterectomy or oophorectomy solely to prevent endometrial or ovarian cancer. Certainly, unexplained signs/symptoms of endometrial or ovarian cancer should be evaluated appropriately.

Statement 15.10

We recommend health care professionals offer cervical cancer screening to transgender and

gender diverse people who currently have or previously had a cervix, following local guidelines for cisgender women.

Individuals with a cervix should undergo routine cervical cancer screening and prevention according to age-based regional practices and guidelines. This includes vaccination against the human papilloma virus (HPV) and screening according to local guidelines, including cytologic, high-HPV co-testing if available. It is important HCPs be mindful of performing pelvic speculum examinations in a manner that minimizes pain and distress for transgender masculine people.

TGD people with a cervix are less likely to have had conventional cervical cancer screening, either because the exam can cause worsening of dysphoria and/or because general practitioners and patients are misinformed about the need for this screening (Agenor et al., 2016; Potter et al., 2015). In addition, testosterone therapy can result in atrophic changes of the genital tract, and the duration of testosterone use has been associated with a greater likelihood of obtaining an inadequate sample for cytologic screening of cervical cancer (Peitzmeier et al., 2014). Alternatives to speculum exams and cervical cytology, such as provider- or self-collected high-risk HPV swabs, may be of particular benefit for screening people with a cervix. Research underway in the US is investigating the use of self-collected vaginal high-risk HPV testing among transgender masculine populations. HPV swabs were found to be highly acceptable among transgender men with a sensitivity to high-risk HPV of 71.4% (negative predictive value of 94.7%) and a specificity of 98.2% (Reisner et al., 2018). Further study is needed to evaluate the harms of HPV primary screening in transgender men in terms of the potential increased harms associated with invasive examinations and colposcopies.

Statement 15.11

We recommend health care professionals counsel transgender and gender diverse people that the use of antiretroviral medications is not a contraindication to gender-affirming hormone therapy.

Human immunodeficiency virus (HIV) prevalence is disproportionately high in TGD populations. A recent large metanalysis found a global odds ratio for HIV infection of sixty-six for trans feminine individuals and 6.8 for trans masculine individuals (Stutterheim et al., 2021). PCPs have unique opportunities to provide crucial education and implement prevention strategies, especially related to decreasing HIV burden among TGD people. Mistrust of health care providers due to past experiences of discrimination and transphobia impacts HIV prevention and disrupts the linkage to care efforts (Sevelius et al., 2016). Stigma, lack of adequate training, and innate power hierarchies within medical establishments, all contribute to ambivalence and uncertainty among HCPs when caring for TGD people (Poteat et al., 2013). Finally, a lack of inclusiveness and gender-affirming practices in the health care setting may lead to TGD people feeling unsafe discussing sensitive topics, such as HIV diagnosis and avoiding care out of fear (Bauer et al., 2014; Gibson et al., 2016; Seelman et al., 2017).

HCPs should be aware of this broader context within which many TGD people are seeking care for either gender-affirming hormones, HIV pre-exposure chemoprophylaxis/treatment (PrEP), or both. There may be various misconceptions about the safety of taking gender-affirming hormones concurrently with antiretroviral therapy for HIV chemoprophylaxis or treatment.

Direct study of antiretroviral/gender-affirming hormone therapy (ART/GAHT) interactions has been limited. A subanalysis of transgender women and trans feminine persons in the multinational iPrEx trial found poor effectiveness in this group in the intention-to-treat analysis, although effectiveness was similar to that in cisgender gay men among those transgender participants who adhered to the medication as prescribed, suggesting that uptake and adherence to PrEP remain challenging in this population. Two studies of the effects of GAHT on tenofovir diphosphate (Grant et al., 2021) and tenofovir diphosphate and emtricitabine (Shieh et al., 2019) found the significantly lowered ART drug levels were unlikely to be of clinical significance. Overall, data on the interactions between hormonal contraceptives and antiretrovirals are reassuring in terms of the impact of hormones on ART (Nanda

et al., 2017). Because estradiol is partially metabolized by cytochrome P450 (CYP) 3A4 and 1A2 enzymes, potential drug interactions with other medications that induce or inhibit these pathways, such as non-nucleoside reverse transcriptase inhibitors (NNRTIs, e.g., efavirenz (EFV) and nevirapine (NVP)), may exist (Badowski et al., 2021). However, the preferred first-line ART regimens in most countries include integrase inhibitors, which have minimal to no drug interactions with gender-affirming hormones and can be used safely (Badowski, 2021; Department of Health and Human Services. Panel on Antiretroviral Guidelines for Adults and Adolescents, 2021). If concerns exist about potential interactions, HCPs should monitor blood hormone levels as needed. Therefore, TGD people living with HIV and taking antiretroviral medications should be counseled that taking antiretrovirals alongside GAHT is safe.

Statement 15.12

We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people that includes past and present use of hormones, gonadal surgeries as well as the presence of traditional osteoporosis risk factors, to assess the optimal age and necessity for osteoporosis screening. For supporting text, see Statement 15.13.

Statement 15.13

We recommend health care professionals discuss bone health with transgender and gender diverse people including the need for active weight bearing exercise, healthy diet, calcium, and vitamin D supplementation.

Estrogen and testosterone both support bone formation and turnover. Decreased sex hormone levels are associated with a greater risk of osteoporosis in older age (Almeida et al., 2017). TGD individuals may receive medical and/or surgical interventions that have the potential to influence bone health, such as sex hormone treatment, androgen blockade, and gonadectomy. Therefore, a detailed medical history, including past and present use of hormones along with gonadal surgeries, is necessary to establish the need for osteoporosis screening.

Several observational studies have compared bone mineral density (BMD) of TGD adults before and after gender-affirming hormone therapy along with in TGD individuals compared with sex-at-birth matched cisgender controls.

Low BMD may exist before the initiation of hormones. One study showed a lower mean areal BMD at the femoral neck, total hip, and spine in transgender women than in age-matched cisgender male controls (Van Caenegem, Taes et al., 2013). Another study revealed a high prevalence of low BMD scores among TGD youth before starting puberty blockers (Lee, Finlayson et al., 2020). The authors of both studies concluded low rates of physical activity may be an important contributor to these findings.

Acceleration of bone loss can occur after gonadectomy if hormones are stopped or if hormones levels are suboptimal. In one study, thirty percent of transgender women who had undergone gonadectomy had low bone mass, and this correlated with lower 17-ß estradiol levels and adherence to GAHT (Motta et al., 2020).

Investigation of the effects of GAHT on BMD have revealed TGD women receiving estrogen therapy show improvements in BMD. A systematic review and meta-analysis on the impact of sex hormones on bone health of transgender individuals included 9 eligible studies in transgender women (n = 392) and 8 eligible studies in transgender men (n = 247) published between 2008 and 2015. The meta-analysis revealed transgender women showed a statistically significant increase in lumbar spine BMD (but not femoral neck BMD) compared with baseline measures. Among transgender men, there were no statistically significant changes in the lumbar spine, femoral neck, and total hip BMD at 12 and 24 months after starting testosterone compared with baseline measures (Singh-Ospina et al., 2017). Since the publication of this study, the European Network for Investigation of Gender Incongruence (ENIGI) study, a multicenter prospective observational study (Belgium, Norway, Italy, and the Netherlands) published results on BMD outcomes for 231 transgender women and 199 transgender men one year after initiating GAH (Wiepjes et al., 2017). Transgender women had an increase in BMD of the lumbar spine, total hip and

femoral neck, and increased BMD of the total hip occurred in transgender men. One study reported no fractures in transgender individuals at 12 months following initiation of hormones in 53 transgender men and 53 transgender women (Wierckx, van Caenegem et al., 2014). No studies suggest GAHT should be an indication for enhanced osteoporosis screening. Rather, gaps in GAHT in those who have undergone prior gonadectomy would be a consideration for such screening.

Clinical practice guidelines include recommendations for osteoporosis screening in TGD individuals (Deutsch, 2016a; Hembree et al., 2017; Rosen et al., 2019). For TGD people, both the International Society for Clinical Densitometry and the Endocrine Society suggest consideration of baseline BMD screening before initiation of hormones. Further recommendations for BMD screening are based on several factors including sex reported at birth and age along with the presence of traditional risk factors for osteoporosis, such as prior fracture, high risk medication use, conditions associated with bone loss, and low body weight (Rosen et al., 2019). Specifically, the ISCD guidelines state BMD testing is indicated for TGD individuals if they have a history of gonadectomy or therapy that lowers endogenous gonadal steroid levels prior to the initiation of GAHT, hypogonadism with no plan to take GAHT or known indications for BMD testing (Rosen et al., 2019). However, the evidentiary basis for these recommendations is weak.

The recommended screening modality for osteoporosis is dual energy x-ray absorptiometry (DXA) of the lumbar spine, total hip, and femoral neck (Kanis, 1994). However in many low- and middle-income countries, BMD tests using DXA are not available, and routine DXA-based screening is conducted in few countries, the US being an exception.

PCPs should discuss ways to optimize bone health with TGD people. In addition, PCPs should provide information about the importance of nutrition and exercise on maintaining bone health. TGD individuals with (or at risk) for osteoporosis should be informed about the benefits of weight bearing exercise along with strength and resistance exercises in limiting bone loss (Benedetti et al., 2018). Nutrition is integral to bone health. Nutritional deficiencies, including insufficient calcium intake and low vitamin D, can result in low bone mineralization. Vitamin D and calcium supplementation have been shown to reduce hip as well as total fracture incidence (Weaver et al., 2016). Although relevant to all populations, this discussion is pertinent as a high prevalence of hypovitaminosis D has been observed in TGD populations (Motta et al., 2020; Van Caenegem, Taes et al., 2013).

Statement 15.14

We recommend health care professionals offer transgender and gender diverse people referrals for hair removal from the face, body, and genital areas for gender-affirmation or as part of a preoperative preparation process.

Hair removal is necessary both for the elimination of facial hair (Marks et al., 2019) as well as in preparation for certain gender-affirming surgeries (GAS) such as vaginoplasty, phalloplasty, and metoidioplasty (Zhang et al., 2016). Preoperative permanent hair removal is required for any skin area that will either be brought into contact with urine (e.g., used to construct a neourethra) or be moved to reside within a partially closed cavity within the body (e.g., used to line the neovagina) (Zhang et al., 2016). Hair removal techniques used in gender-affirming care are electrolysis hair removal (EHR) and laser hair removal (LHR) (Fernandez et al., 2013). EHR is currently the only US Food and Drug Administration–approved method of permanent hair removal, whereas LHR is approved for permanent hair reduction (Thoreson et al., 2020).

EHR involves the use of an electric current with a very fine probe that is manually inserted sequentially into individual hair follicles (Martin et al., 2018). Since this method uses direct mechanical destruction of the blood supply to the hair, it can be used on all hair colors and skin types (Martin et al., 2018). EHR is time consuming and costly as it requires each hair follicle to be treated individually, but is effective for permanent hair removal. For genital permanent hair removal prior to GAS, this treatment needs to be performed by a practitioner competent in genital hair removal as this method differs

from that of the face and body. EHR is more painful than LHR, with possible side effects of erythema, crusting, and swelling (Harris et al., 2014). Postinflammatory hyperpigmentation is a risk for dark-skinned individuals (Richards & Meharg, 1995). Pain can be controlled with topical local anesthetic and cooling techniques, and tolerance to EHR does develop to some degree with many persons able to tolerate longer sessions (Richards & Meharg, 1995).

LHR uses laser energy to target hair follicles. It is beneficial for larger surface areas. The mechanism is photo-thermolysis, whereby light from a laser selectively targets melanin in the hair shaft (Gao et al., 2018). This energy is converted to heat, which damages the follicles within the skin that produce hairs and results in the destruction of hair growth. Further treatments are needed to achieve best results and are typically spaced six weeks apart to allow for hair cycling (Zhang et al., 2016). Because LHR targets melanin, results may be limited for those with grey, blonde, or red hair.

There are specific considerations for using LHR in dark-skinned individuals (Fitzpatrick skin types IV to VI) (Fayne et al., 2018)). The higher melanin content of the epidermis can compete with the target chromophore of the light or laser, which is the melanin in the hair shaft of the hair follicle. For selective thermolysis to occur, heat diffuses from the hair shaft to the follicular stem cells to cause damage. In darker skin types, rather than reaching the target melanin in the hair shaft, light is absorbed in the epidermis where it is then converted to heat. This may result in poorer clinical outcomes and a higher rate of thermally induced adverse effects, such as hypo- or hyperpigmentation, blistering, and crust formation (Fayne et al., 2018). The selection of laser wavelength is critical in reducing this risk, with longer wavelength recommended to minimize the absorption of light in epidermal melanin and thus maximize efficacy and minimize adverse effects in patients with dark skin (Zhang et al., 2016). Side effects from LHR can include the feeling of sunburnt after treatment, as well as inflammation, redness, hyperpigmentation, and swelling. Flashing lights have been known to induce seizures in susceptible patients, so patients should be screened for this risk. Pain and discomfort during the procedure can also represent a significant barrier, and PCPs should be prepared to prescribe topical or systemic analgesics, such as a eutectic mixture of local anesthetics (EMLA) or a low dose systemic opioid. For genital GAS, some have recommended a 3-month wait after the last planned hair removal treatment before proceeding with surgery to confirm that no further hair regrowth will occur (Zhang et al., 2016).

CHAPTER 16 Reproductive Health

All humans, including transgender individuals, have the reproductive right to decide whether or not to have children (United Nations Population Fund, 2014). Medically necessary gender-affirming hormonal treatments (GAHTs) and surgical interventions (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1) that alter reproductive anatomy or function may limit future reproductive options to varying degrees (Hembree et al., 2017; Nahata et al., 2019). It is thus critical to discuss infertility risk and fertility preservation (FP) options with transgender individuals and their families prior to initiating any of these treatments and to continue these conversations on an ongoing basis thereafter (Hembree et al., 2017). Established FP options, such as embryo, oocyte, and sperm cryopreservation, may be available for postpubertal transgender individuals (Nahata et al., 2019). Research protocols for ovarian and testicular tissue cryopreservation have also been developed and studied (Borgström et al., 2020; Nahata et al., 2019; Rodriguez-Wallberg, et al., 2019). Whereas the use of embryos, mature oocytes, and sperm have all proven to be efficacious when employed within clinical treatments, cryopreserved gonadal tissues would require either future retransplantation aimed at obtaining fully functional gametes or the application of laboratory methods for culture, which are still under development in basic science research settings. Of note, recent American Society for Reproductive Medicine guidelines have lifted the experimental label on ovarian tissue cryopreservation, but evidence remains limited in prepubertal children (Practice Committee of the American Society for Reproductive Medicine, 2019).

Individualized care should be provided in the context of each person's parenthood goals. Some research suggests transgender and gender diverse (TGD) people may be less likely to desire genetically related children or children at all when compared with cisgender peers (Defreyne, van Schuvlenbergh et al., 2020; Russell et al., 2016; von Doussa et al., 2015). Yet, several other studies have shown many TGD individuals 1) desire genetically related children; 2) regret missed opportunities for FP; and 3) are willing to delay or interrupt hormone therapy to preserve fertility and/or conceive (Armuand, Dhejne et al., 2017; Auer et al., 2018; De Sutter et al., 2002; Defreyne, van Schuylenbergh et al., 2020; Tornello & Bos, 2017).

Many barriers to FP have been reported, such as cost (which is exacerbated when insurance coverage is lacking), urgency to start treatment, inability to make future-oriented decisions, inadequate provider knowledge/provider biases that affect offering FP, and difficulties accessing FP (Baram et al., 2019; Defreyne, van Schuylenbergh et al., 2020). Additionally, transgender individuals may have worsening dysphoria due to various steps in the FP process that are inseparably connected with the gender assigned at birth (Armuand, Dhejne, et al., 2017; Baram et al., 2019). When available, a multidisciplinary team approach, where both medical and mental health providers collaborate with gender-affirming fertility specialists, can help overcome some of these barriers (Tishelman et al., 2019). TGD individuals should be educated about the distinction between fertility (utilizing one's own gametes/reproductive tissues) and pregnancy. In addition to fertility considerations, efforts to ensure equitable high-quality care for all forms of family planning and building throughout the full reproductive continuum must be maintained. This includes procreative options such as perinatal care, pregnancy, delivery, and postpartum care, as well as family planning and contraceptive options to prevent unplanned pregnancies, and pregnancy termination if sanctioned (Bonnington et al., 2020; Cipres et al., 2017; Krempasky et al., 2020; Light et al., 2018; Moseson, Fix et al., 2020). TGD people who wish to carry a pregnancy should undergo standard of care preconception care and prenatal counseling and should receive counseling about breast/chest feeding in environments supportive of people with diverse gender identities and experiences (MacDonald et al., 2016; Obedin-Maliver & Makadon, 2016).

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and

Statements of Recommendations

16.1- We recommend health care professionals who are treating transgender and gender diverse people and prescribing or referring patients for hormone therapies/surgeries advise their patients about:
16.1.a- Known effects of hormone therapies/surgery on future fertility;
16.1.b- Potential effects of therapies that are not well studied and are of unknown reversibility;
16.1.c- Fertility preservation (FP) options (both established and experimental);
16.1.d- Psychosocial implications of infertility.
16.2- We recommend health care professionals refer transgender and gender diverse people interested in fertility preservation to providers with expertise in fertility preservation for further discussion.
16.3- We recommend transgender care teams partner with local reproductive specialists and facilities to provide specific and timely information and fertility preservation services prior to offering medical and surgical interventions that may impact fertility.
16.4- We recommend health care professionals counsel pre- or early-pubertal transgender and gender diverse youth seeking gender-affirming therapy and their families that currently evidence-based/established fertility preservation options are limited.
16.5- We recommend transgender and gender diverse people with a uterus who wish to carry a pregnancy undergo preconception care, prenatal counseling regarding use and cessation of gender-affirming hormones, pregnancy care, labor and delivery, chest/breast feeding supportive services, and postpartum support according to local standards of care in a gender-affirming way.
16.6. We recommend medical providers discuss contraception methods with transgender and gender diverse people who engage in sexual activity that can result in pregnancy.
16.7. We recommend providers who offer pregnancy termination services ensure procedural options are gender-affirming and serve transgender people and those of diverse genders.

harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 16.1

We recommend health care professionals who are treating transgender and gender diverse people and prescribing or referring patients for hormone therapies/surgeries advise their patients about:

a. **Known effects of hormone therapies/surgeries on future fertility;**
b. **Potential effects of therapies that are not well studied and are of unknown reversibility;**
c. **Fertility preservation (FP) options (both established and experimental;**
d. **Psychosocial implications of infertility.**

TGD individuals assigned female at birth

GAHT may negatively impact future reproductive capacity (Hembree et al., 2017). Based on current evidence in transgender men and gender diverse people assigned female at birth, these risks are as follows:

Gonadotropin-releasing hormone agonists (GnRHas) may be used for pubertal suppression to prevent further pubertal progression until adolescents are ready for masculinizing treatment. GnRHas may also be used for menstrual suppression. GnRHas impact the maturation of gametes but do not cause permanent damage to gonadal function. Thus, if GnRHas are discontinued, oocyte maturation would be expected to resume.

There are few studies detailing the effects of testosterone therapy on reproductive function in transgender men (Moravek et al., 2020). Restoration of normal ovarian function with oocyte maturation after testosterone interruption has been demonstrated in transgender men who have achieved natural conception. A retrospective study on oocyte cryopreservation showed no differences in the total number of oocytes retrieved or in the number of mature oocytes between transgender men and age- and BMI-matched cisgender women (Adeleye et al., 2018, 2019). The first results have recently been published evaluating live birth rates after controlled ovarian stimulation in transgender men compared with cisgender women (Leung et al., 2019). Testosterone was discontinued prior to ovarian stimulation. Overall, the results concerning the influence of testosterone on reproductive organs and their function appear to be reassuring. However, there have been no prospective studies to date evaluating the effect of long-term hormone therapy on fertility (i.e., started in adolescence) or in those treated with GnRHas in early puberty followed by testosterone therapy. It is important to take into consideration that required medications and procedures for cryopreserving oocytes (a

pelvic examination, vaginal ultrasound monitoring, and oocyte retrievals) may lead to increasing gender dysphoria in transgender men (Armuand, Dhejne et al., 2017).

Surgical interventions among transgender men will have obvious implications for reproductive capacity. If patients desire a hysterectomy, the option should be offered of preserving the ovaries to retain the possibility of having a genetically related child. Alternatively, if the ovaries are removed either separately or concurrently with the hysterectomy, egg freezing should be offered prior to surgery and/or ovarian tissue cryopreservation can be done at the time of oophorectomy. Although this procedure is no longer considered experimental, many transgender men may desire *in vitro* maturation of primordial follicles, which is still investigational. Studies evaluating oocyte function have shown oocytes isolated from transgender men with testosterone exposure at the time of oophorectomy can be matured *in vitro* to develop normal metaphase II meiotic spindle structure (De Roo et al., 2017; Lierman et al., 2017).

TGD individuals assigned male at birth

Based on current evidence in transgender women and gender diverse people assigned male at birth (AMAB), the influence of medical treatment is as follows:

GnRHas inhibit spermatogenesis. Data suggest discontinuation of treatment results in a re-initiation of spermatogenesis, although this may take at least 3 months and most likely longer (Bertelloni et al., 2000). Furthermore, the psychological burden of re-exposure to testosterone should be considered.

Anti-androgens and estrogens result in an impaired sperm production (de Nie et al., 2020; Jindarak et al., 2018; Kent et al., 2018). Spermatogenesis might resume after discontinuation of prolonged treatment with anti-androgens and estrogens, but data are limited (Adeleye et al., 2019; Alford et al., 2020; Schneider et al., 2017). Testicular volumes diminish under the influence of gender-affirming hormone treatment (Matoso et al., 2018). Semen quality in transgender women may also be negatively affected by specific life-style factors, such as a low frequency of masturbation, wearing the genitals tight against the body (e.g., with use of tight undergarments for tucking) (Jung & Schuppe, 2007; Mieusset et al., 1985, 1987; Rodriguez-Wallberg, Häljestig et al., 2021).

Statement 16.2

We recommend health care professionals refer transgender and gender diverse people interested in fertility preservation to providers with expertise in fertility preservation for further discussion.

Research shows many transgender adults desire biological children (De Sutter et al., 2002; Defreyne, van Schuylenbergh et al., 2020; Wierckx, Van Caenegem et al., 2012), yet FP rates remain widely variable, particularly in youth (< 5%–40%) (Brik et al., 2019; Chen et al., 2017; Chiniara et al., 2019; Nahata et al., 2017; Segev-Becker et al., 2020). In a recent survey, many youth acknowledged their feelings about having a biological child might change in the future (Strang, Jarin et al., 2018). Non-elective sterilization is a violation of human rights (Ethics Committee of the American Society for Reproductive Medicine, 2015; Equality and Human Rights Commission, 2021; Meyer III et al., 2001) and due to advances in social attitudes, fertility medicine, and affirmative transgender health care, opportunities for biological parenthood during transition should be supported for transgender people. Due to the influence clinical opinion may have on transgender or nonbinary people's FP and on parenting decisions, FP options should be explored by health care providers alongside options such as fostering, adoption, coparenting, and other parenting alternatives (Bartholomaeus & Riggs, 2019). Transgender patients who have been offered this type of discussion and have been given the choice to undergo procedures for FP have reported the experience to be an overall positive one (Armuand, Dhejne et al., 2017; De Sutter et al., 2002; James-Abra et al., 2015).

In other patient populations, fertility referrals and formal fertility programs have been shown to increase FP rates and improve patient satisfaction (Kelvin et al., 2016; Klosky, Anderson et al., 2017; Klosky, Wang et al., 2017;

Shnorhavorian et al., 2012) Physician attitudes have been investigated, and recent studies indicate both an awareness and a desire to provide fertility-related information to children and their families (Armuand et al., 2020). However, barriers have also been identified, including lack of knowledge, comfort, and resources (Armuand, Nilsson et al., 2017; Frederick et al., 2018). Thus, the need for appropriate training of health care providers has been highlighted, with emphasis placed on fertility counseling and offering FP options to all at-risk individuals in an unbiased way (Armuand, Nilsson et al., 2017). Parents' recommendations have also been shown to significantly influence FP rates in adolescent and young adult males with cancer (Klosky, Flynn et al., 2017). While there are clear clinical differences in these populations, these findings can help inform best practices for fertility counseling and FP referrals for transgender individuals.

Statement 16.3

We recommend transgender care teams partner with local reproductive specialists and facilities to provide specific and timely information and fertility preservation services prior to offering medical and surgical interventions that may impact fertility.

Cryopreservation of sperm and oocytes are established FP techniques and can be offered to pubertal, late pubertal, and adult birth assigned males and birth assigned females, respectively, preferably prior to the initiation of GAHT (Hembree et al., 2017; Practice Committee of the American Society for Reproductive Medicine, 2019). Cryopreservation of embryos can be offered to adult (post-pubertal) TGD people who wish to have a child and have an available partner. The future use of cryopreserved gametes is also dependent on the gametes and reproductive organs of the future partner (Fischer, 2021; Maxwell et al., 2017)

Although semen parameters have been shown to be compromised when FP is performed after initiation of GAH medication (Adeleye et al., 2019), one small study showed when the treatment was discontinued, semen parameters were comparable to those in TGD patients who had never undergone GAH treatment. With regard to ovarian stimulation, oocyte vitrification yield and subsequent use of the oocytes in in-vitro fertilization (IVF), there is no reason to anticipate a different outcome in assisted reproductive technology (ART) treatments for TGD patients than that obtained in cisgender patients undergoing ART—other than individual confounding factors related to (in)fertility—when gametes are banked prior to any medical treatment (Adeleye et al., 2019). The use of oocytes in ART treatment resulted in similarly successful outcomes in TGD compared with controlled, matched cisgender patients (Adeleye et al., 2019; Leung et al., 2019; Maxwell et al., 2017).

Although these are established options, few pubertal, late pubertal or adult TGD people undergo FP (Nahata et al., 2017), and many experience challenges while undergoing FP interventions. Not only is access and cost of these methods a barrier (particularly in regions without insurance coverage), but these procedures are often physically and emotionally uncomfortable, and many express concerns about postponing the transitioning process (Chen et al., 2017; De Sutter et al., 2002; Nahata et al., 2017; Wierckx, Stuyver et al., 2012). Especially for the birth assigned females, the invasiveness of endovaginal ultrasound follow-up of the ovarian stimulation and oocyte retrieval procedures (and associated psychological distress) have been cited as a barrier (Armuand, Dhejne et al., 2017; Chen et al., 2017). There is also the concern young adults going through transitioning may not have a clear vision of parenting and are therefore likely to decline the opportunity to use FP at that time—while as adults, they may have different opinions about parenthood (Cauffman & Steinberg, 2000). The reduction of gender dysphoria during transitioning could also influence the decision-making process surrounding FP (Nahata et al., 2017). Based on research showing TGD youths' fertility perspectives may change over time (Nahata et al., 2019; Strang, Jarin et al., 2018), FP options should be discussed on an ongoing basis.

Statement 16.4

We recommend health care professionals counsel pre- or early-pubertal transgender and

gender diverse youth seeking gender-affirming therapy and their families that currently evidence-based/established fertility preservation options are limited.

For prepubertal and early-pubertal children, FP options are limited to the storage of gonadal tissue. Although this option is available for TGD children in the same way that it is available for cisgender prepubertal and early-pubertal oncological patients, there is no literature describing the utilization of this approach in the transgender population. Ovarian tissue autotransplantation has resulted in over 130 live births in cisgender women. Most of these patients conceived naturally without ART (Donnez & Dolmans, 2015; Jadoul et al., 2017), and the majority stored their ovarian tissue either as adults or during puberty. Although the recent American Society for Reproductive Medicine guideline has lifted the experimental label from ovarian tissue cryopreservation (Practice Committee of the American Society for Reproductive Medicine, 2019), there are very few case reports describing a successful pregnancy in a woman following the transplantation of ovarian tissue cryopreserved before puberty. Demeestere et al. (2015) and Rodriguez-Wallberg, Milenkovic et al. (2021) described cases of successful pregnancies following transplantation of tissue procured at the age of 14, and recently Matthews et al. (2018) described the case of a girl diagnosed with thalassemia who had ovarian tissue stored at the age of 9 and transplantation 14 years late. She subsequently conceived through IVF and delivered a healthy baby.

Currently, the only future clinical application for storing ovarian tissue is autotransplantation, which might be undesirable in a transgender man (due to the potentially undesirable effects of estrogen). A laboratory procedure that would make it possible to mature oocytes *in vitro* starting with ovarian tissue would be the ideal future application of stored ovarian tissue for transgender people, but this technique is currently only being investigated and optimized in basic science research settings (Ladanyi et al., 2017; Oktay et al., 2010).

Prepubertal procurement of testicular tissue has been documented as a low-risk procedure (Borgström et al., 2020; Ming et al., 2018). Some authors have also described this approach as a theoretical option in transgender people (De Roo et al., 2016; Martinez et al., 2017; Nahata, Curci et al., 2018). However, there are no reports in the literature describing the clinical or investigational utilization of this FP option for TGD patients. Moreover, the viability of the clinical application of autotransplantation of testicular tissue remains unknown in humans, and *in vitro* maturation techniques are still in the realm of basic science research. Thus, specialists currently consider this technique experimental (Picton et al., 2015). The possibility of storing gonadal tissue should be discussed prior to any genital surgery that would result in sterilization, although the probability of being able to use this tissue must be clearly addressed.

Statement 16.5

We recommend transgender and gender diverse people with a uterus who wish to carry a pregnancy undergo preconception care and prenatal counseling regarding the use and cessation of gender-affirming hormones, pregnancy care, labor and delivery, chest/breast feeding supportive services, and postpartum support according to local standards of care in a gender-affirming way.

Most transgender men and gender diverse people (AFAB) retain their uterus and ovaries and thus can conceive and carry a pregnancy even after long-term testosterone use (Light et al., 2014). Many transgender men desire children (Light et al., 2018; Wierckx, van Caenegem et al., 2012) and are willing to carry a pregnancy (Moseson, Fix, Hastings et al., 2021; Moseson, Fix, Ragosta et al., 2021). ART has expanded the opportunity for many transgender men to conceive and fulfill their family planning wishes (De Roo et al., 2017; Ellis et al., 2015; Maxwell et al., 2017). Some transgender men report psychological isolation, dysphoria related to the gravid uterus and chest changes, and depression (Charter, 2018; Ellis et al., 2015; Hoffkling et al., 2017; Obedin-Maliver & Makadon, 2016). Conversely, other studies have reported some positive experiences during pregnancy as well (Fischer, 2021; Light et al., 2014). Mental health providers should be involved to provide support, and counseling should be

provided addressing when to stop and when to resume gender-affirming hormones, what options are available for the mode of delivery and for chest/breast feeding (Hoffkling et al., 2017). Finally, system-level and interpersonal-level interventions should be implemented to ensure person-centered reproductive health care for all people (Hahn et al., 2019; Hoffkling et al., 2017; Moseson, Zazanis et al., 2020; Snowden et al., 2018).

Given the potential harmful effects of testosterone on the developing embryo, discontinuing testosterone or masculinizing hormone therapy prior to conception and during the entire pregnancy is recommended. However, the optimal time for both the discontinuation of testosterone prior to pregnancy and its resumption after pregnancy is unknown. Since stopping gender-affirming hormones may cause distress and exacerbate dysphoria in transgender men, when and how to stop this therapy should be discussed during prenatal counseling (Hahn et al., 2019). Because information about the duration of testosterone exposure and the risk of teratogenicity is lacking, testosterone use should be discontinued prior to attempting pregnancy and before stopping contraception. Moreover, there is limited information regarding health outcomes of infants born to transgender men. Small case series attempting to evaluate this question have revealed no adverse physical or psychosocial differences between infants born to transgender men and infants in the general population (Chiland et al., 2013).

Chest/Breast feeding

In the limited studies evaluating lactation and chest/breast feeding, the majority of transgender men and TGD individuals AFAB who chose to chest/breast feed postpartum were successful, with research suggesting induction of lactation is in part dependent on preconception counseling and experienced lactation nursing support (MacDonald et al., 2016; Wolfe-Roubatis & Spatz, 2015). Specifically, transgender men and TGD people who use testosterone should be informed 1) although quantities are small, testosterone does pass through chest/breast milk; and 2) the impact on the developing neonate/child is unknown, and therefore gender-affirming testosterone use is not recommended during lactation but may be resumed after discontinuation of chest/breast feeding (Glaser et al., 2009). Transgender men and other TGD individuals AFAB should be made aware some patients who carry a pregnancy may experience undesired chest growth and/or lactation even after chest reconstruction and should therefore be supported if they desire to suppress lactation (MacDonald et al., 2016).

There is limited information concerning lactation in transgender women as well as other TGD AMAB but many also express the desire to chest/breast feed. While there is a case report of a transgender woman successfully lactating and chest/breast feeding her infant after hormonal support using a combination of estrogen, progesterone, domperidone, and breast pumping (Reisman & Goldstein, 2018), the nutritional and immunological profile of chest/breast milk under these conditions has not been studied. Therefore, patients need to be informed about the risks and benefits of this approach to child feeding (Reisman & Goldstein, 2018).

Statement 16.6

We recommend medical providers discuss contraception methods with transgender and gender diverse people who engage in sexual activity that can result in pregnancy.

Many TGD individuals may retain reproductive capacity, and they (if they retain a uterus, ovaries, and tubes) or their sexual partners (for sperm producing individuals) may experience unplanned pregnancies (James et al., 2016; Light et al., 2014; Moseson, Fix et al., 2020). Therefore, intentional family planning counseling, including contraception and abortion conducted in gender-expansive ways is needed (Klein, Berry-Bibee et al., 2018; Obedin-Maliver, 2015; Stroumsa & Wu, 2018). TGD people AFAB may not use contraception due to an erroneous assumption that testosterone is a reliable form of contraception (Abern & Maguire, 2018; Ingraham et al., 2018; Jones, Wood et al., 2017; Potter et al., 2015). However, based on current understanding, testosterone should not be considered a reliable form of contraception because of its incomplete suppression of the hypothalamic-pituitary-adrenal axis (Krempasky et al., 2020). Furthermore, pregnancies have occurred while individuals are amenorrheic due

to testosterone use, which may outlast active periods of administration (Light et al., 2014). Pregnancy can also occur in TGD people after long-term testosterone use (at least up to 10 years), although the effect on oocytes and baseline fertility is still unknown (Light et al., 2014).

TGD people AFAB may use a variety of contraceptive methods (Abern & Maguire, 2018; Bentsianov et al., 2018; Bonnington et al., 2020; Chrisler et al., 2016; Cipres et al., 2017; Jones, Wood et al., 2017; Krempasky et al., 2020; Light et al., 2018).These methods may be used explicitly for pregnancy prevention, menstrual suppression, abnormal bleeding, or other gynecological needs (Bonnington et al., 2020; Chrisler et al., 2016; Krempasky et al., 2020; Schwartz et al., 2019). Contraceptive research gaps within this population are profound. No studies have examined how the use of exogenous androgens (e.g., testosterone) may modify the efficacy or safety profile of hormonal contraceptive methods (e.g., combined estrogen and progestin hormonal contraceptives, progestin-only based contraceptives) or non-hormonal and barrier contraceptive methods (e.g., internal and external condoms, non-hormonal intrauterine devices, diaphragms, sponges, etc.).

Gender diverse individuals who currently have a penis and testicles may engage in sexual activity with individuals who have a uterus, ovaries, and tubes of any gender. Gender diverse people who have a penis and testicles can produce sperm even while on gender-affirming hormones (i.e., estrogen), and although semen parameters are diminished among those who are currently using or who have previously used gender-affirming hormones, azoospermia is not complete and sperm activity is not totally suppressed (Adeleye et al., 2019; Jindarak et al., 2018; Kent et al., 2018). Therefore, contraception needs to be considered if pregnancy is to be avoided in penis-in-vagina sexual activity between a person with a uterus, ovaries, and tubes and one with a penis and testicles, irrespective of the use of gender-affirming hormones by either partner. Currently, contraceptive methods available for use by the sperm-producing partner are primarily mechanical barriers (i.e., external condoms, internal condoms), permanent sterilization (i.e., vasectomy), and gender-affirming surgery (e.g., orchiectomy, which also results in sterilization). Contraceptive counseling that considers sperm producing, egg producing, and gestating partners (as relevant) is recommended.

Statement 16.7

We recommend providers who offer pregnancy termination services ensure procedural approaches are gender-affirming and serve transgender people and those of diverse genders.

Unplanned pregnancies and abortions have been reported among TGD individuals with a uterus (Abern & Maguire, 2018; Light et al., 2014; Light et al., 2018; Moseson, Fix et al., 2020) and documented through surveys of abortion-providing facilities (Jones et al., 2020). However, the population-based epidemiology of abortion provision and the experiences and preferences of TGD individuals AFAB undergoing abortion still represents a critical gap in research (Fix et al., 2020; Moseson, Fix et al., 2020; Moseson, Lunn et al., 2020). Nonetheless, given that pregnancy capacity exists among many TGD people and pregnancies may not always be planned or desired, access to safe, legal, and gender-affirming pregnancy medical and surgical termination services is necessary.

CHAPTER 17 Sexual Health

Sexual health has a profound impact on physical and psychological well-being, regardless of one's sex, gender, or sexual orientation. However, stigma about sex, gender and sexual orientation influences individual's opportunities to live out their sexuality and to receive appropriate sexual health care. Specifically, in most societies, cisnormativity and heteronormativity lead to the assumption that all people are cisgender and heterosexual (Bauer et al., 2009), and that this combination is superior to all other genders and sexual orientations (Nieder, Güldenring et al., 2020; Rider, Vencill et al., 2019). Hetero-cisnormativity negates the complexity of gender, sexual orientation, and sexuality and disregards diversity and fluidity. This is all the more important since sexual identities, orientations, and practices of transgender and gender diverse (TGD) people are characterized by an enormous diversity (Galupo et al., 2016; Jessen et al., 2021; Thurston & Allan, 2018; T'Sjoen et al., 2020). Likewise, a strong cross-cultural tendency toward allonormativity—the assumption that all people experience sexual attraction or interest in sexual activity—negates the diverse experiences of TGD people, especially those who locate themselves on the asexual spectrum (McInroy et al., 2021; Mollet, 2021; Rothblum et al., 2020).

The World Health Organization (WHO, 2010) emphasizes sexual health depends on respect for the sexual rights of all people, including the right to express diverse sexualities and to be treated respectfully, safely, and with freedom from discrimination and violence. Sexual health discourses have focused on agency and body autonomy, which include consent, sexual pleasure, sexual satisfaction, partnerships, and family life (Cornwall & Jolly, 2006; Lindley et al., 2021). In light of this, the WHO defines sexual health as "a state of physical, emotional, mental, and social well-being in relation to sexuality and not merely the absence of disease, dysfunction, or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination, and violence. For sexual health to be attained and maintained, the sexual rights of all persons must be respected, protected, and fulfilled" (WHO, 2006, p. 5). This includes individuals on the asexual spectrum, who may not experience sexual attraction to others but may still choose to be sexual at times (e.g., via self-stimulation) and/or experience interest in forming and building romantic relationships (de Oliveira et al., 2021).

Scientific attention to the sexual experiences and behaviors of TGD people has grown in recent years (Gieles et al., 2022; Holmberg et al., 2019; Klein & Gorzalka, 2009; Kloer et al., 2021; Mattawanon et al., 2021; Stephenson et al., 2017; Tirapegui et al., 2020; Thurston & Allan, 2018). This expansion within the literature reflects a sex-positive framework (Harden, 2014), a framework that recognizes both the positive aspects such as sexual pleasure (Laan et al., 2021) and potential risks associated with sexuality (Goldhammer et al., 2022; Mujugira et al., 2021). Studies of TGD people's sexuality, however, often lack validated measures, an appropriate control group, or a prospective design (Holmberg et al., 2019). Additionally, most focus exclusively on sexual functioning (Kennis et al., 2022), and thus neglecting sexual satisfaction and broader operationalizations of sexual pleasure beyond functioning. The effects of current TGD-related medical treatments on sexuality are heterogeneous (Özer et al., 2022; T'Sjoen et al., 2020), and there has been little research on the sexuality of TGD adolescents (Bungener et al., 2017; Maheux et al., 2021; Ristori et al., 2021; Stübler & Becker-Hebly, 2019; Warwick et al., 2022). While sex-positive approaches to counseling and treatment for sexual difficulties experienced by TGD individuals have been proposed (Fielding, 2021; Jacobson et al., 2019; Richards, 2021), to date there is insufficient research on the effectiveness of such interventions. Focusing on the promotion of sexual health, the World Association for Sexual Health (WAS) asserts the importance of sexual pleasure and considers self-determination, consent, safety, privacy, confidence, and the ability to communicate and negotiate sexual relations as major facilitators (Kismödi et al., 2017). WAS asserts sexual pleasure is integral to sexual rights and human rights (Kismödi et al., 2017). To contribute to

Statements of Recommendations

17.1- We recommend health care professionals who provide care to transgender and gender diverse people acquire the knowledge and skills needed to address sexual health issues (relevant to their care provision).
17.2- We recommend health care professionals who provide care to transgender and gender diverse people discuss the impact of gender-affirming treatments on sexual function, pleasure, and satisfaction.
17.3- We recommend health care professionals who provide care to transgender and gender diverse people offer the possibility of including the partner(s) in sexuality-related care, if appropriate.
17.4- We recommend health care professionals counsel transgender and gender diverse people about the potential impact of stigma and trauma on sexual risk behavior, sexual avoidance, and sexual functioning.
17.5- We recommend any health care professional who offers care that may impact sexual health provide information, ask about the expectations of the transgender and gender diverse individual and assess their level of understanding of possible changes.
17.6.-We recommend health care professionals who provide care to transgender and gender diverse people counsel adolescents and adults regarding prevention of sexually transmitted infections.
17.7- We recommend health care professionals who provide care to transgender and gender diverse people follow local and World Health Organization guidelines for human immunodeficiency virus/sexual transmitted infections (HIV/STIs) screening, prevention, and treatment.
17.8- We recommend health care professionals who provide care to transgender and gender diverse people address concerns about potential interactions between antiretroviral medications and hormones.

the sexual health of TGD people, health care professionals (HCPs) need both transgender-related expertise and sensitivity (Nieder, Güldenring et al., 2020). With the goal of improving sexual health care for TGD people to an ethically-sound, evidence-based and high-quality level, HCPs must provide their health services with the same care (i.e., with transgender-related expertise), respect (i.e., with transgender-related sensitivity), and investment in sexual pleasure and sexual satisfaction as they provide for cisgender people (Holmberg et al., 2019).

In many societies, nonconforming gender expressions can elicit strong (emotional) reactions, including in HCPs. Thus, when initiating a health-related contact or establishing a therapeutic relationship, a nonjudgmental, open and welcoming manner is most likely ensured when HCPs reflect on their emotional, cognitive, and interactional reactions to the person (Nieder, Güldenring et al., 2020). In addition, transgender-related expertise refers to identifying the impact the TGD person's intersectional identities and experiences of marginalization and stigma may have had on their whole self (Rider, Vencill et al., 2019). To adequately address the specific physical, psychological, and social conditions of TGD people, HCPs must be aware these conditions are generally overlooked due to hetero-cis-normativity, lack of knowledge, and lack of skills (Rees et al., 2021). It is also important to consider cultural norms in relation to sexuality. For example, in some African cultures, the idea of sex as taboo restricts the number of acceptable terms to be used when taking a sexual history (Netshandama et al., 2017). Culturally respectful language can facilitate talking openly about one's sexual history and reduce ambiguity or shame (Duby et al., 2016). In addition, HCPs must be sensitive to the history of (mis)use of sexual identity and orientation as a gatekeeping function to exclude transgender people from gender-affirming health care (Nieder & Richter-Appelt, 2011; Richards et al., 2014). The following recommendations aim to improve sexual health care for TGD people.

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 17.1

We recommend health care professionals who provide care to transgender and gender diverse people acquire the knowledge and skills to address sexual health issues (relevant to their care provision).

It is important HCPs addressing the sexual health of TGD people be familiar with commonly used terminology (see Chapter 1—Terminology) and invite those seeking care to explain terms with which the provider may not be familiar. In this context, it is also important HCPs (are

prepared to) take a sexual history and offer treatment (according to their competencies) in a gender-affirming way with a sex-positive approach (Centers for Disease Control, 2020; Tomson et al., 2021). However, HCP's should apply greater importance to the terminology that the TGD person uses for their own body over more traditionally accepted or used medical terminology (Wesp, 2016). When talking about sexual practices, it is advisable to focus on body parts (e.g., "Do you have sex with people with a penis, people with a vagina, or both?"; ACON, 2022) and what role they play in their sexuality (e.g., "During Sex, do any parts of your body enter your partners body, such as their genitals, anus, or mouth?"; ACON, 2022).

Statement 17.2

We recommend health care professionals who provide care to transgender and gender diverse people discuss the impact of gender-affirming treatments on sexual function, pleasure, and satisfaction.

To achieve gender-affirming care, it is crucial HCPs providing transition-related medical interventions be sufficiently informed about the possible effects on sexual function, pleasure, and satisfaction (T'Sjoen et al., 2020). Since clinical data indicate that TGD people score significantly lower in sexual pleasure compared to cisgender individuals, this is even more important (Gieles et al., 2022). If the HCP cannot provide information about the effects of their treatment on sexual function, pleasure, and satisfaction, they are at least expected to refer the individual to someone qualified to do so. If the sexuality-related effects of their treatment are unknown, HCPs should inform their patients accordingly. As introduced above, the sexuality of TGD people often challenges heteronormative views. Nevertheless, there is a large amount of literature (e.g., Bauer, 2018; Laube et al., 2020; Hamm & Nieder, 2021; Stephenson et al., 2017) highlighting the spectrum character of sexuality that does not fit into expectations of what male and female sexuality entails (neither cis- nor transgender), let alone that of gender diverse people (e.g., nonbinary, agender, genderqueer). Thus, these aspects should be carefully considered by HCPs as cisnormativity, heteronormativity, and transition-related medical interventions, all have a strong impact on sexual health.

Sexual pleasure has been well documented as a factor in improving sexual, mental, and physical health outcomes (Anderson, 2013). Next to sexual function, HCPs providing sexual health care must address sexual pleasure and satisfaction as a key factor within sexual health. Historically sexual health care has been disease focused, and this is particularly true for research and clinical practice in working with TGD patients. Although competent sexual health care regarding HIV and STIs is necessary, integration of valuing sexual pleasure of TGD patients is also necessary. Calls for integrating sexual pleasure as a focal point in STI prevention education and interventions rest on the understanding that pleasure is a motivator of behavior (Philpott et al., 2006). TGD people are concerned about their sexual pleasure and need HCPs who are knowledgeable about the diversity of sexual practices and anatomical functioning particular to TGD health care.

Statement 17.3

We recommend health care professionals who provide care to transgender and gender diverse people offer the possibility of including the partner(s) in sexuality-related care, if appropriate.

When appropriate and relevant to clinical concerns, inclusion of a sexual and/or romantic partner(s) in sexual health care decision-making can increase TGD patients' sexual well-being and satisfaction outcomes (Kleinplatz, 2012). TGD people may choose a range of transition-related medical interventions, and these interventions may have mixed results in shifting experiences of anatomical dysphoria (Bauer & Hammond, 2015). When discussing the impact of medical interventions on sexual functioning, pleasure, and satisfaction, inclusion of partner(s) can increase knowledge of potential changes and encourage communication between partners (Dierckx et al., 2019). Because the process of transitioning is often not a completely solitary endeavor, the inclusion of sexual and/or romantic partners in transition-related health care can facilitate the process of "co-transitioning" (Lindley et al., 2020;

Siboni et al., 2022; Theron & Collier, 2013) and can also support sexual growth and adjustment both in the individual as well as in the relationship. Social and psychological barriers to sexual functioning and pleasure, including experiences of gender dysphoria, stigmatization, lack of sexual and relationship role models, and limited skills, can have negative impacts on overall sexual health (Kerckhof et al., 2019). Supportive, gender-affirming sexual communication between partners improves sexual satisfaction outcomes for TGD people (Stephenson et al., 2017; Wierckx, Elaut et al., 2011).

Inclusion of sexual and/or romantic partners offers an additional opportunity to set realistic expectations, disseminate helpful and accurate information, and facilitate gender-affirming positive communication related to sexual health. Ultimately, however, it is important to recognize individual choices related to gender health and transition are the patients to make, not a partner's decision. It is important the inclusion of partners in sexual health-related care occur only when appropriate and as desired by patients. Contraindications might include interpersonal dynamics that are abusive or violent, in which case patient safety overrides partner involvement. Finally, it is critical HCPs treat all people in an affirming and inclusive manner, including sexual and romantic partners. This means, for example, monitoring and addressing assumptions and potential biases about the gender or sexual orientation of a patient's partner(s) or a patient's relationship structure.

Statement 17.4

We recommend health care professionals counsel transgender and gender diverse people about the potential impact of stigma and trauma on sexual risk behavior, sexual avoidance, and sexual functioning.

The TGD community is disproportionately impacted by stigma, discrimination, and violence (de Vries et al., 2020; European Union Agency for Fundamental Rights, 2020; McLachlan, 2019). These experiences are often traumatic in nature (Burnes et al., 2016; Mizock & Lewis, 2008) and can create barriers to sexual health, functioning, and pleasure (Bauer & Hammond, 2015). For example, stigmatizing narratives about transgender sexualities can increase dysphoria and sexual shame, increasing potential avoidance of the sexual communication needed for safety and optimizing pleasure (Stephenson et al., 2017). Research demonstrates stigma, a history of sexual violence, and body image concerns can negatively impact sexual self-esteem and agency, for example the ability to assert what is pleasurable or to negotiate condom use (Clements-Nolle et al., 2008; Dharma et al., 2019). Additionally, gender dysphoria can be exacerbated by past trauma experiences and ongoing trauma-related symptoms (Giovanardi et al., 2018). It may be difficult for some TGD individuals to engage sexually using the genitals with which they were born, and they may choose to avoid such stimulation altogether, disrupting arousal and/or orgasmic processes (Anzani et al., 2021; Bauer & Hammond, 2015; Iantaffi & Bockting, 2011) or result in complex feelings about orgasm (Chadwick et al., 2019). HCPs providing gender-affirming counseling and interventions must be knowledgeable about the spectrum of sexual orientations and identities (including asexual identities and practices) to avoid assumptions based in heteronormative, cisnormative, allonormative modes of behavior or satisfaction while also affirming the potential impacts of stigma and trauma on sexual health and pleasure (Nieder, Güldenring et al., 2020). Some level of disconnect or dissociation may at times be present, particularly in the case of acute trauma symptoms (Colizzi et al., 2015). It is important HCPs be aware of these potential impacts on sexual health, functioning, pleasure, and satisfaction, so they may refer patients as needed to trauma-informed sexual counselors, mental health providers, or both, who may be of further assistance and may also normalize and validate TGD patients exploring multiple diverse pathways of healing and accessing sexual pleasure.

Statement 17.5

We recommend any health care professional who offers care that may impact sexual health provide information, ask about the expectation of the transgender and gender diverse individual, and assess their level of understanding of possible changes.

Transition-related care can affect sexual function, pleasure, and satisfaction, both in positive and negative ways (Holmberg et al., 2018; Kerckhof et al., 2019; Thurston & Allan, 2018; Tirapegui et al., 2020). On the positive side, gender-affirming care can help TGD people improve their sexual functioning and increase their sexual pleasure and satisfaction (Kloer et al., 2021; Özer et al., 2022; T'Sjoen et al., 2020). On the negative side, however, data indicate problematic sexual health outcomes due to hormonal and surgical treatments (Holmberg et al., 2018; Kerckhof et al., 2019, Stephenson et al., 2017; Weyers et al., 2009). Transition-related hormones may affect mood, sexual desire, the ability to have an erection and ejaculation, and genital tissue health, which in turn can impact sexual function, pleasure and sexual self-expression (Defreyne, Elaut et al., 2020; Garcia & Zaliznyak, 2020; Kerckhof et al., 2019; Klein & Gorzalka, 2009; Wierckx, Elaut et al., 2014). TGD people who wish to use their original genital anatomy for penetrative sex may benefit from medications that address sexual health side effects of hormone therapy, such as erectile dysfunction, medications for TGD persons taking estrogen or antiandrogens, and topical estrogen and/or moisturizers for TGD persons experiencing vaginal atrophy or dryness due to testosterone therapy.

Sexual desire, arousal, and function may also be affected by the use of psychotropic drugs (Montejo et al., 2015). As some TGD people are prescribed medication to treat depression (Heylens, Elaut et al., 2014), anxiety (Millet et al., 2017) or other mental health concerns (Dhejne et al., 2016), their potential side effects on sexual health should be considered.

Many gender-affirming surgeries can have significant effects on erogenous sensation, sexual desire and arousal as well as sexual function and pleasure. The impact of these changes for patients may be mixed (Holmberg et al., 2018). Chest surgeries (breast reduction, mastectomy, and breast augmentation) and body contouring surgeries, for example, may offer desired changes in form and appearance thereby reducing psychological distress that can disrupt sexual functioning but may adversely affect erogenous sensation (Bekeny et al., 2020; Claes et al., 2018; Rochlin et al., 2020). Genital surgeries in particular can potentially affect sexual function and pleasure in adverse ways, although they are likely to be experienced positively as the patient's body becomes more aligned with their gender, potentially opening new avenues for sexual pleasure and satisfaction (Hess et al., 2018; Holmberg et al., 2018; Kerckhof et al., 2019).

There are numerous examples of this in the extant literature:

- Surgery may result in a decrease, a total loss, or a possible increase in erogenous stimulation and/or experienced sensation compared with the patient's presurgery anatomy (Garcia, 2018; Sigurjónsson et al., 2017).
- A particular surgical option may be associated with specific limitations to sexual function that may manifest immediately, in the future, or at both timepoints, and which patients should consider before finalizing their choice when considering different surgical options (Frey et al., 2016; Garcia, 2018; Isaacson et al., 2017).
- Postsurgical complications can adversely affect sexual function by either decreasing the quality of sexual function (e.g., discomfort or pain with sexual activity) or by precluding satisfactory intercourse (Kerckhof et al., 2019; Schardein et al., 2019).

In general, satisfaction with any medical treatment is heavily influenced by the patient's expectations (Padilla et al., 2019). Furthermore, when patients have unrealistic expectations before treatment, they are much more likely to be dissatisfied with the outcome, their care, and with their HCP (Padilla et al., 2019). Therefore, it is important to both provide patients with adequate information about their treatment options and to understand and consider what is important to the patient with regard to outcomes (Garcia, 2021). Finally, it is important the HCP ensure patients understand the potential adverse effects of a treatment on their sexual function and pleasure so that a well-informed decision can be made. This is relevant for both meeting the standard of informed consent (i.e.,

discussion and understanding) and for providing an opportunity to offer further clarification to patients and, if desired, to their partners (Glaser et al., 2020).

Statement 17.6

We recommend health care professionals who provide care to transgender and gender diverse people counsel adolescents and adults regarding prevention of sexually transmitted infections.

The WHO (2015) recommends HCPs implement brief sexuality-related communication in primary care for all adolescents and adults. Therefore, TGD persons who are sexually active or considering sexual activity may benefit from sexuality-related communication or counseling for the purpose of HIV/STI prevention. These conversations are particularly important as TGD persons are disproportionately impacted by human immunodeficiency virus (HIV) and other sexually transmitted infections (STIs) relative to cisgender persons (Baral et al., 2013; Becasen et al., 2018; Poteat et al., 2016). However, few data are available for non-HIV STIs, such as chlamydia, gonorrhea, syphilis, viral hepatitis, and herpes simplex virus (Tomson et al., 2021). The United Nations Joint Programme on HIV/AIDS estimates transgender women are 12 times more likely than other adults to be living with HIV (UNAIDS, 2019). A meta-analysis estimated a pooled global HIV prevalence of 19% among transgender women who have sex with men (Baral et al., 2013). HIV/STI risk is concentrated among TGD subgroups at the confluence of multiple biological, psychological, interpersonal, and structural vulnerabilities. In particular, transfeminine persons who have sex with cisgender men, belong to minoritized racial/ethnic groups, live in poverty, and engage in survival sex work are at elevated HIV/STI risk (Becasen et al., 2018; Poteat et al., 2015; Poteat et al., 2016). Less is known about HIV/STI risk among transgender men or gender diverse persons AFAB. Small studies in high-income countries indicate a laboratory-confirmed HIV prevalence of 0-4% among transmasculine people (Becasen et al., 2018; Reisner & Murchison, 2016). Almost no research has been conducted with transmasculine people who have sex with cisgender men in high-HIV-prevalence countries. Despite limited epidemiologic data, transmasculine persons who have sex with cisgender men frequently report HIV/STI risk related to receptive vaginal and/or anal sex (Golub et al., 2019; Reisner et al., 2019; Scheim et al., 2017) and may be more susceptible to HIV acquisition from vaginal intercourse than (pre-menopausal) cisgender women due to hormone-related vaginal atrophy.

HCPs will need to supplement general guidelines by developing the knowledge and skills needed for discussing sexual health issues with TGD people, such as the use of gender-affirming language (see Statement 17.1 in this chapter). It is critical HCPs avoid assumptions about HIV/STI risk based solely on a patient's gender identity or anatomy. For example, many transgender people are not sexually active, and TGD persons may use prosthetics or toys for sex. To provide appropriate prevention counseling, HCPs should inquire about the specific sexual activities TGD people engage in, and the body parts (or prosthetics) involved in those activities (ACON, 2022). Well-prepared HCPs (including, but not limited to mental health providers) may also engage in in-depth counseling with their patients to address the underlying drivers of HIV/STI risk (see Statement 17.3 in this chapter).

In all cases, HCPs should be sensitive to the collective and individual histories of TGD people (e.g., stereotypes and stigma about trans sexualities and gender dysphoria) and should explain to patients the reasons for sexuality-related inquiries and the voluntary nature of such inquiries. In discussing HIV/STI prevention, HCPs should refer to the full range of prevention options including barrier methods, post-exposure prophylaxis, pre-exposure prophylaxis, and HIV treatment to prevent onwards transmission (WHO, 2021). Trans-specific considerations for pre-exposure prophylaxis are addressed in Statement 17.8.

Statement 17.7

We recommend health care professionals who provide care to transgender and gender diverse people follow local and World Health Organization guidelines for human immunodeficiency virus/sexual transmitted infections (HIV/STIs) screening, prevention, and treatment.

Like cisgender patients, TGD adolescents and adults should be offered screening for HIV/STIs in accordance with existing guidelines and based on their individual risk of HIV/STI acquisition, considering anatomy and behavior rather than gender identity alone. Where local or national guidelines are unavailable, WHO (2019a) offers global recommendations; more frequent screening is recommended for transgender people who have sex with cisgender men as a key population affected by HIV.

Gender-affirming genital surgeries and surgical techniques have implications for STI risks and screening needs, as outlined in recent guidelines from the US Centers for Disease Control (Workowski et al., 2021). For instance, transfeminine persons who have had penile inversion vaginoplasty using only penile and scrotal skin to line the vaginal canal are likely at lower risk of urogenital Chlamydia trachomatis *(C. trachomatis)* and Neisseria gonorrhoeae *(N. gonorrhoeae)*, but newer surgical techniques that employ buccal or urethral mucosa or peritoneum flaps could in theory increase susceptibility to bacterial STIs relative to the use of penile/scrotal skin alone (Van Gerwen et al., 2021). Routine STI screening of the neovagina (if exposed) is recommended for all transfeminine persons who have had vaginoplasty (Workowski et al., 2021). For transmasculine persons who have had metoidioplasty with urethral lengthening, but not vaginectomy, testing for bacterial urogenital STIs should include a cervical swab because infections may not be detected in urine (Workowski et al., 2021).

Further, it is important for HCPs to offer testing at multiple anatomical sites as STIs in transgender patients are often extragenital (Hiransuthikul et al., 2019; Pitasi et al., 2019). Consistent with WHO (2020) recommendations, self-collection of samples for STI testing should be offered as an option, particularly if patients are uncomfortable or unwilling to undergo provider-collected sampling due to gender dysphoria, trauma histories, or both. Where relevant, integration of HIV/STI testing with regular serology used to monitor hormone therapy may better facilitate access to care (Reisner, Radix et al., 2016; Scheim & Travers, 2017).

Statement 17.8

We recommend health care professionals who provide care to transgender and gender diverse people address concerns about potential interactions between antiretroviral medications and hormones.

For TGD adolescents and adults at substantial risk of HIV infection (generally defined as an ongoing serodiscordant relationship or condomless sex outside of a mutually monogamous relationship with a known HIV-negative partner; WHO, 2017), pre-exposure prophylaxis (PrEP) is an important HIV prevention option (Golub et al., 2019; Sevelius et al., 2016; WHO, 2021). To encourage uptake of PrEP, in 2021 the US Centers for Disease Control recommended all sexually active adolescents and adults be informed about PrEP and offered it if requested (CDC, 2021). For treatment among people living with HIV, transgender-specific guidelines are available in some settings (e.g., Panel on Antiretroviral Guidelines for Adults and Adolescents, 2019).

For both HIV prevention and treatment, there are antiretroviral dosing and administration considerations specific to TGD persons. For oral PrEP, only daily dosing is currently recommended for TGD persons as studies demonstrating the effectiveness of event-driven PrEP with emtricitabine/tenofovir disoproxil fumarate (TDF) have been limited to cisgender men (WHO, 2019c). In addition, while emtricitabine/tenofovir alafenamide (TAF) is a new oral PrEP option, as of early 2022 it is not recommended for people at risk of HIV acquisition through receptive vaginal sex due to a lack of evidence (CDC, 2021). Finally, long-acting injectable formulations of both PrEP and HIV treatment are increasingly available (e.g., cabotegravir for PrEP), and while they are recommended for all patients who might benefit from injectable options, indicated injection sites (i.e., the gluteal muscle) may be unsuitable for individuals who have used soft tissue fillers (Rael et al., 2020).

There is little evidence supporting the occurrence of drug-drug interactions between gender-affirming hormones and PrEP medications. A few small studies, primarily relying on self-reported PrEP use, have shown reduced PrEP drug concentrations in transgender women undergoing hormone therapy, although

concentrations remained in the protective range (Yager & Anderson, 2020). A subsequent drug-drug interaction study using directly observed PrEP therapy failed to detect an impact of hormone therapy on PrEP drug concentrations in transgender women and found transgender women and men taking hormone therapy achieved high levels of protection against HIV infection (Grant et al., 2020). Most importantly, for many TGD people, no impact of PrEP on hormone concentrations has been detected. With regard to HIV treatment, specific antiretroviral medications may impact hormone concentrations; however, these can be managed by selecting alternative agents, monitoring and adjusting hormone dosing, or both (Cirrincione et al., 2020) as detailed in guidelines from the US Department of Health and Human Services (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2019). Nevertheless, concerns about drug-drug interactions, particularly interactions that may limit hormone concentrations, represent a barrier to the implementation and adherence to antiretroviral therapy for HIV prevention or treatment (Radix et al., 2020; Sevelius et al., 2016). Therefore, it is advisable for HCPs to proactively address such concerns with those who are candidates for PrEP or HIV treatment. Integration of PrEP or HIV treatment with hormone therapy may further reduce barriers to implementation and adherence (Reisner, Radix et al., 2016). Integration may be achieved through colocation or through coordination with an HIV specialist if the primary care provider does not have the necessary expertise. Some TGD persons may benefit from standalone PrEP or sexual health services that provide greater privacy and flexibility, and thus differentiated service delivery models are needed (Wilson et al., 2021).

CHAPTER 18 Mental Health

This chapter is intended to provide guidance to health care professionals (HCPs) and mental health professionals (MHPs) who offer mental health care to transgender and gender diverse (TGD) adults. It is not meant to be a substitute for chapters on the assessment or evaluation of people for hormonal or surgical interventions. Many TGD people will not require therapy or other forms of mental health care as part of their transition, while others may benefit from the support of mental health providers and systems (Dhejne et al., 2016).

Some studies have shown a higher prevalence of depression (Witcomb et al., 2018), anxiety (Bouman et al., 2017), and suicidality (Arcelus et al., 2016; Bränström & Pachankis, 2022; Davey et al., 2016; Dhejne, 2011; Herman et al., 2019) among TGD people (Jones et al., 2019; Thorne, Witcomb et al., 2019) than in the general population, particularly in those requiring medically necessary gender-affirming medical treatment (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1). However, transgender identity is not a mental illness, and these elevated rates have been linked to complex trauma, societal stigma, violence, and discrimination (Nuttbrock et al., 2014; Peterson et al., 2021). In addition, psychiatric symptoms lessen with appropriate gender-affirming medical and surgical care (Aldridge et al., 2020; Almazan and Keuroghlian; 2021; Bauer et al., 2015; Grannis et al., 2021) and with interventions that lessen discrimination and minority stress (Bauer et al., 2015; Heylens, Verroken et al., 2014; McDowell et al., 2020).

Mental health treatment needs to be provided by staff and implemented through the use of systems that respect patient autonomy and recognize gender diversity. MHPs working with transgender people should use active listening as a method to encourage exploration in individuals who are uncertain about their gender identity. Rather than impose their own narratives or preconceptions, MHPs should assist their clients in determining their own paths. While many transgender people require medical or surgical interventions or seek mental health care, others do not (Margulies et al., 2021). Therefore, findings from research involving clinical populations should not be extrapolated to the entire transgender population.

Addressing mental illness and substance use disorders is important but should not be a barrier to transition-related care. Rather, these interventions to address mental health and substance use disorders can facilitate successful outcomes from

Statements of Recommendations

18.1- We recommend mental health professionals address mental health symptoms that interfere with a person's capacity to consent to gender-affirming treatment before gender-affirming treatment is initiated.
18.2- We recommend mental health professionals offer care and support to transgender and gender diverse people to address mental health symptoms that interfere with a person's capacity to participate in essential perioperative care before gender-affirmation surgery.
18.3- We recommend when significant mental health symptoms or substance abuse exists, mental health professionals assess the potential negative impact that mental health symptoms may have on outcomes based on the nature of the specific gender-affirming surgical procedure.
18.4- We recommend health care professionals assess the need for psychosocial and practical support of transgender and gender diverse people in the perioperative period surrounding gender- affirmation surgery.
18.5- We recommend health care professionals counsel and assist transgender and gender diverse people in becoming abstinent from tobacco/nicotine prior to gender-affirmation surgery.
18.6- We recommend health care professionals maintain existing hormone treatment if a transgender and gender diverse individual requires admission to a psychiatric or medical inpatient unit, unless contraindicated.
18.7- We recommend health care professionals ensure if transgender and gender diverse people need in-patient or residential mental health, substance abuse or medical care, all staff use the correct name and pronouns (as provided by the patient), as well as provide access to bathroom and sleeping arrangements that are aligned with the person's gender identity.
18.8- We recommend mental health professionals encourage, support, and empower transgender and gender diverse people to develop and maintain social support systems, including peers, friends, and families.
18.9- We recommend health care professionals should not make it mandatory for transgender and gender diverse people to undergo psychotherapy prior to the initiation of gender-affirming treatment, while acknowledging psychotherapy may be helpful for some transgender and gender diverse people.
18.10- We recommend "reparative" and "conversion" therapy aimed at trying to change a person's gender identity and lived gender expression to become more congruent with the sex assigned at birth should not be offered.

transition-related care, which can improve quality of life (Nobili et al., 2018).

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 18.1

We recommend mental health professionals address mental health symptoms that interfere with a person's capacity to consent to gender-affirming treatment before gender-affirming treatment is initiated.

Because patients generally are assumed to be capable of providing consent for care, whether the presence of cognitive impairment, psychosis, or other mental illness impairs the ability to give informed consent is subject to individual examination (Applebaum, 2007). Informed consent is central to the provision of health care. The health care provider must educate the patient about the risks, benefits, and alternatives to any care that is offered so the patient can make an informed, voluntary choice (Berg et al., 2001). Both the primary care provider or endocrinologist prescribing hormones and the surgeon performing surgery must obtain informed consent. Similarly, MHPs obtain informed consent for mental health treatment and may consult on a patient's capacity to give informed consent when this is in question. Psychiatric illness and substance use disorders, in particular cognitive impairment and psychosis, may impair an individual's ability to understand the risks and benefits of the treatment (Hostiuc et al., 2018). Conversely, a patient may also have significant mental illness, yet still be able to understand the risks and benefits of a particular treatment (Carpenter et al., 2000). Multidisciplinary communication is important in challenging cases, and expert consultation should be utilized as needed (Karasic & Fraser, 2018). For many patients, difficulty understanding the risks and benefits of a particular treatment can be overcome with time and careful explanation. For some patients, treatment of the underlying condition that is interfering with the capacity to give informed consent—for example treating an underlying psychosis—will allow the patient to gain the capacity to consent to the required treatment. However, mental health symptoms such as anxiety or depressive symptoms that do not affect the capacity to give consent should not be a barrier for gender-affirming medical treatment, particularly as this treatment has been found to reduce mental health symptomatology (Aldridge et al., 2020).

Statement 18.2

We recommend mental health professionals offer care and support to transgender and gender diverse people to address mental health symptoms that interfere with a person's capacity to participate in essential perioperative care before gender-affirmation surgery.

The inability to adequately participate in perioperative care due to mental illness or substance use should not be viewed as an obstacle to needed transition care, but should be seen as an indication mental health care and social support be provided (Karasic, 2020). Mental illness and substance use disorders may impair the ability of the patient to participate in perioperative care (Barnhill, 2014). Visits to health care providers, wound care, and other aftercare procedures (e.g., dilation after vaginoplasty) may be necessary for a good outcome. A patient with a substance use disorder might have difficulty keeping necessary appointments to the primary care provider and the surgeon. A patient with psychosis or severe depression might neglect their wound or not be attentive to infection or signs of dehiscence (Lee, Marsh et al., 2016). Active mental illness is associated with a greater need for further acute medical and surgical care after the initial surgery (Wimalawansa et al., 2014).

In these cases, treatment of the mental illness or substance use disorder may assist in achieving successful outcomes. Arranging more support for the patient from family and friends or a home health care worker may help the patient participate sufficiently in perioperative care for surgery to proceed. The benefits of mental health treatments that may delay surgery should be weighed against the risks of delaying surgery and should

include an assessment of the impact on the patients' mental health delays may cause in addressing gender dysphoria (Byne et al., 2018).

Statement 18.3

We recommend when significant mental health symptoms or substance abuse exists, mental health professionals assess the potential negative impact mental health symptoms may have on outcomes based on the nature of the specific gender-affirming surgical procedure.

Gender-affirming surgical procedures vary in terms of their impact on the patient. Some procedures require a greater ability to follow preoperative planning as well as engage in peri- and postoperative care to achieve the best outcomes (Tollinche et al., 2018). Mental health symptoms can influence a patient's ability to participate in the planning and perioperative care necessary for any surgical procedure (Paredes et al., 2020). The mental health assessment can provide an opportunity to develop strategies to address the potential negative impact mental health symptoms may have on outcomes and to plan support for the patient's ability to participate in the planning and care. Gender-affirming surgical procedures have been shown to relieve symptoms of gender dysphoria and improve mental health (Owen-Smith et al., 2018; van de Grift, Elaut et al., 2017). These benefits are weighed against the risks of each procedure when the patient and provider are deciding whether to proceed with the treatment. HCPs can assist TGD people in reviewing preplanning and perioperative care instructions for each surgical procedure (Karasic, 2020). Provider and patient can collaboratively determine the necessary support or resources needed to assist with keeping appointments for perioperative care, obtaining necessary supplies, addressing financial issues, and handling other preoperative coordination and planning. In addition, issues surrounding appearance-related and functional expectations, including the impact of these various factors on gender dysphoria, can be explored.

Statement 18.4

We recommend health care professionals assess the need for psychosocial and practical support of transgender and gender diverse people in the perioperative period surrounding gender-affirmation surgery.

Regardless of specialty, all HCPs have a responsibility to support patients in accessing medically necessary care. When HCPs are working with TGD people as they prepare for gender-affirming surgical procedures, they should assess the levels of psychosocial and practical support required (Deutsch, 2016b). Assessment is the first step in recognizing where additional support may be needed and enhancing the ability to work collaboratively with the individual to successfully navigate the pre-, peri-, and postsurgical periods (Tollinche et al., 2018). In the perioperative period, it is important to help patients optimize functioning, secure stable housing, when possible, build social and family supports by assessing their unique situation, plan ways of responding to medical complications, navigate the potential impact on work/income, and overcome additional hurdles some patients may encounter, such as coping with electrolysis and tobacco cessation (Berli et al., 2017). In a complex medical system, not all patients will be able to independently navigate the procedures required to obtain care, and HCPs and peer navigators can support patients through this process (Deutsch, 2016a).

Statement 18.5

We recommend health care professionals counsel and assist transgender and gender diverse people in becoming abstinent from tobacco/nicotine prior to gender-affirmation surgery.

Transgender populations have higher rates of tobacco and nicotine use (Kidd et al., 2018). However, many are unaware of the well-documented smoking-associated health risks (Bryant et al., 2014). Tobacco consumption increases the risk of developing health problems (e.g., thrombosis) in individuals receiving gender-affirming hormone treatment, particularly estrogens (Chipkin & Kim, 2017).

Tobacco use has been associated with worse outcomes in plastic surgery, including overall complications, tissue necrosis, and the need for surgical revision (Coon et al., 2013). Smoking also increases the risk for postoperative infection (Kaoutzanis et al., 2019). Tobacco use has been shown to affect

the healing process following any surgery, including gender-related surgeries (e.g., chest reconstructive surgery, genital surgery) (Pluvy, Garrido et al., 2015). Tobacco users have a higher risk of cutaneous necrosis, delayed wound healing, and scarring disorders due to hypoxia and tissue ischemia (Pluvy, Panouilleres et al., 2015). In view of this, surgeons recommend stopping the use of tobacco/nicotine prior to gender-affirmation surgery and abstaining from smoking up to several weeks postoperatively until the wound has completely healed (Matei & Danino, 2015). Despite the risks, cessation may be difficult. Tobacco smoking and nicotine use is addictive and is also used as a coping mechanism (Matei et al., 2015). HCPs who see patients longitudinally before surgery, including mental health and primary care providers, should address the use of tobacco/nicotine with individuals in their care, and either assist TGD people in accessing smoking cessation programs or provide treatment directly (e.g., varenicline or bupropion).

Statement 18.6

We recommend health care professionals maintain existing hormone treatment if a transgender and gender diverse individual requires admission to a psychiatric or medical inpatient unit, unless contraindicated.

TGD people entering inpatient psychiatric, substance use treatment, or medical units should be maintained on their current hormone regimens. There is an absence of evidence supporting routine cessation of hormones prior to medical or psychiatric admissions. Rarely, a newly admitted patient may be diagnosed with a medical complication necessitating suspension of hormone treatment, for example an acute venous thromboembolism (Deutsch, 2016a). There is no strong evidence for routinely stopping hormone treatment prior to surgery, and the risks and benefits for each individual patient should be assessed before doing so (Boskey et al., 2018).

Hormone treatment has been shown to improve quality of life and to decrease depression and anxiety (Aldridge et al., 2020; Nguyen et al., 2018; Nobili et al., 2018; Owen-Smith et al., 2018, Rowniak et al., 2019). Access to gender-affirming medical treatment is associated with a substantial reduction in the risk of suicide attempt (Bauer et al., 2015). Halting a patient's regularly prescribed hormones denies the patient of these salutary effects, and therefore may be counter to the goals of hospitalization.

Some providers may be unaware of the low risk of harm and the high potential benefit of continuing transition-related treatment in the inpatient setting. A study of US and Canadian medical schools revealed that students received an average of 5 hours of LGBT-related course content over their entire four years of education (Obedin-Maliver et al., 2011). According to a survey of Emergency Medicine physicians, who are often responsible for making quick decisions about medications as patients are being admitted, while 88% reported caring for transgender patients, only 17.5% had received any formal training about this population (Chisolm-Straker et al., 2018). As education about transgender topics increases, more providers will become aware of the importance of maintaining transgender patients on their hormone regimens during hospitalization.

Statement 18.7

We recommend health care professionals ensure if transgender and gender diverse people need inpatient or residential mental health, substance abuse, or medical care, all staff use the correct name and pronouns (as provided by the patient), as well as provide access to bathroom and sleeping arrangements that are aligned with the person's gender identity.

Many TGD patients encounter discrimination in a wide range of health settings, including hospitals, mental health treatment settings, and drug treatment programs (Grant et al., 2011). When health systems fail to accommodate TGD individuals, they reinforce the longstanding societal exclusion many have experienced (Karasic, 2016). Experiences of discrimination in health settings lead to avoidance of needed health care due to anticipated discrimination (Kcomt et al., 2020).

The experience of discrimination experienced by TGD individuals is predictive of suicidal ideation (Rood et al., 2015; Williams et al., 2021). Gender minority stress associated with rejection and nonaffirmation has also been associated with suicidality (Testa et al., 2017). Denial of access to gender appropriate bathrooms has been

associated with increased suicidality (Seelman, 2016). However, the use of chosen names for TGD people has been associated with lower depression and suicidality (Russell et al., 2018). Structural as well as internalized transphobia must be addressed to reduce the incidence of suicide attempts in TGD people (Brumer et al., 2015). To successfully provide care, health settings must minimize the harm done to patients because of transphobia by respecting and accommodating TGD identities.

Statement 18.8

We recommend mental health professionals encourage, support, and empower transgender and gender diverse people to develop and maintain social support systems, including peers, friends, and families.

While minority stress and the direct effects of discriminatory societal discrimination can be harmful to the mental health of TGD people, strong social support can help lessen this harm (Trujillo et al., 2017). TGD children often internalize rejection from family and peers as well as the transphobia that surrounds them (Amodeo et al., 2015). Furthermore, exposure to transphobic abuse may be impactful across a person's lifespan and may be particularly acute during the adolescent years (Nuttbrock et al., 2010).

The development of affirming social support is protective of mental health. Social support can act as a buffer against the adverse mental health consequences of violence, stigma, and discrimination (Bockting et al., 2013), can assist in navigating health systems (Jackson Levin et al., 2020), and can contribute to psychological resilience in TGD people (Bariola et al., 2015; Başar and Öz, 2016). Diverse sources of social support, especially LGBTQ + peers and family, have been found to be associated with better mental health outcomes, well-being, and quality of life (Bariola et al., 2015; Başar et al., 2016; Kuper, Adams et al., 2018; Puckett et al., 2019). Social support has been proposed to facilitate the development of coping mechanisms and lead to positive emotional experiences throughout the transition process (Budge et al., 2013).

HCPs can support patients in developing social support systems that allow them to be recognized and accepted as their authentic identity and help them cope with symptoms of gender dysphoria. Interpersonal problems and lack of social support have been associated with a greater incidence of mental health difficulties in TGD people (Bouman, Davey et al., 2016; Davey et al., 2015) and have been shown to be an outcome predictor of gender-affirming medical treatment (Aldridge et al., 2020). Therefore, HCPs should encourage, support, and empower TGD people to develop and maintain social support systems. These experiences can foster the development of interpersonal skills and help with coping with societal discrimination, potentially reducing suicidality and improving mental health (Pflum et al., 2015).

Statement 18.9

We recommend health care professionals should not make it mandatory for transgender and gender diverse people to undergo psychotherapy prior to the initiation of gender-affirming treatment, while acknowledging psychotherapy may be helpful for some transgender and gender diverse people.

Psychotherapy has a long history of being used in clinical work with TGD people (Fraser, 2009b). The aims, requirements, methods and principles of psychotherapy have been an evolving component of the Standards of Care from the initial versions (Fraser, 2009a). At present, psychotherapeutic assistance and counseling with adult TGD people may be sought to address common psychological concerns related to coping with gender dysphoria and may also help some individuals with the coming-out process (Hunt, 2014). Psychological interventions, including psychotherapy, offer effective tools and provide context for the individual, such as exploring gender identity and its expression, enhancing self-acceptance and hope, and improving resilience in hostile and disabling environments (Matsuno and Israel, 2018). Psychotherapy is an established alternative therapeutic approach for addressing mental health symptoms that may be revealed during the initial assessment or later during the follow-up for gender-affirming medical interventions. Recent research shows, although mental health symptoms are reduced following gender-affirming medical treatment, levels of anxiety remain high (Aldridge et al., 2020) suggesting psychological therapy can play a role in helping

individuals suffering from anxiety symptoms following gender-affirming treatment.

In recent years, the uses and potential benefits of specific psychotherapeutic modalities have been reported (Austin et al., 2017; Budge, 2013; Budge et al., 2021; Embaye, 2006; Fraser, 2009b; Heck et al., 2015). Specific models of psychotherapy have been proposed for adult transgender and nonbinary individuals (Matsuno & Israel, 2018). However, more empiric data is needed on the comparative benefits of different psychotherapeutic models (Catelan et al., 2017). Psychotherapy can be experienced by transgender persons as a fearful as well as a beneficial experience (Applegarth & Nuttall, 2016) and presents challenges to the therapist and to alliance formation when it is associated with gatekeeping for medical interventions (Budge, 2015).

Experience suggests many transgender and nonbinary individuals decide to undergo gender-affirming medical treatment with little or no use of psychotherapy (Spanos et al., 2021). Although various modalities of psychotherapy may be beneficial for different reasons before, during, and after gender-affirming medical treatments and varying rates of desire for psychotherapy have been reported during different stages of transition (Mayer et al., 2019), a requirement for psychotherapy for initiating gender-affirming medical procedures has not been shown to be beneficial and may be a harmful barrier to care for those who do not need this type of treatment or who lack access to it.

Statement 18.10

We recommend "reparative" and "conversion" therapy aimed at trying to change a person's gender identity and lived gender expression to become more congruent with the sex assigned at birth should not be offered.

The use of "reparative" or "conversion" therapy or gender identity "change" efforts is opposed by many major medical and mental health organizations across the world, including the World Psychiatric Association, Pan American Health Organization, American Psychiatric and American Psychological Associations, Royal College of Psychiatrists, and British Psychological Society. Many states in the US have instituted bans on practicing conversion therapy with minors. Gender identity change efforts refers to interventions by MHPs or others that attempt to change gender identity or expression to be more in line with those typically associated with the person's sex assigned at birth (American Psychological Association, 2021).

Advocates of "conversion therapy" have suggested it could potentially allow a person to fit better into their social world. They also point out some clients specifically ask for help changing their gender identities or expressions and therapists should be allowed to help clients achieve their goals. However, "conversion therapy" has not been shown to be effective (APA, 2009; Przeworski et al., 2020). In addition, there are numerous potential harms. In retrospective studies, a history of having undergone conversion therapy is linked to increased levels of depression, substance abuse, suicidal thoughts, and suicide attempts, as well as lower educational attainment and less weekly income (Ryan et al., 2020; Salway et al., 2020; Turban, Beckwith et al., 2020). In 2021, the American Psychological Association resolutions states that "scientific evidence and clinical experience indicate that GICEs [gender identity change efforts] put individuals at significant risk of harm" (APA, 2021).

While there are barriers to ending gender identity "change" efforts, education about the lack of benefit and the potential harm of these practices may lead to fewer providers offering "conversion therapy" and fewer individuals and families choosing this option.

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Conflict of Interest

Conflict of interests were reviewed as part of the selection process for committee members and at the end of the process before publication. No conflicts of interest were deemed significant or consequential.

Ethical Approval

This manuscript does not contain any studies with human participants performed by any of the authors.

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Appendix A METHODOLOGY

1. Introduction

This version of the Standards of Care (SOC-8) is based upon a more rigorous and methodological evidence-based approach than previous versions. This evidence is not only based on the published literature (direct as well as background evidence) but also on consensus-based expert opinion. Evidence-based guidelines include recommendations intended to optimize patient care and are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options. Evidence-based research provides the basis for sound clinical practice guidelines and recommendations but must be balanced by the realities and feasibility of providing care in diverse settings. The process for development of the SOC-8 incorporated recommendations on clinical practice guideline development from the National Academies of Medicine and The World Health Organization that addressed transparency, the conflict-of-interest policy, committee composition and group process. (Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice, 2011; World Health Organization, 2019a).

The SOC-8 revision committee was multidisciplinary and consisted of subject matter experts, health care professionals, researchers and stakeholders with diverse perspectives and geographic representation. All committee members completed conflict of interest declarations.*

A guideline methodologist assisted with the planning and development of questions, and an independent team undertook systematic reviews that were used to inform some of the statements for recommendations. Additional input to the guidelines was provided by an international advisory committee, legal experts, and feedback received during a public comment period. Recommendations in the SOC-8 are based on available evidence supporting interventions, a discussion of risks and harms, as well as feasibility and acceptability within different contexts and country settings. Consensus of the final recommendations was attained using a Delphi process that included all members of the Standards of Care Revision committee and required that recommendation statements were approved by 75% of members. Supportive and explanatory text of the evidence for the statements were written by chapter members. Drafts of the chapters were reviewed by the Chair and the Co-Chairs of the SOC Revision Committee to ensure the format was consistent, evidence was properly provided, and recommendations were consistent across chapters. An independent team checked the references used in the SOC-8 before the guidelines were fully edited by a single professional. A detailed overview of the SOC-8 Methodology is described below.

2. Difference between the methodology of the SOC-8 and previous editions

The main differences in the methodology of the SOC-8 when compared with other versions of the SOC are:

- The involvement of a larger group of professionals from around the globe;
- A transparent selection process to develop the guidelines steering committee as well as to select chapter leads and members;
- The inclusion of diverse stakeholders in the development of the SOC-8
- Management of conflicts of interest
- The use of a Delphi process to reach agreement on the recommendations among SOC-8 committee members
- The involvement of an independent body from a reputable university to help develop the methodology and undertake independent systematic literature reviews where possible
- Recommendations were graded as either "recommend" or "suggest" based upon the strength of the recommendations.
- The involvement of an independent group of clinical academics to review citations.
- The involvement of international organizations working with the transgender and gender diverse (TGD) community, members of WPATH and other professional organizations as well as the general public who provided feedback through a public comment period regarding the whole SOC-8.

3. Overview of SOC-8 development Process

The steps for updating the Standards of Care are summarized below:

1. Establishing Guideline Steering Committee including Chair, and Co-Chairs (July 19, 2017)
2. Determining chapters (scope of guidelines)
3. Selecting Chapter Members based upon expertise (March 2018)
4. Selecting the Evidence Review Team: John Hopkins University (May 2018)
5. Refining topics included in the SOC-8 and review questions for systematic reviews
6. Conducting systematic reviews (March 2019)
7. Drafting the recommendation statements
8. Voting on the recommendation statements using a Delphi process (September 2019–February 2022)
9. Grading of the recommendations statements
10. Writing the text supporting the statements
11. Independently validating the references used in the supportive text
12. Finalizing a draft SOC-8 (December 1, 2021)
13. Feedback on the statements by International Advisory Committee
14. Feedback on the entire draft of the SOC-8 during a public comment period (November 2021–January 2022)
15. Revision of Final Draft based on comments (January 2022- May 2022)
16. Approval of final Draft by Chair and Co-Chairs (June 10, 2022)
17. Approval by the WPATH Board of Directors
18. Publication of the SOC-8
19. Dissemination and translation of the SOC-8

3.1. Establishment of Guideline Steering Committee

The WPATH Guideline Steering Committee oversaw the guideline development process for all chapters of the Standards of Care. Except for the Chair (Eli Coleman) who was appointed by the WPATH board to maintain a continuity from previous SOC editions, members of the Guideline Steering Committee were selected by the WPATH Board from WPATH members applying for these positions. Job descriptions were developed for the positions of Co-Chairs, Chapter Leads, Chapter Members and Stakeholder. WPATH members were eligible to apply by completing an application form and submitting their CV. The Board of WPATH voted for the position of co-chair (one member of the board did not participate in view of conflict of interest). The chairs and co-chairs selected the chapter leads and members (as well as stakeholders) based on the application form and CVs.

The Guideline Steering Committee for Standards of Care 8th Version are:

- Eli Coleman, PhD (Chair) Professor, Director and Academic Chair, Institute for Sexual and Gender Health, Department of Family Medicine and Community Health, University of Minnesota Medical School (USA)
- Asa Radix, MD, PhD, MPH (Co-chair) Senior Director, Research and Education Callen-Lorde Community Health Center Clinical Associate Professor of Medicine New York University, USA
- Jon Arcelus, MD, PhD (Co-chair) Professor of Mental Health and Well-being Honorary Consultant in Transgender Health University of Nottingham, UK
- Karen A. Robinson, PhD (Lead, Evidence Review Team) Professor of Medicine, Epidemiology and Health Policy & Management Johns Hopkins University, USA

3.2. Determination of topics for chapters

The Guideline Steering Committee determined the chapters for inclusion in the Standards of Care by reviewing the literature and by reviewing the previous edition of the SOC. The chapters in the Standards of Care 8th Version:

1. Terminology
2. Global Applicability
3. Population estimates
4. Education*
5. Assessment of Adults
6. Adolescent
7. Children
8. Nonbinary
9. Eunuch
10. Intersex
11. Institutional environments
12. Hormone Therapy
13. Surgery and Postoperative Care
14. Voice and communication
15. Primary care
16. Reproductive Health
17. Sexual Health
18. Mental Health

* The Education Chapter was originally intended to cover both education and ethics. A decision was made to create a separate committee to write a chapter on ethics. In the course of writing the chapter, it was later determined topic of ethics was best placed external to the SOC8 and required further in-depth examination of ethical considerations relevant to transgender health.

3.3. Selection of chapter members

A call for applications to be part of the SOC-8 review committee (chapter lead or member) was sent to the WPATH membership. The Chairs of the Guideline Steering Committee appointed the members for each chapter, ensuring representation from a variety of disciplines and perspectives.

Chapter Leads and Members were required to be WPATH Full Members in good standing and content experts in transgender health, including in at least one chapter topic. Chapter Leads reported to the Guideline Steering Committee and were responsible for coordinating the participation of Chapter Members. Chapter members reported directly to the Chapter Lead.

Each chapter also included stakeholders as members who bring perspectives of transgender health advocacy or work in the community, or as a member of a family that included a transgender child, sibling, partner, parent, etc. Stakeholders were not required to be full members of WPATH.

The Chapter Members were expected to:

- Participate in the development refinement of review questions
- Read and provide comments on all materials from the Evidence Review Team
- Critically review draft documents, including the draft evidence report
- Review and assess evidence and draft recommendations
- Participate in the Delphi consensus process
- Develop the text to back up the recommendation statements
- Grade each statement to describe the strength of the recommendation
- Review and address the comments from the Chairs during the whole process
- Develop the content of the chapters
- Review comments from public comments and assist in the development of a revision of guidelines
- Provide input and participate in the dissemination of guidelines

Training and orientation for Chapter Leads and Members was provided, as needed. Training content included formulation and refinement of questions (i.e., use of PICO), reviewing the evidence, developing recommendation state-

ments, grading the evidence and the recommendations, and information about the guideline development program and process.

A total of 26 chapter-leads were appointed (some chapters required co-leads), 77 chapter members and 16 stakeholders. A total of 127 were selected. During the SOC process, 8 people left, due to personal or work-related issues. Therefore, there were 119 final authors of the SOC-8.

3.4. Selection of the evidence review team

The WPATH Board issued a request for applications to become the Evidence Review Team. For Standards of Care 8th Version the WPATH Board engaged the Evidence Review Team at Johns Hopkins University under the leadership of Karen Robinson.

- Karen A. Robinson, PhD (Lead, Evidence Review Team) Professor of Medicine, Epidemiology and Health Policy & Management Johns Hopkins University, USA

Dr Robinson also guided the steering committee in the development of the SOC-8 by providing advice and training in the development of PICO questions, statements, and the Delphi process as well as undertaking a very rigorous systematic literature review where direct evidence was available.

Conflict of interest

Members of the Guideline Steering Committee, Chapter Leads and Members, and members of the Evidence Review Team were asked to disclose any conflicts of interest. Also reported, in addition to potential financial and competing interests or conflicts, are personal or direct reporting relationships with a chair, co-chair or a WPATH Board Member or the holding of a position on the WPATH Board of Directors.

3.5. Refinement of topics and review of questions

The Evidence Review Team abstracted the recommendation statements from the prior version of the Standards of Care. With input from the Evidence Review Team, the Guideline Steering Committee and Chapter Leads determined:

- Recommendation statements that needed to be updated
- New areas requiring recommendation statements

3.6. Conduct the systematic reviews

Chapter Members developed questions to help develop recommendation statements. For the questions eligible for systematic review, the Evidence Review Team drafted review questions, specifying the Population, Interventions, Comparisons, and Outcomes (PICO elements). The Evidence Review Team undertook the systematic reviews. The Evidence Review Team presented evidence tables and other results of the systematic reviews to the members of the relevant chapter for feedback.

Protocol

A separate detailed systematic review protocol was developed for each review question or topic, as appropriate. Each protocol was registered on PROSPERO.

Literature search

The Evidence Review Team developed a search strategy appropriate for each research question including MEDLINE®, Embase™, and the Cochrane Central Register of Controlled Trials (CENTRAL). The Evidence Review Team searched additional databases as deemed appropriate for the research question. The search strategy included MeSH and text terms and was not limited by language of publication or date.

The Evidence Review Team hand searched the reference lists of all included articles and recent, relevant systematic reviews. The Evidence Review Team searched ClinicalTrials.gov for any additional relevant studies.

Searches were updated during the peer review process.

The literature included in the systematic review was mostly based on quantitative studies conducted in Europe, the US or Australia. We acknowledge a bias towards perspectives from the global north that does not pay sufficient attention to the diversity of lived experiences and perspectives within transgender and gender diverse (TGD) communities across the world. This imbalance of visibility in the literature points to a research and practice gap that needs to be addressed by researchers and practitioners in the future in order to do justice to the support needs of all TGD people independent of gender identification.

Study selection

The Evidence Review Team, with input from the Chapter Workgroup Leads, defined the eligibility criteria for each research question *a priori*.

Two reviewers from the Evidence Review Team independently screened titles and abstracts and full-text articles for eligibility. To be excluded, both reviewers needed to agree that the study met at least one exclusion criteria. Reviewers resolved differences regarding eligibility through discussion.

Data extraction

The Evidence Review Team used standardized forms to abstract data on general study characteristics, participant characteristics, interventions, and outcome measures. One reviewer abstracted the data, and a second reviewer confirmed the abstracted data.

Assessment of risk of bias

Two reviewers from the Evidence Review Team independently assessed the risk of bias for each included study. For

randomized controlled trials, the Cochrane Risk of Bias Tool was used. For observational studies, the Risk of Bias in Non-Randomized Studies—of Interventions (ROBINS-I) tool was used. Where deemed appropriate, existing recent systematic reviews were considered and evaluated using ROBIS.

Data synthesis and analysis

The Evidence Review Team created evidence tables detailing the data abstracted from the included studies. The members of the Chapter Workgroups reviewed and provided comments on the evidence tables.

Grading of the evidence

The Evidence Review Team assigned evidence grades using the GRADE methodology. The strength of the evidence was obtained using predefined critical outcomes for each question and by assessing the limitations to individual study quality/risk of bias, consistency, directness, precision, and reporting bias.

3.7. Drafting of the Recommendation Statements

Chapter Leads and Members drafted recommendation statements. The statements were crafted to be feasible, actionable, and measurable.

Evidence-based recommendation statements were based on the results of the systematic, and background literature reviews plus consensus-based expert opinions.

The Chair and Co-Chairs and Chapter Leads reviewed and approved all recommendation statements for clarity and consistency in wording. During this review and throughout the process any overlap between chapters was also addressed.

Many chapters had to work closely together to ensure consistency of their recommendations. For example, as there are now separate chapters for childhood and adolescence, to ensure consistency between both chapters, some authors were part of both chapters. For a similar reason, when applicable, a workgroup collaborated with other Chapter Workgroups on topics shared between the chapters (i.e., Assessment of Children, Assessment of Adults, Hormone Therapy, Surgery and Postoperative Care and Reproductive Health).

3.8. Approval of the recommendations using the Delphi process

Formal consensus for all statements was obtained using the Delphi process (a structured solicitation of expert judgements in three rounds). For a recommendation to be approved, a minimum of 75% of the voters had to approve the statement. A minimum of 65% of the SOC-8 members had to take part in the Delphi process for each statement. People who did not approve the statement had to provide information as to the reasons for their disapproval, so the statement could be modified (or removed) according to this feedback. Once modified, the statement was put through the Delphi process again. If after 3 rounds the statement was not approved, the statement was removed from the SOC. Every member of the SOC voted for each statement. There was a response rate between (74.79% and 94.96%) for the statements.

3.9. Grading criteria for statements

Once the statements passed the Delphi process, chapter members graded each statement using a process adapted from the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework. This a transparent framework for developing and presenting summaries of evidence and provides a systematic approach for making clinical practice recommendations (Guyatt et al., 2011). The statements were graded based on factors such as:

- The balance of potential benefits and harms
- Confidence in that balance or quality of evidence
- Values and preferences of providers and patients
- Resource use and feasibility

The statements were classified as:

- Strong recommendations ("we recommend") are for those interventions/therapy/strategies where:
  - the evidence is of high quality
  - estimates of the effect of an intervention/therapy/strategy (i.e., there is a high degree of certainty effects will be achieved in practice)
  - there are few downsides of therapy/intervention/strategy
  - there is a high degree of acceptance among providers and patients or those for whom the recommendation applies.
- Weak recommendations ("we suggest") are for those interventions/therapy/strategies where:
  - there are weaknesses in the evidence base
  - there is a degree of doubt about the size of the effect that can be expected in practice
  - there is a need to balance the potential upsides and downsides of interventions/therapy/strategies
  - there are likely to be varying degrees of acceptance among providers and patients or those for whom the recommendation applies.

3.10. Writing of the text supporting the statements

Following the grading of the statements, the Chapter Workgroups wrote the text providing the rationale or reasoning for the recommendation. This included providing the available evidence, providing details about potential benefits and harms, describing uncertainties, and information about implementation of the recommendation, including expected barriers or challenges among others. References use APA-7 style, to support the information in the text. Links to resources are also provided, as appropriate. The text, including whether a recommendation has been described as strong or weak, was reviewed and approved by the Chair and Co-Chairs.

3.11. External validation of references used to support the statements

A group of independent clinical academics working in the field of transgender health reviewed the references used in every chapter in order to validate that the references were appropriately used to support the text. Any queries regarding the references were sent back to the chapters for review.

3.12. Finalizing a draft SOC-8

A final SOC-8 draft was made available for comments.

3.13. Distribute Standards of Care for review by international advisors

The statements of the recommendations of Standards of Care 8th were circulated among the broader Standards of Care Revision Committee and the WPATH International Advisory Group, which included the Asia Pacific Transgender Network (APTN), the Global Action for Transgender Equality (GATE), the International Lesbian, Gay, Bisexual, Transgender, Intersex Association (ILGA), and Transgender Europe (TGEU).

3.14. Public comment period

The revised draft version of the Standards of Care document was posted online for comment from the public, including WPATH members, on the WPATH website. A 6-week period was allocated for comments. A total of 1,279 people made comments on the draft with a total of 2,688 comments.

3.15. Revision of final draft based on comments

The Chapter Leads and Guideline Steering Committee considered the feedback and made any necessary revisions. All public comments were read and, where appropriate, integrated into the background text.

As part of this process, 3 new Delphi statements were developed and 2 were modified enough to require a new vote by the SOC-8 committee. This meant a new Delphi process was initiated in January 2022. The results of this Delphi process were accepted by the chapters, and the new statements were added or modified accordingly. The new supportive text was added.

All the new versions of the chapters were reviewed again by the Chair and Co-Chairs and changes or modifications were suggested. Finally, once the Chairs and the Chapter Members were satisfied with the draft, the chapter was finalized.

All new references were double checked by an independent member.

3.16. Approval of final draft by Chair and Co-Chairs

Modifications were reviewed by the Chairs and were accepted by them.

3.17. Approval by the WPATH Board of Directors

The final document was presented to the WPATH Board of Directors for approval and it was approved on the 20th of June 2022.

3.18. Publication of the SOC-8 and dissemination of the Standards of Care

The Standards of Care was disseminated in a number of venues and in a number of formats including publication in the International Journal of Transgender Health (the official scientific journal of WPATH).

4. Plan to Update

A new edition of the SOC (SOC-9) will be developed in the future, when new evidence and/or significant changes in the field necessitating a new edition is substantial.

*The development of SOC-8 was a complex process at a time of COVID-19 and political uncertainties in many parts of the world. Members of the SOC-8 worked on the SOC-8 on top of their day-to-day job, and most of the meetings took place out of their working time and during their weekends via Zoom. There were very few face-to-face meetings, most of them linked to WPATH, USPATH or EPATH conferences. Committee members of the SOC-8 were not paid as part of this process.

Appendix B GLOSSARY

CISGENDER refers to people whose current gender identity corresponds to the sex they were assigned at birth.

DETRANSITION is a term sometimes used to describe an individual's retransition to the gender stereotypically associated with their sex assigned at birth.

EUNUCH refers to an individual assigned male at birth whose testicles have been surgically removed or rendered non-functional and who identifies as a eunuch. This differs from the standard medical definition by excluding those who do not identify as eunuch.

EUNUCH-IDENTIFIED: An individual who feels their true self is best expressed by the term eunuch. Eunuch-identified individuals generally desire to have their reproductive organs surgically removed or rendered non-functional.

GENDER: Depending on the context, gender may reference gender identity, gender expression, and/or social gender role, including understandings and expectations culturally tied to people who were assigned male or female at birth. Gender identities other than those of men and women (who can be either cisgender or transgender) include transgender, nonbinary, genderqueer, gender neutral, agender, gender fluid, and "third" gender, among others; many other genders are recognized around the world.

GENDER-AFFIRMATION refers to being recognized or affirmed in a person's gender identity. It is usually conceptualized as having social, psychological, medical, and legal dimensions. Gender affirmation is used as a term in lieu of transition (as in medical gender-affirmation) or can be used as an adjective (as in gender-affirming care).

GENDER-AFFIRMATION SURGERY (GAS) is used to describe surgery to change primary and/or secondary sex characteristics to affirm a person's gender identity.

GENDER BINARY refers to the idea there are two and only two genders, men and women; the expectation that everyone must be one or the other; and that all men are males, and all women are females.

GENDER DIVERSE is a term used to describe people with gender identities and/or expressions that are different from social and cultural expectations attributed to their sex assigned at birth. This may include, among many other culturally diverse identities, people who identify as nonbinary, gender expansive, gender nonconforming, and others who do not identify as cisgender.

GENDER DYSPHORIA describes a state of distress or discomfort that may be experienced because a person's gender identity differs from that which is physically and/or socially attributed to their sex assigned at birth. Gender Dysphoria is also a diagnostic term in the DSM-5 denoting an incongruence between the sex assigned at birth and experienced gender accompanied by distress. Not all transgender and gender diverse people experience gender dysphoria.

GENDER EXPANSIVE is an adjective often used to describe people who identify or express themselves in ways that broaden the socially and culturally defined behaviors or beliefs associated with a particular sex. Gender creative is also sometimes used. The term gender variant was used in the past and is disappearing from professional usage because of negative connotations now associated with it.

GENDER EXPRESSION refers to how a person enacts or expresses their gender in everyday life and within the context of their culture and society. Expression of gender through physical appearance may include dress, hairstyle, accessories, cosmetics, hormonal and surgical interventions as well as mannerisms, speech, behavioral patterns, and names. A person's gender expression may or may not conform to a person's gender identity.

GENDER IDENTITY refers to a person's deeply felt, internal, intrinsic sense of their own gender.

GENDER INCONGRUENCE is a diagnostic term used in the ICD-11 that describes a person's marked and persistent experience of an incompatibility between that person's gender identity and the gender expected of them based on their birth-assigned sex.

INTERSEX refers to people born with sex or reproductive characteristics that do not fit binary definitions of female or male.

MISGENDER/MISGENDERING refers to when language is used that does not correctly reflect the gender with which a person identifies. This may be a pronoun (he/him/his, she/her/hers, they/them/theirs) or a form of address (sir, Mr.).

NONBINARY refers to those with gender identities outside the gender binary. People with nonbinary gender identities may identify as partially a man and partially a woman or identify as sometimes a man and sometimes a woman, or identify as a gender other than a man or a woman, or as not having a gender at all. Nonbinary people may use the pronouns they/them/theirs instead of he/him/his or she/her/hers. Some nonbinary people consider themselves to be transgender or trans; some do not because they consider transgender to be part of the gender binary. The shorthand NB or "enby" is sometimes used as a descriptor for nonbinary. Examples of nonbinary gender identities are genderqueer, gender diverse, genderfluid, demigender, bigender, and agender.

RETRANSITION refers to second or subsequent gender transition whether by social, medical, or legal means. A retransition may be from one binary or nonbinary gender to another binary or nonbinary gender. People may retransition more than once. Retransition may occur for many reasons, including evolving gender identities, health concerns, family/societal concerns, and financial issues.

SEX ASSIGNED AT BIRTH refers to a person's status as male, female, or intersex based on physical characteristics. Sex is usually assigned at birth based on appearance of the external genitalia. AFAB is an abbreviation for "assigned female at birth." AMAB is an abbreviation for "assigned male at birth."

SEXUAL ORIENTATION refers to a person's sexual identity, attractions, and behaviors in relation to people on the basis of their gender(s) and or sex characteristics and those of their partners. Sexual orientation and gender identity are distinct terms.

TRANSGENDER or trans are umbrella terms used to describe people whose gender identities and/or gender expressions are not what is typically expected for the sex to which they were assigned at birth. These words should always be used as adjectives (as in "trans people") and never as nouns (as in "transgenders") and never as verbs (as in "transgendered").

TRANSGENDER MEN or **TRANS MEN** or **MEN OF TRANS EXPERIENCE** are people who have gender identities as men and who were assigned female at birth. They may or may not have undergone any transition. FTM or Female-to-Male are older terms that are falling out of use.

TRANSGENDER WOMEN or **TRANS WOMEN** or **WOMEN OF TRANS EXPERIENCE** are people who have gender identities as women and who were assigned male at birth. They may or may not have undergone any transition. MTF or Male-to-Female are older terms that are falling out of use.

TRANSITION refers to the process whereby people usually change from the gender expression associated with their assigned sex at birth to another gender expression that better matches their gender identity. People may transition socially by using methods such as changing their name, pronoun, clothing, hair styles, and/or the ways that they move and speak. Transitioning may or may not involve hormones and/or surgeries to alter the physical body. Transition can be used to describe the process of changing one's gender expression from any gender to a different gender. People may transition more than once in their lifetimes.

TRANSPHOBIA refers to negative attitudes, beliefs, and actions concerning transgender and gender diverse people as a group. Transphobia may be enacted in discriminatory policies and practices on a structural level or in very specific and personal ways. Transphobia can also be internalized, when transgender and gender diverse people accept and reflect such prejudice about themselves or other transgender and gender diverse people. While transphobia sometimes may be a result of unintentional ignorance rather than direct hostility, its effects are never benign. Some people use the term anti-transgender bias in place of transphobia.

Appendix C GENDER-AFFIRMING HORMONAL TREATMENTS

Table 1. Expected time course of physical changes in response to gender-affirming hormone therapy

Testosterone Based Regimen		
Effect	**Onset**	**Maximum**
Skin Oiliness/acne	1–6 months	1–2 years
Facial/body hair growth	6–12 months	>5 years
Scalp hair loss	6–12 months	>5 years
Increased muscle mass/ strength	6–12 months	2–5 years
Fat redistribution	1–6 months	2–5 years
Cessation of menses	1–6 months	1–2 years
Clitoral enlargement	1–6 months	1–2 years
Vaginal atrophy	1–6 months	1–2 years
Deepening of voice	1–6 months	1–2 years
Estrogen and testosterone-lowering based regimens		
Effect	**Onset**	**Maximum**
Redistribution of body fat	3–6 months	2–5 years
Decrease in muscle mass and strength	3–6 months	1–2 years
Softening of skin/ decreased oiliness	3–6 months	Unknown
Decreased sexual desire	1–3 months	Unknown
Decreased spontaneous erections	1–3 months	3–6 months
Decreased sperm production	Unknown	2 years
Breast growth	3–6 months	2–5 years
Decreased testicular volume	3–6 months	Variable
Decreased terminal hair growth	6–12 months	> 3 years
Increased scalp hair	Variable	Variable
Voice changes	None	

Adapted from Hembree et al., 2017.

Table 2. Risks associated with gender affirming hormone therapy (bolded items are clinically significant) (Updated from SOC-7)

RISK LEVEL	Estrogen-based regimens	Testosterone-based regimens
Likely increased risk	**Venous Thromboembolism** **Infertility** Hyperkalemia[S] Hypertrigyceridemia Weight Gain	**Polycythemia** **Infertility** Acne Androgenic Alopecia Hypertension Sleep Apnea Weight Gain Decreased HDL Cholesterol and increased LDL Cholesterol
Likely increased risk with presence of additional risk factors	Cardiovascular Disease Cerebrovascular Disease Meningioma[C] Polyuria/Dehydration[S] Cholelithiasis	Cardiovascular Disease Hypertriglyceridemia
Possible increased risk	Hypertension Erectile Dysfunction	
Possible increased risk with presence of additional risk factors	Type 2 Diabetes Low Bone Mass/ Osteoporosis Hyperprolactinemia	Type 2 Diabetes Cardiovascular Disease
No increased risk or inconclusive	Breast and Prostate Cancer	Low Bone Mass/ Osteoporosis Breast, Cervical, Ovarian, Uterine Cancer

[C]cyproterone-based regimen
[S]spironolactone-based regimen

Table 3. Gender-Affirming Hormone Regimens In Transgender And Gender Diverse Youth (Adapted from the Endocrine Society Guidelines; Hembree et al., 2017)

Induction of female puberty (estrogen-based regimen) with oral 17ß-estradiol

Initiate at 5µg/kg/d and increase every 6 months by 5 µg/kg/d up to 20 µg/kg/d according to estradiol levels
Adult dose = 2-6 mg/day
In postpubertal TGD adolescents, the dose of 17ß-estradiol can be increased more rapidly:
1 mg/d for 6 months followed by 2 mg/d and up according to estradiol levels

Induction of female puberty (estrogen-based regimen) with transdermal 17ß-estradiol

Initial dose 6.25-12.5 µg/24 h (cutting 24 g patch to ¼ then ½)
Titrate up by every 6 months by 12.5 µg/24 h according to estradiol levels
Adult dose = 50-200 µg/24 hours
For alternatives once at adult dose (Table 4)

Induction of male puberty (testosterone-based regimen) with testosterone esters

25 mg/m^2/2 weeks (or alternatively half this dose weekly)
Increase by 25 mg/m^2/2 weeks every 6 months until adult dose and target testosterone levels are achieved. See alternatives for testosterones (Table 4)

Table 4. Hormone regimens in transgender and gender diverse adults*

Estrogen-based regimen (Transfeminine)	
Estrogen	
Oral or sublingual	
Estradiol	2.0-6.0 mg/day
Transdermal	
Estradiol transdermal patch	0.025-0.2 mg/day
Estradiol gel various	‡ daily to skin
Parenteral	
Estradiol valerate or cypionate	5-30 mg IM every 2 weeks 2-10 IM every week
Anti-Androgens	
Spironolactone	100–300 mg/day
Cyproterone acetate	10 mg/day**
GnRH agonist	3.75–7.50 mg SQ/IM monthly
GnRH agonist depot formulation	11.25/22.5 mg SQ/IM 3/6 monthly
‡ Amount applied varies to formulation and strength	
Testosterone-Based Regimen (Transmasculine)	
Transgender males	
Testosterone	
Parenteral	
Testosterone enanthate/ cypionate	50–100 IM/SQ weekly or 100–200 IM every 2 weeks
Testosterone undecanoate	1000 mg IM every 12 weeks or 750 mg IM every 10 weeks
Transdermal testosterone	
Testosterone gel	50-100 mg/day
Testosterone transdermal patch	2.5–7.5 mg/day

Doses are titrated up or down until sex steroid hormone levels are in the therapeutic range. Hormone regimens do not reflect all formulations that are available in all pharmacies throughout the world. Hormone regimens may have to be adapted to what is available in local pharmacies.
**Kuijpers et al (2021).

Table 5. Hormone monitoring of transgender and gender diverse people receiving gender-affirming hormone therapy (Adapted from the Endocrine Society Guidelines)

Transgender male or trans masculine (including gender diverse/nonbinary) individuals

1. Evaluate patient approximately every 3 months (with dose changes) in the first year and 1 to 2 times per year thereafter to monitor for appropriate physical changes in response to testosterone.
2. Measure serum total testosterone every 3 months (with dose changes) until levels are at goal
   a. For parenteral testosterone, the serum total testosterone should be measured midway between injections. The target level is 400-700 ng/dL. Alternatively, measure peak and trough peaks to ensure levels remain in the range of reference men.
   b. For parenteral testosterone undecanoate, testosterone should be measured just before injection. If the level is < 400 ng/dL, adjust the dosing interval.
   c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 week of daily application (at least 2 hours after application of product).
3. Measure hematocrit or hemoglobin concentrations at baseline and approximately 3 months (with dose changes) for the first year and then one to two times a year.

Transgender Female or trans feminine (including gender diverse/nonbinary) individuals

1. Evaluate patient approximately every 3 months (with dose changes) in the first year and one to two times per year thereafter to monitor for appropriate physical changes in response to estrogen.
   a. Serum testosterone levels should be less than 50 ng/dL.
   b. Serum estradiol should be in the range of 100-200 pg/mL.
2. For individuals receiving spironolactone, serum electrolytes, in particular potassium, and kidney function, in particular creatinine, should be monitored.
3. Follow primary care screening per primary care chapter recommendations

Appendix D SUMMARY CRITERIA FOR HORMONAL AND SURGICAL TREATMENTS FOR ADULTS AND ADOLESCENTS

The SOC-8 guidelines are intended to be flexible in order to meet the diverse health care needs of TGD people globally. While adaptable, they offer consensus-based standards derived from the best available scientific evidence for promoting optimal health care and guiding the treatment of people experiencing gender incongruence. As in all previous versions of the SOC, the criteria put forth in this document for gender affirming interventions are clinical guidelines; individual health care professionals and programs, in consultation with the TGD person, may modify them. Clinical departures from the SOC may occur due to a TGD person's unique anatomic, social, or psychological situation; an experienced health care professional's evolving method of handling a common situation; a research protocol; lack of resources in various parts of the world; or the need for specific harm-reduction strategies. These departures should be recognized as such, discussed with the TGD person, and documented. This documentation is also valuable for the accumulation of new data, which can be retrospectively examined to allow for health care—and the SOC—to evolve. This summary criteria needs to be read in conjunction with the relevant chapters (see Adult Assessment and Adolescent chapters).

SUMMARY CRITERIA FOR ADULTS

Related to the assessment process

- Health care professionals assessing transgender and gender diverse adults seeking gender-affirming treatment should liaise with professionals from different disciplines within the field of trans health for consultation and referral, if required*
- If written documentation or a letter is required to recommend gender affirming medical and surgical treatment (GAMST), only one letter of assessment from a health care professional who has competencies in the assessment of transgender and gender diverse people is needed.

Criteria for hormones

a. Gender incongruence is marked and sustained;
b. Meets diagnostic criteria for gender incongruence prior to gender-affirming hormone treatment in regions where a diagnosis is necessary to access health care;
c. Demonstrates capacity to consent for the specific gender-affirming hormone treatment;
d. Other possible causes of apparent gender incongruence have been identified and excluded;
e. Mental health and physical conditions that could negatively impact the outcome of treatment have been assessed, with risks and benefits discussed;
f. Understands the effect of gender-affirming hormone treatment on reproduction and they have explored reproductive options.

Criteria for surgery

a. Gender incongruence is marked and sustained;
b. Meets diagnostic criteria for gender incongruence prior to gender-affirming surgical intervention in regions where a diagnosis is necessary to access health care;
c. Demonstrates capacity to consent for the specific gender-affirming surgical intervention;
d. Understands the effect of gender-affirming surgical intervention on reproduction and they have explored reproductive options;
e. Other possible causes of apparent gender incongruence have been identified and excluded;
f. Mental health and physical conditions that could negatively impact the outcome of gender-affirming surgical intervention have been assessed, with risks and benefits have been discussed;
g. Stable on their gender affirming hormonal treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).*

*These were graded as suggested criteria

SUMMARY CRITERIA FOR ADOLESCENTS

Related to the assessment process

- A comprehensive biopsychosocial assessment including relevant mental health and medical professionals;
- Involvement of parent(s)/guardian(s) in the assessment process, unless their involvement is determined to be harmful to the adolescent or not feasible;
- If written documentation or a letter is required to recommend gender-affirming medical and surgical treatment (GAMST), only one letter of assessment from a member of the multidisciplinary team is needed. This letter needs to reflect the assessment and opinion from the team that involves both medical and mental health professionals (MHPs).

Puberty blocking agents

a. Gender diversity/incongruence is marked and sustained over time;
b. Meets the diagnostic criteria of gender incongruence in situations where a diagnosis is necessary to access health care;
c. Demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment;
d. Mental health concerns (if any) that may interfere with diagnostic clarity, capacity to consent, and gender-affirming medical treatments have been addressed; sufficiently so that gender-affirming medical treatment can be provided optimally.
e. Informed of the reproductive effects, including the potential loss of fertility and the available options to preserve fertility;
f. Reached Tanner stage 2.

Hormonal treatments

a. Gender diversity/incongruence is marked and sustained over time;
b. Meets the diagnostic criteria of gender incongruence in situations where a diagnosis is necessary to access health care;
c. Demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment;
d. Mental health concerns (if any) that may interfere with diagnostic clarity, capacity to consent, and gender-affirming medical treatments have been addressed; sufficiently so that gender-affirming medical treatment can be provided optimally.
e. Informed of the reproductive effects, including the potential loss of fertility and the available options to preserve fertility;
f. Reached Tanner stage 2.

Surgery

a. Gender diversity/incongruence is marked and sustained over time;
b. Meets the diagnostic criteria of gender incongruence in situations where a diagnosis is necessary to access health care;
c. Demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment;
d. Mental health concerns (if any) that may interfere with diagnostic clarity, capacity to consent, and gender-affirming medical treatments have been addressed; sufficiently so that gender-affirming medical treatment can be provided optimally.
e. Informed of the reproductive effects, including the potential loss of fertility and the available options to preserve fertility;
f. At least 12 months of gender-affirming hormone therapy or longer, if required, to achieve the desired surgical result for gender-affirming procedures, including breast augmentation, orchiectomy, vaginoplasty, hysterectomy, phalloplasty, metoidioplasty, and facial surgery as part of gender-affirming treatment unless hormone therapy is either not desired or is medically contraindicated.

Appendix E GENDER-AFFIRMING SURGICAL PROCEDURES

As the field's understanding of the many facets of gender incongruence expands, and as technology develops which allows for additional treatments, it is imperative to understand this list is not intended to be exhaustive. This is particularly important given the often lengthy time periods between updates to the SOC, during which evolutions in understanding and treatment modalities may occur.

FACIAL SURGERY	
Brow	• Brow reduction • Brow augmentation • Brow lift
Hair line advancement and/or hair transplant	
Facelift/mid-face lift (following alteration of the underlying skeletal structures)	
Facelift/mid-face lift (following alteration of the underlying skeletal structures)	• Platysmaplasty
Blepharoplasty	• Lipofilling
Rhinoplasty (+/- fillers)	
Cheek	• Implant • Lipofilling
Lip	• Upper lip shortening • Lip augmentation (includes autologous and non-autologous)
Lower jaw	• Reduction of mandibular angle • Augmentation
Chin reshaping	• Osteoplastic • Alloplastic (implant-based)
Chondrolaryngoplasty	• Vocal cord surgery (see voice chapter)
BREAST/CHEST SURGERY	
Mastectomy	• Mastectomy with nipple-areola preservation/reconstruction as determined medically necessary for the specific patient • Mastectomy without nipple-areola preservation/reconstruction as determined medically necessary for the specific patient
Liposuction	
Breast reconstruction (augmentation)	• Implant and/or tissue expander • Autologous (includes flap-based and lipofilling)
GENITAL SURGERY	
Phalloplasty (with/without scrotoplasty)	• With/without urethral lengthening • With/without prosthesis (penile and/or testicular) • With/without colpectomy/colpocleisis
Metoidioplasty (with/without scrotoplasty)	• With/without urethral lengthening • With/without prosthesis (penile and/or testicular) • With/without colpectomy/colpocleisis
Vaginoplasty (inversion, peritoneal, intestinal)	• May include retention of penis and/or testicle
Vulvoplasty	• May include procedures described as "flat front"
GONADECTOMY	
Orchiectomy	
Hysterectomy and/or salpingo-oophorectomy	
BODY CONTOURING	
Liposuction	
Lipofilling	
Implants	• Pectoral, hip, gluteal, calf
Monsplasty/mons reduction	
ADDITIONAL PROCEDURES	
Hair removal: Hair removal from the face, body, and genital areas for gender affirmation or as part of a preoperative preparation process. (see Statement 15.14 regarding hair removal)	• Electrolysis • Laser epilation
Tattoo (i.e., nipple-areola)	
Uterine transplantation	
Penile transplantation	

EXHIBIT 117

WPATH
WORLD PROFESSIONAL ASSOCIATION FOR TRANSGENDER HEALTH

USPATH
UNITED STATES PROFESSIONAL ASSOCIATION FOR TRANSGENDER HEALTH

Joint Letter from USPATH and WPATH

The United States Professional Association for Transgender Health (USPATH) and the World Professional Association for Transgender Health (WPATH) stand behind the appropriate care of transgender and gender diverse youth, which includes, when indicated, the use of "puberty blockers" such as gonadotropin releasing hormone analogs and other medications to delay puberty, and, when indicated, the use of gender- affirming hormones such as estrogen or testosterone. Guidelines for the assessment of transgender and gender diverse youth, as well as for the use of pubertal delay and gender affirming hormone medications have been published by reputable professional bodies, including the Endocrine Society, the World Professional Association for Transgender Health, and the American Psychiatric Association.

USPATH and WPATH support scientific discussions on the use of pubertal delay and hormone therapy for transgender and gender diverse youth. We believe that such discussions should occur among experts and stakeholders in this area, based on scientific evidence, and in fora such as peer-reviewed journals or scientific conferences, and among colleagues and experts in the assessment and care of transgender and gender diverse youth. USPATH and WPATH oppose the use of the lay press, either impartial or of any political slant or viewpoint, as a forum for the scientific debate of these issues, or the politicization of these issues in any way. Furthermore, individual decisions about gender- affirming interventions and treatments for transgender and gender diverse youth should be made only among the patient, their parent(s) or guardian(s), their medical and mental health provider(s), and any other identified stakeholders on a case-by-case basis, and opposes any attempts to dictate or restrict, by statute, judiciary, or otherwise, access to such treatment when recommended according to accepted standards and guidelines.

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EXHIBIT 118

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Meta-Analysis

Meta-Analysis

Hormone Therapy, Mental Health, and Quality of Life Among Transgender People: A Systematic Review

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Abbreviations: BDI, Beck Depression Inventory; ENIGI, European Network for the Investigation of Gender Incongruence; GnRH, gonadotropin-releasing hormone; HADS, Hospital Anxiety and Depression Scale; QOL, quality of life; RCT, randomized controlled trial; SF-36, Short Form-36 Health Survey; WPATH, World Professional Association for Transgender Health.

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Abstract

We sought to systematically review the effect of gender-affirming hormone therapy on psychological outcomes among transgender people. We searched PubMed, Embase, and PsycINFO through June 10, 2020 for studies evaluating quality of life (QOL), depression, anxiety, and death by suicide in the context of gender-affirming hormone therapy among transgender people of any age. We excluded case studies and studies reporting on less than 3 months of follow-up. We included 20 studies reported in 22 publications. Fifteen were trials or prospective cohorts, one was a retrospective cohort, and 4 were cross-sectional. Seven assessed QOL, 12 assessed depression, 8 assessed anxiety, and 1 assessed death by suicide. Three studies included trans-feminine people only; 7 included trans-masculine people only, and 10 included both. Three studies focused on adolescents. Hormone therapy was associated with increased QOL, decreased depression, and decreased anxiety. Associations were similar across gender identity and age. Certainty in this conclusion is limited by high risk of bias in study designs, small sample sizes, and confounding with other interventions. We could not draw any conclusions about death by suicide. Future studies should investigate the psychological benefits of hormone therapy among larger and more diverse groups of transgender people using study designs that more effectively isolate the effects of hormone treatment.

Key Words: Transgender, hormone therapy, sex hormones, mental health, systematic review

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Transgender people are those whose gender identity is different from the sex they were assigned at birth. Estimates of the size of the transgender population vary depending on how the data are collected [1]. In studies that rely on clinical records, estimates range between 1 and 30 people per 100 000 (0.001% to 0.03%) [2]. Studies that focus instead on self-report among nonclinical populations find estimates that range between 0.1% and 2% [2].

Many transgender people seek medical services to affirm their gender identity. According to the *Standards of Care for Transsexual, Transgender, and Gender Non-Conforming People* maintained by the World Professional Association for Transgender Health (WPATH), gender-affirming medical care is different for each individual and may include a variety of services and procedures, such as psychological support, hormone therapy, and surgeries [3]. Hormone therapy, which typically involves estrogens and anti-androgens for transgender women and other trans-feminine people and testosterone for transgender men and other trans-masculine people, is a common component of medical gender affirmation [4]. Because hormone treatment can have a powerful effect on physical appearance, it is often a priority for transgender people seeking medical gender affirmation [5]. Gender-affirming hormone therapy can be managed for most patients by primary care providers, as it typically involves long-term maintenance on doses similar to those used for cisgender patients with conditions such as hypogonadism [6, 7]. Some clinicians require a minimum period of psychological counseling before hormone therapy can be initiated, while others provide hormone therapy on the basis of informed consent [8].

The need for gender-affirming care is often characterized using psychiatric diagnoses such as gender dysphoria, which replaced gender identity disorder in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) [9]. The 11th International Classification of Diseases (ICD-11) replaces these terms with a diagnosis called gender incongruence (codes: HA60, HA61, HA6Z), which is located in a new chapter on sexual health. These changes clarify that the target of gender-affirming medical interventions is not the person's gender identity itself but rather the clinically significant distress that can accompany a misalignment between gender identity and sex assigned at birth [10]. Some countries have further underscored that transgender identity is not a pathology by recognizing gender affirmation as fundamental to the human right to self-definition and removing requirements that transgender people seeking gender-affirming medical care present with a diagnosis such as gender dysphoria [11].

Several previous reviews have indicated that gender-affirming hormone therapy is associated with psychological benefits that include reductions in depression and anxiety and improvements in quality of life (QOL) among transgender people [12-17]. Most of these reviews did not require a minimum duration of hormone therapy [14-17]. One review that did impose a minimum follow-up requirement is 10 years old [12]. The other that required a minimum of 3 months of therapy included only uncontrolled prospective cohorts, which resulted in a sample of only 3 studies [13]. A comprehensive review without a minimum follow-up period assessed gender-affirming hormone therapy and surgeries only in adolescents [17]. By requiring a minimum duration of hormone treatment but considering all ages and a variety of study designs, we sought to update and more completely summarize the growing evidence base regarding the relationship between gender-affirming hormone therapy and psychological outcomes in transgender people.

Search Strategy and Selection Criteria

This review is one of a series of systematic reviews on gender-affirming care conducted for WPATH to inform the eighth revision of the *Standards of Care*. The protocol is registered on PROSPERO (CRD42018115379) [18], and we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in reporting our findings [19].

We searched PubMed, Embase, and PyscINFO from inception to October 2018 and updated the search through June 10, 2020, for studies assessing QOL, depression, anxiety, and death by suicide among transgender participants of any age in the context of gender-affirming hormone therapy [20]. We also reviewed the reference lists of previous reviews and hand-searched the *International Journal of Transgenderism*. Using DistillerSR [21], 2 reviewers independently screened titles, abstracts, and full-text articles. Differences were resolved through consensus adjudication.

We included studies that evaluated the psychological effects of any testosterone, estrogen, or anti-androgen formulation used for gender affirmation. We also considered gonadotropin-releasing hormone (GnRH) analogues used as anti-androgens or for puberty delay. Study participants must have been on hormone therapy for at least 3 months in order to reflect a minimum time for expected onset of effects [3]. Health care provider supervision was not required. We excluded studies that did not state therapy type and duration, including the range for cross-sectional studies. We included studies regardless of language (the search terms were in English) and country of origin, and we accepted any study design except case reports.

We created standardized forms for data extraction using the Systematic Review Data Repository system. The data extracted included participant demographics; study design

and methods; hormone therapy type, dose, and duration; potential confounders such as gender-affirming surgery status; outcome scales [20]; and psychological outcomes. From studies that used the Short Form-36 Health Survey (SF-36) to measure QOL, we extracted scores in all domains [22]. For studies that used measures with depression or anxiety subscales, we extracted only the subscale scores corresponding to the psychological outcomes of interest (eg, the depression subscale of the Minnesota Multiphasic Personality Inventory [MMPI]). We extracted comparisons with cisgender controls or general population norms only when longitudinal findings in a transgender population or comparisons with an untreated transgender control group were not reported. We used WebPlotDigitizer to extract data reported only in figures [23].

Two reviewers independently assessed risk of bias [20]. For randomized controlled trials (RCTs), we used the revised Cochrane tool [24]. For non-randomized studies, we used the Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions (ROBINS-I) [25]. One reviewer graded strength of evidence for each outcome using the Agency for Healthcare Research and Quality Methods Guide for Conducting Comparative Effectiveness Reviews [26]. We considered the directionality and magnitude of effects reported in cross-sectional studies as additional context for our evaluation of evidence from trials and prospective and retrospective cohorts. Each strength of evidence assessment was confirmed by a second reviewer.

WPATH provided the research question and reviewed the protocol, evidence tables, and report. WPATH had no role in study design, data collection, analysis, interpretation, or drafting. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication. The authors are responsible for all content, and statements in this report do not necessarily reflect the official views of or imply endorsement by WPATH.

Results

We retrieved 1753 nonduplicate studies for the broader systematic review project of which this review was a part (Fig. 1). After screening and full-text review for the specific research question on the psychological effects of gender-affirming hormone therapy, 20 studies reported in 22 publications were included (Table 1): 1 RCT [27], 2 before-after trials [28, 29], 12 prospective cohorts reported in 13 publications [30-42], 1 retrospective cohort reported in 2 publications [43, 44], and 4 cross-sectional studies [45-48]. De Vries (2014) [35] reported on a subset of the participants in de Vries (2011) [34] who continued in care. We counted these publications as a single study but extracted and reported data separately because the characteristics of the study's adolescent population changed substantially in the period between the 2 publications. Similarly, Asscheman (2011) [44] reported on an extension of Asscheman (1989) [43]; we counted these as a single study but extracted data separately. In Table 1 and in the subsequent tables for each outcome, studies are ordered first by study design (RCTs, before-after trials, prospective cohorts, retrospective cohorts, and cross-sectional studies); within these categories, studies are presented in the following order according to how the study results were reported: adult transgender women only, adult transgender men only, adult transgender women and transgender men together, and transgender adolescents (no study reported separate results by gender identity for transgender youth). Where multiple studies shared the same study design and population, they are additionally ordered chronologically.

The time frame covered in the included studies began in 1972 [43], but most studies dated from post-2000. Eight studies were conducted in Italy [27-29, 31, 32, 36, 39, 41]; 2 each in Belgium [37, 48], the Netherlands [34, 35, 43, 44], the United States [30, 47], and Spain [38, 45]; and 1 in the United Kingdom [33], Turkey [42], and France [46]. One study recruited participants from Switzerland and Germany [40]. One study was part of the European Network for the Investigation of Gender Incongruence (ENIGI), which is a research collaborative between clinics providing gender-affirming care to transgender people in Ghent (Belgium), Amsterdam (Netherlands), Oslo (Norway), and Hamburg (Germany). The ENIGI study included in this review drew participants only from the Ghent clinic [37].

The study sizes ranged from 20 to 1331, although most had fewer than 60 participants. Fourteen studies reported on testosterone formulations in adult transgender men [27, 29, 31-33, 36, 39-46, 48]. These formulations were typically injectable testosterone cypionate or enanthate, although some studies used long-acting injectable testosterone undecanoate or daily transdermal gels. Ten studies reported on estrogen formulations in adult transgender women, usually in conjunction with an anti-androgen such as cyproterone acetate or spironolactone [28, 31, 33, 36, 37, 39, 43-47]. Estrogen formulations included transdermal, oral, or injectable estradiol (commonly estradiol valerate) or conjugated estrogens. Three studies reported on the psychological effects of GnRH therapy for puberty delay among mixed-gender groups of transgender adolescents [30, 34, 35, 38]. No study reported on hormone therapy among nonbinary people.

All studies that reported information about recruitment drew their participants largely or exclusively from specialized clinics dedicated to providing gender-affirming care for transgender people. These clinics were typically part of larger systems such as university hospitals. Clinic-based

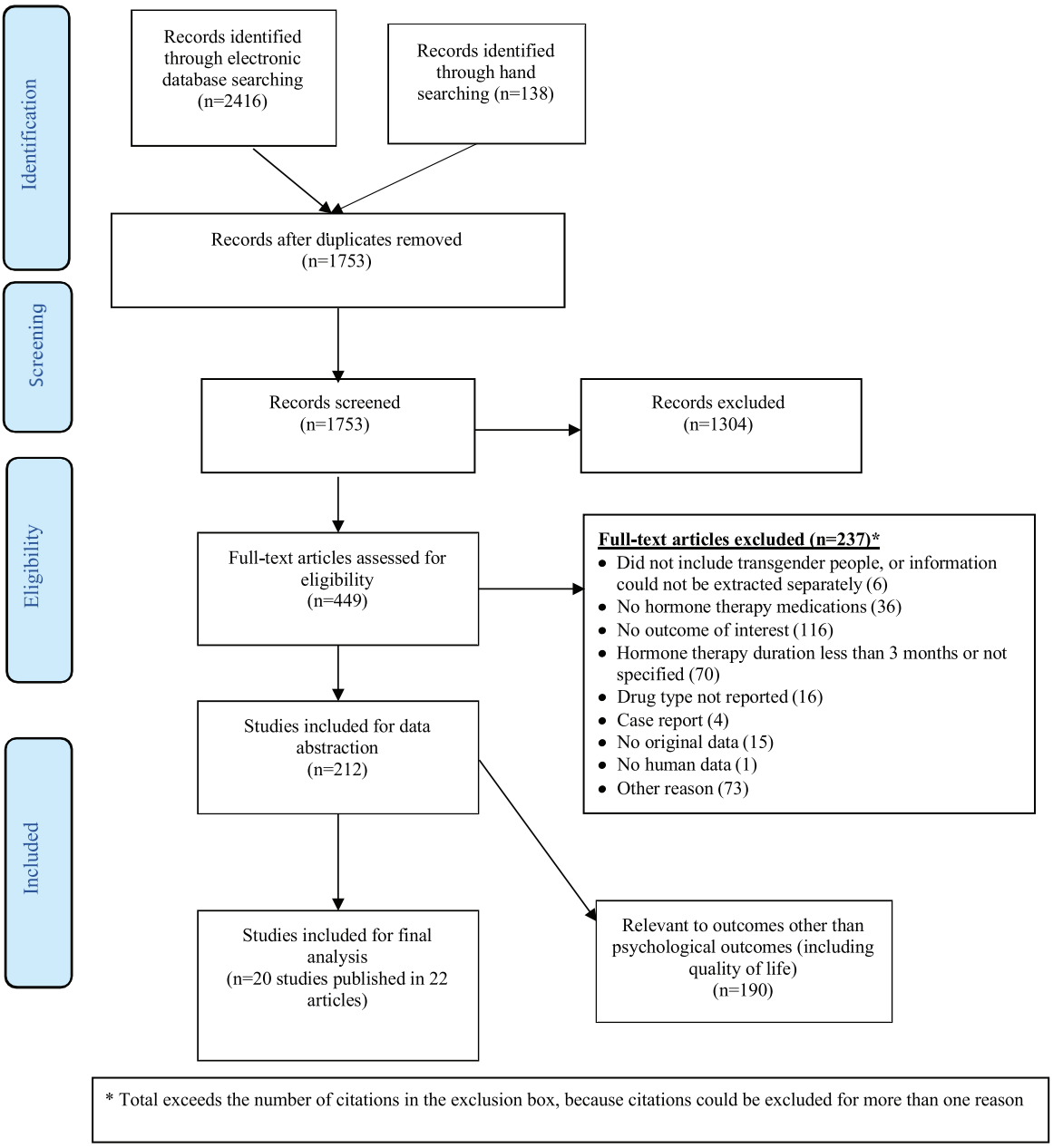

Figure 1. PRISMA flow diagram.

studies often applied strict eligibility criteria that included a period of psychiatric evaluation and a formal diagnosis of gender dysphoria before hormone therapy was initiated. Some studies also reported that psychological counseling was either available or required during the course of hormone therapy. In many cases, hormone therapy was considered a prerequisite for gender-affirming surgeries. The type and timing of gender-affirming surgeries and the proportion of participants for whom hormone therapy and surgeries were assessed simultaneously varied widely: some studies assessed only participants who had not had any type of gender-affirming surgery [27, 28, 30-32, 34, 36, 38-40, 42, 46, 47], while in others some or all participants underwent gender-affirming surgeries during the study period [29, 33, 35, 43-45, 48].

Quality of Life

Seven studies, including 1 RCT [27], 2 before-after trials [28, 29], 2 prospective cohorts [30, 39], and 2 cross-sectional studies [46, 48], assessed QOL (Table 2). An RCT found an improvement of approximately 5.5 points on a 10-point measure of life satisfaction across 3 groups of transgender men (n = 15 each) after 1 year of testosterone treatment ($P < 0.05$) [27]. A before-after trial similarly reported that life satisfaction scores almost

Table 1. Studies Reporting Effects of Gender-Affirming Hormone Therapy on Psychological Outcomes Among Transgender People

Author, year Location Study name	Study design	Start year	Transgender population	Overall N	Age in years	Baseline HT status	Outcomes	GAS status	Risk of bias
Pelusi, 2014 [27] Italy	Randomized controlled trial[a]	NR	Men	45	Mean: 29.5	No previous HT	QOL	No GAS before or during study	High
Gava, 2016 [28] Italy	Before-after trial	NR	Women	40	Mean: 3.2 (range, 19–55)	No previous HT	QOL, Depression	No GAS before or during study	Low
Gava, 2018 [29] Italy	Before-after trial[a]	NR	Men	50	Mean: 30.1 (range, 21–42)	No previous HT	QOL	72% (n = 36) had gonadectomy during study	Serious
Fuss, 2015 [37] Belgium ENIGI (NCT01072825)	Prospective cohort	2010	Women	20	Mean: 33.9 (range, 17–48)	No previous HT	Anxiety	NR	Serious
Costantino, 2013 [32] Italy	Prospective cohort	2001	Men	50	Mean: 29.8	No previous HT	Depression	No GAS before or during study	Serious
Motta, 2018 [41] Italy	Prospective cohort	2013	Men	52	Mean: 28.3	No previous HT	Anxiety	NR	Moderate
Turan, 2018 [42] Turkey	Prospective cohort[b]	NR	Men	37	Mean: 24.6	No previous HT	Depression, Anxiety	No GAS before or during study	Moderate
Metzger, 2019 [40] Switzerland, Germany	Prospective cohort[b]	2013	Men	23	Mean: 27.2 (range, 18–51)	No previous HT	Depression	No GAS before or during study	Moderate
Colizzi, 2014 [31] Italy	Prospective cohort	2008	Women and men	107	Mean: 29.2	No previous HT	Depression, Anxiety	No GAS before or during study	Low
Manieri, 2014 [39] Italy	Prospective cohort	NR	Women and men	83	Mean: 32.7 (women), 30.2 (men)	No previous HT	QOL	No GAS before or during study	Moderate
Fisher, 2016 [36] Italy	Prospective cohort	2012	Women and men	54	Mean: 32.5 (women), 26.3 (men)	No previous HT	Depression	No GAS before or during study	Low
Defreyne, 2018 [33] UK	Prospective cohort	2012	Women and men	155	Median: 27 (range, 18–52)	No previous HT	Depression, Anxiety	Some had GAS during study; % and type NR	Serious
Asscheman, 1989 [43] Netherlands	Retrospective cohort[b,d]	1972	Women and men	425	Median: 32 (women, range, 16–67); 25.4 (men, range, 16–54)	Previous HT for at least 6 months	Death by suicide	78% (n = 235) of transgender women had GAS during study; data NR for transgender men	Serious

Table 1. Continued

Author, year Location Study name	Study design	Start year	Transgender population	Overall N	Age in years	Baseline HT status	Outcomes	GAS status	Risk of bias
Asscheman, 2011 [44] Netherlands	Retrospective cohort[b,d]	1975	Women and men	1331	Mean: 31.4 (women, range, 16–76); 26.1 (men, range, 16–57)	Previous HT for at least 1 year	Death by suicide	87% (n = 834) of transgender women and 94% (n = 343) of transgender men had GAS during study	Serious
Leavitt, 1980 [47] US	Cross-sectional	1976	Women	41	Range, 18–35	54% (n = 22) on HT	Depression	No previous GAS	Serious
Wierckx, 2011 [48] Belgium	Cross-sectional[b]	2009	Men	47	Mean: 37 (range, 22–54)	100% on HT	QOL	100% had GAS, but not within previous year	Serious
Gómez-Gil, 2012 [45] Spain	Cross-sectional	NR	Women and men	187	Mean: 29.9 (range, 15–61)	64% (n = 120) on HT	Depression, Anxiety	42% (n = 79) of all participants and 64% (n = 77) of participants on HT had previous GAS	Serious
Gorin-Lazard, 2012 [46] France	Cross-sectional[b]	NR	Women and men	61	Mean: 34.7	72% (n = 44) on HT	QOL	No previous GAS	Serious
de Vries, 2011 [34] Netherlands	Prospective cohort	2000	Girls and boys	70	Mean: 14.8 (range, 11.3–18.6)	No previous HT	Depression, Anxiety	No GAS before or during study	Moderate
de Vries, 2014 [35] Netherlands	Prospective cohort[b,c]	2000	Girls and boys	55	Mean: 14.8 (range, 11.5–18.5)	No previous HT	Depression, Anxiety	100% had GAS during study	Serious
Achille, 2020 [30] US	Prospective cohort	2013	Girls and boys	50	Mean: 16.2	No previous HT	QOL, Depression	No GAS before or during study	Moderate
López de Lara, 2020 [38] Spain	Prospective cohort[b]	2018	Girls and boys	23	Mean: 16 (range, 14-18)	No previous HT	Depression, Anxiety	No GAS before or during study	Moderate

Abbreviations: ENIGI, European Network for the Investigation of Gender Incongruence; GAS, gender-affirming surgery; HT, hormone therapy; NR, not reported; QOL, quality of life.
[a]25 participants were included in both Pelusi [27] and Gava (2018) [29]
[b]Included a cisgender control group or a comparison to general population norms
[c]All participants were also included in de Vries (2011) [34]
[d]An unknown number of participants were included in both Asscheman (1989) [43] and Asscheman (2011) [44]

Table 2. Effects of Gender-Affirming Hormone Therapy on Quality of Life Among Transgender People

Author, year Study design	Transgender population	Treatment / comparison (n)	QOL measures	Length of treatment	Findings
Pelusi, 2014 [27] RCT[a]	Men	Testoviron depot (15) vs testosterone gel (15) vs testosterone undecanoate (15)	VAS (general life satisfaction)	54 weeks	Mean QOL scores increased from 2.8 to 8.5 ($P < 0.05$) in the testoviron depot arm, from 3.2 to 8.9 ($P < 0.05$) in the testosterone gel arm, and from 2.6 to 8.0 ($P < 0.05$) in the testosterone undecanoate arm.[d] There was no difference across arms.
Gava, 2016 [28] Before-after trial	Women	Cyproterone acetate + estradiol (20) vs leuprolide acetate + estradiol (20)	VAS (general life satisfaction) SF-36	12 months	Mean QOL scores did not change in either arm. No comparisons across arms were reported.
Gava, 2018 [29] Before-after trial[a]	Men	Testosterone undecanoate (25)[c] vs testosterone enanthate (25)[c]	VAS (general satisfaction)	5 years	Mean QOL scores increased from 4.3 ± 3.1 to 8.1 ± 1.8 ($P < 0.001$) in the testosterone undecanoate arm and from 4.3 ± 3.8 to 8.3 ± 1.7 ($P < 0.001$) in the testosterone enanthate arm. No comparisons across arms were reported.
Manieri, 2014 [39] Prospective cohort	Women	HT (56)	WHOQOL	12 months	Mean QOL scores increased from 62.5 to 72.2 ($P < 0.05$).[d]
Manieri, 2014 [39] Prospective cohort	Men	HT (27)	WHOQOL	12 months	Mean QOL scores did not change.
Wierckx, 2011 [48] Cross-sectional[b]	Men	HT (47)[c]	SF-36	At least 3 years	Mean QOL scores on the VT and MH subscales were lower for transgender men than cisgender men (VT subscale: 62.1 ± 20.7 vs 71.9 ± 18.3, $P = 0.002$; MH subscale: 72.6 ± 19.2 vs 79.3 ± 16.4, $P = 0.020$). There were no other differences between transgender men and either cisgender men or cisgender women.
Gorin-Lazard, 2012 [46] Cross-sectional[b]	Women and men	HT (44) vs no HT (17)	SF-36	Median: 20 months (range, 12–42 months)	Mean QOL scores were generally higher in the group receiving HT vs the group not receiving HT (MCS: 51.0 ± 7.7 vs 39.8 ± 12.7, $P = 0.003$; MH subscale: 76.4 ± 14.1 vs 59.1 ± 19.6, $P = 0.004$; RE subscale: 88.6 ± 22.7 vs 54.9 ± 40.7, $P = 0.001$; SF subscale: 83.2 ± 23.3 vs 69.9 ± 24.2, $P = 0.026$). There were no differences in the other subscales.
Achille, 2020 [30] Prospective cohort	Girls and boys	GnRH treatment + HT (47)	Q-LES-Q-SF	12 months	Mean QOL scores did not change.

Abbreviations: GnRH, gonadotropin-releasing hormone; HT, hormone therapy; MCS, Mental Component Summary; MH, mental health; QOL, quality of life; RCT, randomized controlled trial; RE, role functioning/emotional; SF, social functioning; SF-36, Short Form-36 Health Survey; VAS, visual analog scale; VT, vitality; WHOQOL, World Health Organization Quality of Life measure.

[a]10 participants on testosterone enanthate and 15 participants on testosterone undecanoate were included in both Pelusi [27] and Gava (2018) [29]

[b]Included a cisgender control group or a comparison to general population norms

[c]Included participants who had undergone gender-affirming surgery/surgeries, or surgery status not reported

[d]No standard deviations reported

doubled among transgender men (n = 50) over 5 years [29]. A prospective study found a 16% improvement in QOL scores among transgender women (n = 56) after 1 year of treatment ($P < 0.05$) but no change among transgender men (n = 27) [39]. Another before-after trial reported no difference in SF-36 scores among 2 groups of transgender women (n = 20 each) after 1 year [28]. Among adolescents, a mixed-gender prospective cohort (n = 50) showed no difference in QOL scores after a year of endocrine interventions, which included combinations of GnRH analogues and estrogen or testosterone formulations [30]. No study found that hormone therapy decreased QOL scores. We conclude that hormone therapy may improve QOL among transgender people. The strength of evidence for this conclusion is low due to concerns about bias in study designs, imprecision in measurement because of small sample sizes, and confounding by factors such as gender-affirming surgery status.

Depression

Twelve studies, including 1 before-after trial [28], 9 prospective cohorts [30-36, 38, 40, 42], and 2 cross-sectional studies [45, 47], assessed depression (Table 3). A prospective study found that the proportion of transgender men and transgender women (n = 107) showing symptoms of depression decreased from 42% to 22% over 12 months of treatment ($P < 0.001$) [31]. In 2 other prospective cohorts, Beck Depression Inventory (BDI-II) scores improved by more than half among both transgender men (n = 26) and transgender women (n = 28) after 24 months of therapy ($P < 0.001$) [36] and improved from 15.7 ± 12.3 to 8.1 ± 6.2 among transgender men (n = 23) after 6 months ($P < 0.001$) [40]. A fourth prospective study reported improvements of 1.05 points (95% CI: −1.87, −0.22) and 1.42 points (95% CI: −2.61, −0.24) on the 21-point Hospital Anxiety and Depression Scale (HADS) among 91 transgender women and 64 transgender men after 12 months ($P = 0.013$ and $P = 0.019$, respectively) [33]. A before-after trial, however, found no change in BDI-II scores among 2 groups of transgender women (n = 20 each) after 1 year [28]. Two prospective studies reported no difference among transgender men (n = 37) after 24 weeks [42] or among transgender men (n = 50) after 12 months [32], although in the latter study this outcome did not change from a baseline median of 0.0 ("not at all depressed") on an unvalidated 4-point scale. Among adolescents, 2 mixed-gender prospective cohorts (n = 50 and n = 23, respectively) showed improvements in depression scores after 1 year of treatment with GnRH analogues and estrogen or testosterone formulations (both $P < 0.001$) [30, 38]. Another prospective study reported that BDI scores improved almost by half among adolescents (n = 41) after a mean of 1.88 years of treatment with GnRH analogues to delay puberty ($P = 0.004$) [34]. The overall improvement after several subsequent years of testosterone or estrogen therapy in this cohort (n = 32) was smaller, however, resulting in no significant change from baseline [35]. No study found that hormone therapy increased depression. We conclude that hormone therapy may decrease depression among transgender people. The strength of evidence for this conclusion is low due to concerns about study designs, small sample sizes, and confounding.

Anxiety

Eight studies, including 7 prospective cohorts [31, 33-35, 37, 38, 41, 42] and 1 cross-sectional study [45], assessed anxiety (Table 4). One prospective study found that Symptom Checklist 90-Revised scores indicating a probable anxiety disorder among a mixed-gender group of adults (n = 107) improved from borderline to normal over 12 months ($P < 0.001$) [31]. Another prospective study, however, did not find a difference in HADS anxiety scores among either transgender men (n = 64) or transgender women (n = 91) after 1 year [33], and a third study reported no change in the number of transgender men (6/52, 12%) with a diagnosed anxiety disorder after 7 months [41]. Likewise, 2 other prospective studies found no difference in anxiety scores among transgender men (n = 37) after 24 weeks of treatment [42] or transgender women (n = 20) after 12 months [37], although this latter finding represented no change from a baseline median score of 0 (answering "no" to the question, "do you feel anxious?") on an unvalidated 3-point scale. Among adolescents, 1 prospective study saw mean anxiety scores in a mixed-gender group (n = 23) improve from 33.0 ± 7.2 to 18.5 ± 8.4 after 1 year ($P < 0.001$) [38], but another reported no changes in anxiety after approximately 2 years of puberty delay treatment with GnRH analogues and 4 years of hormone therapy (n = 32) [35]. No study found that hormone therapy increased anxiety. We conclude that hormone therapy may decrease anxiety among transgender people. The strength of evidence for this conclusion is low due to concerns about study designs, small sample sizes, and confounding.

Death by Suicide

One retrospective study reported in 2 publications assessed death by suicide (Table 5) [43, 44]. The first publication reported that 3 transgender women in the Amsterdam gender dysphoria study cohort (n = 303) died by suicide between 1972 and 1986 [43]. The authors calculated the number of suicide deaths expected in an age-matched stratum of

Table 3. Effects of Gender-Affirming Hormone Therapy on Depression Among Transgender People

Author, year Study design	Transgender population	Treatment / comparison (n)	Depression measures	Length of treatment	Findings
Gava, 2016 [28] Before-after trial	Women	Cyproterone acetate + estradiol (20) vs Leuprolide acetate + estradiol (20)	BDI-II	12 months	Mean depression scores did not change in either arm. No comparisons across arms were reported.
Fisher, 2016 [37] Prospective cohort	Women	HT (28)	BDI-II	24 months	Mean depression score decreased from 10.12 to 4.58 ($P < 0.001$).[d,e]
Defreyne, 2018 [33] Prospective cohort	Women	HT (91)[c]	HADS (depression subscale)	1 year	Median depression score decreased by 1.05 (95% CI: −1.87, −0.22) on a 21-point scale ($P = 0.013$).
Costantino, 2013 [32] Prospective cohort	Men	HT (50)	Ad hoc questionnaire	12 months	Depression score did not change from a median of 0.0 at baseline (IQR: 0.0, 1.0).
Fisher, 2016 [36] Prospective cohort	Men	HT (26)	BDI-II	24 months	Mean depression score decreased from 9.31 to 4.25 ($P < 0.001$).[d,e]
Defreyne, 2018 [33] Prospective cohort	Men	HT (64)[c]	HADS (depression subscale)	1 year	Median depression score decreased by 1.42 (95% CI: −2.61, −0.24) on a 21-point scale ($P = 0.019$).
Turan, 2018 [42] Prospective cohort[b]	Men	HT (37)	SCL-90-R (depression subscale)	24 weeks	Mean depression score did not change.
Metzger, 2019 [40] Prospective cohort[b]	Men	HT (23)	BDI-II	6 months	Mean depression score decreased from 15.7 ± 12.3 to 8.1 ± 6.2 ($P < 0.001$).
Colizzi, 2014 [31] Prospective cohort	Women and men	HT (107)	Zung SDS SCL-90-R (depression subscale)	12 months	Mean Zung SDS score improved from 48.40 ± 10.5 to 39.98 ± 10.79 ($P < 0.001$), and the proportion with Zung SDS scores indicating mild, moderate, or severe depression (vs no depression) decreased from 42% to 22% ($\chi^2 = 19.05$, $P < 0.001$). Mean SCL-90-R score decreased from 0.83 ± 0.74 to 0.51 ± 0.49 ($P < 0.001$), which represents an improvement from possible borderline depression to no depression.
Leavitt, 1980 [47] Cross-sectional	Women	HT (22) vs No HT (19)	MMPI (depression subscale)	At least 12 months	Mean depression score was lower in the group receiving HT vs the group not receiving HT (53.1 ± 14.7 vs 65.7 ± 11.2, $P = 0.004$).

Table 3. Continued

Author, year Study design	Transgender population	Treatment / comparison (n)	Depression measures	Length of treatment	Findings
Gómez-Gil, 2012 [45] Cross-sectional	Women and men	HT (120)[c] vs No HT (67)[c]	HADS (depression subscale)	Mean: 11.0 years (women, range, 1–46 years); 4.7 years (men, range, 1–22 years)	Mean depression score was lower in the group receiving HT vs the group not receiving HT (3.3 ± 3.2 vs 5.2 ± 4.2, $P = 0.002$).[f] The proportion with scores indicating depression (vs no depression) was larger in the group not receiving HT (31% vs 8%, $\chi^2 = 16.46$, $P = 0.001$).[f]
de Vries, 2011 [34] Prospective cohort	Girls and boys	GnRH treatment (41)	BDI	1.88 years	Mean depression score decreased from 8.31 ± 7.12 to 4.95 ± 6.72 ($P = 0.004$).
de Vries, 2014 [35] Prospective cohort[a,b]	Girls and boys	GnRH treatment + HT (32)[c]	BDI	5.9 years	Mean depression score did not change.
Achille, 2020 [30] Prospective cohort	Girls and boys	GnRH treatment + HT (47)	CESD-R, PHQ-9 (modified for adolescents)	12 months	Mean CESD-R score decreased from 21.4 to 13.9 ($P < 0.001$);[d] a score of <16 indicates no clinical depression. Mean PHQ-9 score decreased from 9.0 to 5.4 ($P < 0.001$).[d]
López de Lara, 2020 [38] Prospective cohort[b]	Girls and boys	GnRH treatment + HT (23)	BDI-II	1 year	Mean depression score decreased from 19.3 ± 5.5 to 9.7 ± 3.9 ($P < 0.001$).

Abbreviations: BDI/BDI-II, Beck Depression Inventory; GAS, gender-affirming surgery; GnRH, gonadotropin-releasing hormone; HADS, Hospital Anxiety and Depression Scale; HT, hormone therapy; IQR, interquartile range; MMPI, Minnesota Multiphasic Personality Inventory; NA, not applicable; SCL-90-R, Symptom Checklist 90-Revised; Zung SDS, Zung Self-Rating Depression Scale.

[a]All participants were also included in de Vries (2011) [34]

[b]Included a cisgender control group or a comparison to general population norms

[c]Included participants who had undergone gender-affirming surgery/surgeries, or surgery status not reported

[d]No standard deviations reported

[e]Adjusted for age, gender role, and surgery status

[f]Adjusted for age, gender, and education level

Table 4. Effects of Gender-Affirming Hormone Therapy on Anxiety Among Transgender People

Author, year	Transgender population	Treatment / comparison (n)	Anxiety measures	Length of treatment	Findings
Fuss, 2015 [37] Prospective cohort	Women	HT (20)[c]	Ad hoc questionnaire	12 months	Anxiety score did not change from a median of 0.0 at baseline.
Defreyne, 2018 [33] Prospective cohort	Women	HT (91)[c]	HADS (anxiety subscale)	1 year	Median anxiety score did not change.
Defreyne, 2018 [33] Prospective cohort	Men	HT (64)[c]	HADS (anxiety subscale)	1 year	Median anxiety score did not change.
Motta, 2018 [41] Prospective cohort	Men	HT (46)[c]	DSM	7 months	Proportion diagnosed with an anxiety disorder (6/46, 12%) did not change.
Turan, 2018 [42] Prospective cohort[b]	Men	HT (37)	SCL-90-R (anxiety subscale)	24 weeks	Mean anxiety score did not change.
Colizzi, 2014 [31] Prospective cohort	Women and men	HT (107)	SCL-90-R (anxiety subscale) Zung SAS	12 months	Mean SCL-90-R score decreased from 1.05 ± 0.95 to 0.54 ± 0.56 ($P < 0.001$), which represents an improvement from borderline anxiety disorder to no anxiety disorder. Mean Zung SAS score improved from 44.91 ± 9.59 to 37.90 ± 8.97 ($P < 0.001$), and the proportion with Zung SAS scores indicating mild, moderate, or severe anxiety (vs no anxiety) decreased from 50% to 17% ($\chi^2 = 33.03$, $P < 0.001$).
Gómez-Gil, 2012 [45] Cross-sectional	Women and men	HT (120)[c] vs No HT (67)[c]	HADS (anxiety subscale) SADS	Mean: 11.0 years (women, range, 1-46 years); 4.7 years (men, range, 1-22 years)	Mean HADS and SADS scores were lower in the group receiving HT vs the group not receiving HT (6.4 ± 3.7 vs 9.0 ± 4.0, $P = 0.001$; 8.5 ± 7.8 vs 11.0 ± 7.3, $P = 0.038$, respectively).[d] The proportion with scores indicating anxiety (vs no anxiety) was higher in the group not receiving HT ($\chi^2 = 14.46$, $P < 0.001$).[d]
de Vries, 2011 [34] Prospective cohort	Girls and boys	GnRH treatment (41)	STAI (trait subscale)	1.88 years	Mean anxiety score did not change.
de Vries, 2014 [35] Prospective cohort[a,b]	Girls and boys	GnRH treatment + HT (32)[c]	STAI (trait subscale)	5.9 years	Mean anxiety score did not change.
López de Lara, 2020 [38] Prospective cohort[b]	Girls and boys	GnRH treatment + HT (23)	STAI (trait subscale)	1 year	Mean anxiety score decreased from 33.0 ± 7.2 to 18.5 ± 8.4 ($P < 0.001$).

Abbreviations: BAI, Beck Anxiety Inventory; DSM, Diagnostic and Statistical Manual of Mental Disorders; GAS, gender-affirming surgery; GnRH, gonadotropin-releasing hormone; HADS, Hospital Anxiety and Depression Scale; HT, hormone therapy; IQR, interquartile range; SADS, Social Avoidance and Distress Scale; SCL-90-R, Symptom Checklist 90-Revised; STAI, State-Trait Anxiety Inventory; Zung SAS, Zung Self-Rating Anxiety Scale.

[a]All participants were also included in de Vries (2011) [34]

[b]Included a cisgender control group or a comparison to general population norms

[c]Included participants who have undergone gender-affirming surgery/surgeries, or surgery status not reported

[d]Adjusted for age, gender, and education level

the general male Dutch population over this period to be 0.208. No data were reported for transgender men (n = 122). An update to this study reported 17 deaths by suicide among transgender women (n = 966) and 1 among transgender men (n = 365) between 1975 and 2007 [44]. The age- and sex-stratified standardized mortality ratios were 5.70 (95% CI: 4.93, 6.54) and 2.22 (95% CI: 0.53, 6.18), respectively. The risk of bias for this study was serious due to the difficulty of identifying appropriate comparison groups and uncontrolled confounding by surgery

Table 5. Effects of Gender-Affirming Hormone Therapy on Death by Suicide Among Transgender People

Author, year	Transgender population	Treatment / comparison (n)	Measures	Length of treatment	Findings
Asscheman, 1989 [43] Retrospective cohort[a,b]	Women	HT (303)[c]	Death by suicide (confirmed by autopsy report)	Median: 4.4 years (range, 6 months to 13 years)	3 transgender women (1%) died by suicide between 1972 and 1986. The adjusted number of suicide deaths expected among the general Dutch male population was 0.208.
Asscheman, 2011 [44] Retrospective cohort[a,b]	Women	HT (966)[c]	Death by suicide (confirmed by medical report or physician information)	Median: 18.6 years (range, 0.7–44.5 years)	17 transgender women (2%) died by suicide between 1975 and 2007. The age-stratified SMR compared to the general Dutch male population was 5.70 (95% CI: 4.93, 6.54).
Asscheman, 1989 [43] Retrospective cohort[a,b]	Men	HT (122)[c]	Death by suicide (confirmation procedure NR)	Median: 3.6 years (range, 6 months to 13 years)	No deaths by suicide among transgender men were reported during the study period.
Asscheman, 2011 [44] Retrospective cohort[a,b]	Men	HT (365)[c]	Death by suicide (confirmed by medical report or physician information)	Median: 18.4 years (range, 4.7–42.6 years)	1 transgender man (0.3%) died by suicide between 1975 and 2007. The age-stratified SMR compared to the general Dutch female population was 2.22 (95% CI: 0.53, 6.18).

Abbreviations: HT, hormone therapy; NR, not reported; SMR, standardized mortality ratio.
[a]An unknown number of participants were included in both Asscheman (1989) [43] and Asscheman (2011) [44]
[b]Included a cisgender control group or a comparison to general population norms
[c]Includes participants who had undergone gender-affirming surgery/surgeries, or surgery status not reported

status and socioeconomic variables such as unemployment. We cannot draw any conclusions on the basis of this single study about whether hormone therapy affects death by suicide among transgender people.

Discussion

This systematic review of 20 studies found evidence that gender-affirming hormone therapy may be associated with improvements in QOL scores and decreases in depression and anxiety symptoms among transgender people. Associations were similar across gender identity and age. The strength of evidence for these conclusions is low due to methodological limitations (Table 6). It was impossible to draw conclusions about the effects of hormone therapy on death by suicide.

Uncontrolled confounding was a major limitation in this literature. Many studies simultaneously assessed different types of gender-affirming care and did not control for gender-affirming surgery status, making it difficult to isolate the effects of hormone therapy. Others failed to report complete information about surgery status. Additional factors that may influence both access to care and psychological outcomes, including extent of social or legal gender affirmation and exposure to determinants of health such as discrimination, were typically not considered. In addition, some evidence indicates that cyproterone acetate, a common anti-androgen assessed in many studies alongside estrogen therapy, may increase depression, which may be a source of confounding [49].

Another source of potential bias was recruitment of participants from specialized clinics that impose strict diagnostic criteria as a prerequisite for gender-affirming care. The dual role of clinicians and researchers as both gatekeepers and investigators may force transgender study participants to over- or understate aspects of their mental health in order to access gender-affirming care [8]. Similarly, transgender clinic patients may feel that they cannot opt out of research-related activities, which is a serious concern for the validity of psychological outcome measurements.

Clinic-based recruitment also overlooks transgender people who cannot access these clinics for financial or other reasons and misses those whose need for gender affirmation does not fit into current medical models. This is a particular concern for nonbinary and other gender-diverse people, for whom a model of gender affirmation as a linear transition from one binary gender to another is inaccurate [50].

Most studies used well-known scales for measuring psychological outcomes. None of these scales, however, have been specifically validated for use in transgender populations [51]. Furthermore, many scales are normed

Table 6. Strength of Evidence of Studies that Evaluate the Psychological Effects of Hormone Therapy Among Transgender People

Outcome	Number of studies (n)	Strength of evidence	Summary[a]
Quality of life	1 randomized controlled trial [27] (45)[b] 2 before-after trials [28, 29] (65)[b] 2 prospective cohorts [30, 39] (133) 2 cross-sectional studies [46, 48] (108)	Low[e]	Hormone therapy may improve quality of life among transgender people.[g]
Depression	1 before-after trial [28] (40) 9 prospective cohorts [30-36, 38, 40, 42] (569)[c] 2 cross-sectional [45, 47] (228)	Low[e]	Hormone therapy may alleviate depression among transgender people.[g]
Anxiety	7 prospective cohorts [31, 33-35, 37, 38, 41, 42] (464)[c] 1 cross-sectional [45] (187)	Low[e]	Hormone therapy may alleviate anxiety among transgender people.[g]
Death by suicide	1 retrospective cohort [43, 44] (1756)[d]	Insufficient[f]	There is insufficient evidence to draw a conclusion about the effect of hormone therapy on death by suicide among transgender people.

[a]Due to similarity of findings, the summary is the same for transgender men and transgender women and for adolescents and adults
[b]25 participants are included in both Pelusi [27] and Gava (2018) [29] and are counted once
[c]All 55 participants in de Vries (2014) [35] were also included among the 70 participants in de Vries (2011) [34] and are counted once
[d]An unknown number of participants were included in both Asscheman (1989) [43] and Asscheman (2011), [44] so the unique sample size is smaller than indicated here
[e]Evidence downgraded due to study limitations, including uncontrolled confounding, and imprecision because of small sample sizes
[f]Evidence downgraded due to study limitations, including confounding and a lack of meaningful comparison groups, and imprecision in measurement of a rare event
[g]The body of cross-sectional evidence tended to align with the conclusion

separately for (presumed cisgender) men and women [52]. Inconsistency in identification of appropriate general population norms hinders comparisons between transgender and cisgender groups, which is a major related research question that requires further investigation.

Beyond methodological concerns in the studies we assessed, our review has other limitations. First, it is likely subject to publication bias, as we may have missed studies not published in the peer-reviewed literature. Second, a number of potentially relevant studies could not be included because the authors did not report on a minimum of 3 months of treatment or did not clearly state the type and/or duration of therapy, including the range for cross-sectional studies [53-65]. Finally, even where outcome measurements were similar across studies, heterogeneity in study designs, study populations, intervention characteristics, and reporting of results (ie, some studies reported results separately by gender identity, while others did not), prevented us from quantitatively pooling results.

More research is needed to further explore the relationship between gender-affirming hormone therapy and QOL, death by suicide, and other psychological outcomes, especially among adolescents. Future studies should investigate these outcomes in larger groups of diverse participants recruited outside clinical settings. Studies assessing the relationship between gender-affirming hormone therapy and mental health outcomes in transgender populations should be prospective or use strong quasi-experimental designs; consistently report type, dose, and duration of hormone therapy; adjust for possible confounding by gender-affirming surgery status; control for other variables that may independently influence psychological outcomes; and report results separately by gender identity. Despite the limitations of the available evidence, however, our review indicates that gender-affirming hormone therapy is likely associated with improvements in QOL, depression, and anxiety. No studies showed that hormone therapy harms mental health or quality of life among transgender people. These benefits make hormone therapy an essential component of care that promotes the health and well-being of transgender people.

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