No. 23-12155

## UNITED STATES COURT OF APPEALS FOR THE ELEVENTH CIRCUIT

August Dekker et al., Plaintiffs-Appellees,<br>v.<br>Secretary, Florida Agency for Health Care Administration et al., Defendants-Appellants.

U.S. District Court for the Northern District of Florida, No. 4:22-cv-325 (Hinkle, J.)

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Mohammad O. Jazil
Gary Perko
Michael Beato
Holtzman Vogel Baran
TORCHINSKY \& JOSEFLAK PLLC
119 South Monroe Street, Suite 500
Tallahassee, FL 32301
(850) 274-1690

Counsel for Defendants-Appellants

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/s/ Mohammad O. Jazil<br>Mohammad O. Jazil<br>Gary Perko<br>Michael Beato<br>Holtzman Vogel Baran<br>TORCHINSKy \& Josefiak PLLC<br>119 South Monroe Street, Suite 500<br>Tallahassee, FL 32301<br>Phone: (850) 391-0503<br>Facsimile: (850) 741-1023<br>mjazil@holtzmanvogel.com<br>mbeato@holtzmanvogel.com<br>Counsel for Appellants-Defendants

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. $\mathrm{HCPs}_{\mathrm{s}} /$ 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 l) 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 nonbinarywhich first emerged in approximately the late 2000 s (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 $A M A B$ ), 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 genderaffirming 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 $A M A B$, 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 $A F A B$ 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


#### Abstract

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 testos-terone-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 16Reproductive 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


#### Abstract

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 iden-tity-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 nistenporosis, 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 16Reproductive 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 2Global 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 surgerymay 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 nonbinary 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 21 st 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 1:20001:4500 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 100,00046 , 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


#### Abstract

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 transdisciplinaryand 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 20 th 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 $46, \mathrm{XY} 5 a-\mathrm{RD}-2$ 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 hack 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, genderquestioning, 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 decisinns 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.

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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 $5 a$-reductase-2 ( $5 a-\mathrm{RD}-2$ ) 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 12Hormone 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 5a-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., $46, \mathrm{XX} \mathrm{CAH}$ ) 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 $46, \mathrm{XX}$ 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 2Global 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 5Assessment 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 l-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 heaith 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.

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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 hypettension 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-B-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 6.12 d 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 6Adolescents 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 $\mathbf{1 2 . 1 5}$.

## 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-tohead 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 ( $17 \beta$-estradiol gel $1.5 \mathrm{mg} / \mathrm{d}$ or estradiol patch $50 \mathrm{mcg} / \mathrm{d}$ ) or a daily intake of oral estrogens (estradiol $2 \mathrm{mg} / \mathrm{d}$, estriol $2 \mathrm{mg} / \mathrm{d}$, ethinyl estradiol $50 \mathrm{mcg} /$ day, or ethinyl estradiol $30-50 \mathrm{mcg}$ 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 (TLA/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 $2 \mathrm{mg} / \mathrm{d}$, estriol $2 \mathrm{mg} / \mathrm{d}$ or ethinyl estradiol $50-120 \mathrm{mcg} /$ day) or using transdermal estradiol ( $17 \beta$-estradiol $1.5 \mathrm{mg} /$ day or estradiol $50 \mathrm{mcg} /$ day) over a follow-up duration of 9.2 years (Wierckx, Mueller et al., 2012). Twelve percent ( $\mathrm{n}=6$ ) developed either a VTE, MI, or a TIA/CVA. Two of the participants were taking conjugated estrogen $0.625 \mathrm{mg} / \mathrm{d}$ (one per son in combination with cyproterone acetate), 2 participants were taking ethinyl estradiol $20-50 \mathrm{mcg} / \mathrm{d}$, 1 was taking cyproterone acetate $50 \mathrm{mg} / \mathrm{d}$, 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 ( $\mathrm{n}=40$ ) received estradiol valerate $4 \mathrm{mg} / \mathrm{d}$ in combination with cyproterone acetate (CPA) $50 \mathrm{mg} / \mathrm{d}$ and transgender women older than 45 years of age ( $\mathrm{n}=13$ ) received transdermal $17 \beta$-estradiol, also with CPA. No VTE, MI, or TLA/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 catradiol 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 meningio-mas-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 spironolactoneor 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 ( $>10 \mathrm{mg}$ 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 $5 a$-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 $5 \alpha$-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 $5 a$-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 $5 a$-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 $25-250 \mathrm{mg}$ 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 $\mathbf{1 2 . 1 9 .}$

## 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 $\mathbf{1 2 . 2 1}$.

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 $A M A B$, 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


#### Abstract

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 ct al., 2017; Capitán ct 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 5Assessment 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

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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 genderaffirming 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 spec trum, 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

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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

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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 <br> - Brow augmentation <br> - 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 <br> - Lipofilling |
| Lip | - Upper lip shortening <br> - Lip augmentation (includes autologous and non-autologous) |
| Lower jaw | - Reduction of mandibular angle <br> - Augmentation |
| Chin reshaping | - Osteoplastic <br> - 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 <br> - Mastectomy without nipple-areola preservation/reconstruction as determined medically necessary for the specific patient |
| Liposuction |  |
| Breast reconstruction (augmentation) | - Implant and/or tissue expander <br> - Autologous (includes flap-based and lipofiling) |
| GENITAL SURGERY |  |
| Phalloplasty (with/without scrotoplasty) | - With/without urethral lengthening <br> - With/without prosthesis (penile and/or testicular) <br> - With/without colpectomy/colpocleisis |
| Metoidioplasty (with/without scrotoplasty) | - With/without urethral lengthening <br> - With/without prosthesis (penile and/or testicular) <br> - 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 <br> - 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,


#### Abstract

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 $\left(f_{0}\right)$ ) 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 $f_{0}$, 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 genderand 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 $f 0$ 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 'l'il 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 genderaffirming 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.


#### Abstract

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 abtain 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

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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 lifesfan in Trin 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.

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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 testosteronebased 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 ( $\mathrm{n}=85$ ) (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 ${ }_{i P r} E x$ 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 $\operatorname{PrEP}$ 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 gonadectumy. Therefure, 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-B 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 ( $\mathrm{n}=247$ ) 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 resulls un BMD vulcumes 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-relcasing 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 adolcscence) 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 TP 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

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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. (202I) 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 genderaffirming 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-invagina 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 allonorma-tivity-the assumption that all people experience sexual attraction or interest in sexual activitynegates 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


#### Abstract

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 $\operatorname{PrEP}$ 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 $\operatorname{PrEP}$ 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 $\operatorname{PrEP}$ ), 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 $\operatorname{PrEP}$ use, have shown reduced PrEP drug concentrations in transgender women undergoing hormone therapy, although

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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 $\operatorname{PrEP}$ 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

[^0]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 genderaffirming 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 emutional 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 reseancla shuws, 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 genderaffirming 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 ${ }^{\text {e }}$, Embase ${ }^{m}$, 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

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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 pracess

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

| 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)
$\left.\begin{array}{lll}\hline \text { RISK LEVEL }\end{array} \quad \begin{array}{l}\text { Estrogen-based regimens }\end{array} \quad \begin{array}{c}\text { Testosterone-based } \\ \text { regimens }\end{array}\right]$

[^1]${ }^{5}$ 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 17B-estradiol
Initiate at $5 \mu \mathrm{~g} / \mathrm{kg} / \mathrm{d}$ and increase every 6 months by $5 \mu \mathrm{~g} / \mathrm{kg} / \mathrm{d}$ up to $20 \mu \mathrm{~g} / \mathrm{kg} / \mathrm{d}$ according to estradiol levels
Adult dose $=2-6 \mathrm{mg} /$ day
In postpubertal TGD adolescents, the dose of $17 ß$-estradiol can be increased more rapidly:
$1 \mathrm{mg} / \mathrm{d}$ for 6 months followed by $2 \mathrm{mg} / \mathrm{d}$ and up according to estradiol levels
Induction of female puberty (estrogen-based regimen) with transdermal 17ß-estradiol
Initial dose $6.25-12.5 \mu \mathrm{~g} / 24 \mathrm{~h}$ (cutting 24 g patch to $1 / 4$ then $1 / 2$ )
Titrate up by every 6 months by $12.5 \mu \mathrm{~g} / 24 \mathrm{~h}$ according to estradiol levels
Adult dose $=50-200 \mu \mathrm{~g} / 24$ hours
For alternatives once at adult dose (Table 4)
induction of male puberty (testosterone-based regimen) with testosterone esters
$25 \mathrm{mg} / \mathrm{m}^{2} / 2$ weeks (or alternatively half this dose weekly)
Increase by $25 \mathrm{mg} / \mathrm{m}^{2} / 2$ 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 |$\quad 2.0-6.0 \mathrm{mg} /$ day

Transdermal
Estradiol transdermal patch $\quad 0.025-0.2 \mathrm{mg} /$ day Estradiol gel various $\quad \ddagger$ daily to skin Parenteral

Estradial valerate or cypionate $\quad 5-30 \mathrm{mg} \mathrm{IM}$ every 2 weeks 2-10 IM every week
Anti-Androgens
Spironolactone $\quad 100-300 \mathrm{mg} /$ day
Cyproterone acetate $\quad 10 \mathrm{mg} /$ day $^{* *}$
GnRH agonist $\quad 3.75-7.50 \mathrm{mg}$ SQ/M monthly
GnRH agonist depot formulation $\quad 11.25 / 22.5 \mathrm{mg}$ SQ/M $3 / 6$ monthly
₹ Amount applied varies to formulation and strength
Testosterone-Based Regimen (Transmasculine)
Transgender males
Testosterone
Parenteral
Testosterone enanthate/ $\quad 50-100 \mathrm{IM} / \mathrm{SQ}$ weekly or
cypionate $\quad 100-200 \mathrm{IM}$ every 2 weeks Testosterone undecanoate $\quad 1000 \mathrm{mg}$ IM every 12 weeks or 750 mg IM every 10 week
Transdermal testosterone
Testosterone gel $\quad 50-100 \mathrm{mg} /$ day Testosterone transdermal patch $\quad 2.5-7.5 \mathrm{mg} /$ 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 $400-700 \mathrm{ng} / \mathrm{dL}$.

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 $<400 \mathrm{ng} / \mathrm{dL}$, 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 $50 \mathrm{ng} / \mathrm{dL}$.
b. Serum estradiol should be in the range of $100-200 \mathrm{pg} / \mathrm{mL}$.
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.


## Doc. 193-17

Establishing the soc8 Revision committee and meet the chairs and lead evidence team


### 2.1 Establishing SOC Revision

 Committee ProcessThe Standards of Care 8 revision started by identifying a multidisciplinary team of clinicians, researchers and stakeholders using a clearly defined process. The following steps were followed to select the members of the SOC8 review committee:

### 2.1.1 Establish Guideline Steering Committee

The WPATH Guideline Steering Committee provided oversight of the guideline development process for all chapters of the Standards of Care. Except for the Chair (Dr Eli Coleman) who was selected by WPATH to provide continuity from previous SOC, the two co-chairs were selected by the WPATH Board from WPATH members applying for these positions. The Chairs of the Guideline Steering Committee:

- Appointed the Chapter Leads and Members for each chapter
- Selected topics for the chapters

The Guideline Steering Committee (chairs and Co-chairs) provided general oversight of the guideline development process. The Committee reviewed all chapters of the Standards of Care to confirm adherence to the WPATH guideline methodology and to ensure consistency of statements across the Standards of Care.

### 2.1.2 Nomination Procedures and selection for $\mathrm{CO}_{0}$-Chairs

- A member of WPATH proposed a candidate for co-chair by sending a letter of nomination and the address of the recommended co-chair, to the Executive Director of the Society.
- A Member of WPATH could self-nominate, by sending a letter of self-nomination to the Executive Director of the Society.
- The Executive Director (ED) sent a membership application form, including a request for a curriculum vitae, to the nominated individual.
- The ED distributed copies of the nominating letter, completed application, and curriculum vitae to the Board of Directors.
- The BOD discussed each application and assigns a score in a blinded ballot only seen by the office staff across the application criteria with the three top candidates moving to the next round of voting.
- Any conflict of interest was declared and in the case of a conflict of interest, the conflicted person did not vote.
- The BOD discussed the nominees with the Chair, and best fit for the group was chosen.
- The ED corresponded with the candidate and the nominator regarding the action on each nomination.


### 2.1.2.1 Key Criteria Used for the Selection of Co-Chair on the SOC8 Revision Committee (2 positions)

- Longstanding WPATH Full Member in good standing
- Well recognized advocate for WPATH and the SOC
- Well known expert in transgender health
- Extensive experience in leading consensus building projects and guideline development
- Accomplished clinician, scholar, and researcher in trans health with a publication record
- Able to assess the evidence-based and peer review literature and peer and contribute specific recommendations from an evidence-based perspective
- Able to select and supervise chapter leads


### 2.1.2.1 Results

A total of 8 individuals applied for two positions and 2 people were selected, Dr. Asa Radix and Dr. Jon Arcelus.

### 2.1.3 Nomination and selection procedures for Chapter Leads

- A member of WPATH proposed a candidate for a chapter lead by sending a letter of nomination, including address of the recommended chapter lead (and indicated chapter(s)), to the Executive Director (ED) of the Society.
- A member of WPATH could self-nominate by sending a letter of self-nomination to the ED of the Society.
- The ED sent a membership application form, including a request for a curriculum vitae, to the nominated individual.
- The ED distributes copies of the nominating letter, completed application, and curriculum vitae to the Chair and Co-Chairs.
- The Chair and Co-Chairs discussed the applications and assign a score in a blinded ballot only seen by the office staff across the application criteria with the top 2 candidates moving to the next round of voting. The Chair and Co-Chairs discussed the top 2 candidates with the goal of selecting the best fit for the topic and the other members of the workgroup.
- The Chair and Co-Chairs informed the BOD of their decisions.
- The ED corresponded with the candidate and the nominator regarding the action on each nomination.


### 2.1.3.1 Key Criteria for Chapter Lead on the SOC Revision Committee

- WPATH Full Member in good standing
- Well recognized advocate for WPATH and the SOC
- Well known expert in transgender health
- Accomplished scholar and researcher in trans health with a publication record related to the chapter
- Accomplished clinician, scholar, and researcher in trans health with a publication record
- Able to assess the evidence-based literature and write chapters based on peer review or contribute


### 2.1.3.2 Results

A total of 39 applicants and 24 were selected.

### 2.1.4 Nomination Procedures and selection for Chapter Workgroup Members

- A member of WPATH proposed a candidate for a chapter workgroup member by sending a letter of nomination, including address of the recommended new member, to the Executive Director (ED) of the Society
- A member of WPATH could self-nominate, by sending a letter of self-nomination to the ED of the Society
- The ED sent a membership application form, including a request for a curriculum vitae, to the nominated individual.
- The ED distributed copies of the nominating letter, completed application, and curriculum vitae to the Chapter Leads.
- The Chair and Co-Chairs and Chapter Leads discuss the applications and assign a score in a blinded ballot only seen by the office staff across the application criteria with the top 5-7 candidates (number to be determined prior to voting) within each chapter being chosen.
- The Chair, Co-Chairs and Chapter Lead informed the BOD of their decisions.
- The ED corresponded with the candidate and the nominator regarding the action on each nomination.


### 2.1.4.1 Key Criteria for Chapter Workgroup Member on the SOC8 Revision Committee (5-7 people per chapter)

- WPATH Full Member in good standing
- Well known expert in transgender health
- Accomplished scholar and researcher in trans health with a publication record related to the chapter
- Able to assess the evidence-based literature and write chapters related to peer review or contribute specific recommendations from an evidence-based perspective
- Able and willing to work collaboratively with chapter leads and other committee members
- Applicants could apply to work on more than one workgroup and rank their chapter interests.


### 2.1.4.2 Results

A total of 149 applicants for workgroup members applied and 127 were selected (link it to a page with names of the chairs, leads)

### 2.1.5 Nomination and selection procedures for Chapter Stakeholder Members

- A member of WPATH proposed a candidate for a chapter workgroup member by sending a letter of nomination, including address of the recommended new member, to the Executive Dircctor (ED) of the Socicty
- A person could self-nominate, by sending a letter of self-nomination to the ED of the Society
- The ED sent a committee membership application form, including a request for a curriculum vitae, to the nominated individual.
- The ED distributed copies of the nominating letter, completed application, and curriculum vitae to the Chapter Leads.
- The Chair and Co-Chairs and Chapter Leads discussed the applications and assign a score in a blinded ballot only seen by the office staff across the application criteria with the top 2 candidates (number to be determined prior to voting) per chapter being chosen.
- The Chair, Co-Chairs and Chapter Leads discussed the top 2 candidates and the best fit within each chapter group were chosen.
- The Chair, Co-Chairs and Chapter Lead informed the BOD of their decisions.
- The ED corresponded with the candidate and the nominator regarding the action on each nomination.


### 2.1.5.1 Key Criteria for Stakeholder Membership on the SOC8 Revision Committee

Our intent was that by involving experts (with or without lived experience) that work outside of the scientific publishing arena, we will be able to provide input from those working directly in community health or in policy making and in NGOs around the globe.

- Associate Members of WPATH (with or without lived transgender experience) and other individuals (with or without lived transgender experience) with expertise due to accomplishments in trans health advocacy and a history of work in the community, or a member of a family that includes a transgender child, sibling, partner, parent, etc.
- Able to review the drafts of the SOC committee and contribute specific recommendations from a community health perspective


### 2.1.5.2 Results

A total of 57 and 20 were selected.

### 2.1.6 Selection of the evidence review team

The WPATH Board released a request for proposals (RFP) for the WPATH Standards of Care 8th Version Evidence Review Team. The Board received four complete proposals in response to the RFP. After careful review and discussions of each submitted proposal, the WPATH Board selected and engaged an Evidence Review Team at Johns Hopkins University. Dr Karen Robinson was the lead of the evidence-based review.

## Conflict of Interest

Members of the Guideline Steering Committee, Chapter Leads and Members, and members of the Evidence Review Team are asked to disclose any conflicts of interest. Also reported, in addition to potential financial and competing interests or conflicts, were 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.

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## WPATH

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Doc. 193-24

# Endocrine Treatment of Gender-Dysphorid Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline 

Wylie C. Hembree, ${ }^{1}$ Peggy T. Cohen-Kettenis, ${ }^{2}$ Louis Gooren, ${ }^{3}$ Sabine E. Hannema, ${ }^{4}$ Walter J. Meyer, ${ }^{5}$ M. Hassan Murad, ${ }^{6}$ Stephen M. Rosenthal, ${ }^{7}$ Joshua D. Safer, ${ }^{8}$ Vin Tangpricha, ${ }^{9}$ and Guy G. T'Sjoen ${ }^{10}$<br>${ }^{1}$ New York Presbyterian Hospital, Columbia University Medical Center, New York, New York 10032 (Retired); ${ }^{2} \mathrm{~V} U$ University Medical Center, 1007 MB Amsterdam, Netherlands (Retired); ${ }^{3} \mathrm{VU}$ University Medical Center, 1007 MB Amsterdam, Netherlands (Retired); ${ }^{4}$ Leiden University Medical Center, 2300 RC Leiden, Netherlands; ${ }^{5}$ University of Texas Medical Branch, Galveston, Texas 77555; ${ }^{6}$ Mayo Clinic EvidenceBased Practice Center, Rochester, Minnesota 55905; ${ }^{7}$ University of California San Francisco, Benioff Children's Hospital, San Francisco, California 94143; ${ }^{8}$ Boston University School of Medicine, Boston, Massachusetts $02118 ;{ }^{9}$ Emory University School of Medicine and the Atlanta VA Medical Center, Atlanta, Georgia 30322; and ${ }^{10}$ Ghent University Hospital, 9000 Ghent, Belgium

*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 genetidgonadal 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-dysphoridgender-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

[^2]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


#### Abstract

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-dysphoridgender-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-dysphoridgender-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 psychopachology, (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 yourhs 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. ( $1 \oplus \oplus \bigcirc \bigcirc$ )
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. ( $1 \stackrel{\oplus \oplus(\mathrm{O})}{(~)}$

### 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 $\downarrow \nLeftarrow \bigcirc \bigcirc)$
2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty. ( $2 \mathrm{l} \oplus \bigcirc 0$ )
2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. ( $1 \mathrm{\oplus} \oplus \bigcirc \bigcirc$ )
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. ( $1 \mathrm{I} \oplus \in O O$ ).
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 $\geq 16$ years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this trearment. ( $1 \oplus \bigcirc 00$ )
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 $1 \oplus($

### 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. ( $1 \oplus \oplus \oplus \bigcirc$ )
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. ( $1 \oplus \oplus \oplus \bigcirc$ )
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 $\mid \oplus \oplus \bigcirc O$ )
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. ( $2 \mathrm{l} \oplus \mathrm{O} 00$ )

### 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. ( $2 \| \in \bigcirc 0$ )
4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. ( 2 ノ $\odot \bigcirc$ )
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. ( $2 \mathrm{l} \oplus \oplus \bigcirc \bigcirc$ )
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. ( $1 \oplus \oplus \oplus \bigcirc$ )
4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for non-transgender females. ( $21 \oplus \oplus \bigcirc \bigcirc$ )
4.6. We suggest that transgender females treared with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 19000)
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. ( $1 \oplus \oplus \oplus O$ )
5.2. We advise that clinicians approve genital genderaffirming 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 hormonetreated 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. ( $1 \mathrm{l} \oplus \bigcirc \bigcirc \bigcirc$ )
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 $\mid \oplus \oplus \bigcirc \bigcirc$ ).
5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and menral health status of the individual. There is insufficient evidence to recommend a specific age requirement. ( $2 \mid \oplus \bigcirc O O$ )

## Changes Since the Previous Guideline

Bort 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 trear 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 genderconfirming 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 rask 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 $\oplus 000$ denotes very low-quality evidence; $\Theta \ominus \bigcirc \bigcirc$, low quality; $\oplus \oplus \oplus \bigcirc$, moderate quality; and $\oplus \oplus \oplus \oplus$, 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
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 carc 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-ofinterest 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 derreased 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 $46, \mathrm{XX}$ 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 porential role of androgens in the development of gender identity in other individuals with DSD. For example, a review of two groups of $46, \mathrm{XY}$ 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

## 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 surgen): 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 srudies 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 stili 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 rext 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, hormoneprescribing 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 genderaffirming 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:
7. The condition exists with a disorder of sex development.
8. 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).

[^3]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 abour 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 genderaffirming 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) comperence 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) comperence 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 \geqG2/B2),
    - has confirmed that there are no medical contraindications to GnRH agonist treatment.
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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.

[^4]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, parricularly when the conditions may complicate treatment, affect the outcome of genderaffirming 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. ( $1 \mid \oplus \oplus \bigcirc \bigcirc$ )

## 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, sucial 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 gendervariant 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. ( $1 \mid \oplus \oplus \oplus \bigcirc$ )

## 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 $\mathrm{MHP}(\mathrm{s})$, 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 gamere maturation is an option. This option is often not preferred, because mature sperm production is associared 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 genderaffirming 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 $\sim 2$ years later. In boys, the first physical change is testicular growth. A testicular volume $\geq 4 \mathrm{~mL}$ 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 trearment (Table 5), and are requesting treatment should initially undergo treatment to suppress pubertal development. ( $2 \oplus \oplus \oplus \bigcirc \bigcirc$ )
2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty (Tanner stages $\mathrm{G} 2 / \mathrm{B} 2$ ). ( $2 \mid \oplus \oplus \mathrm{O}$ )

## 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 complered ( 60,62 ). Looking like a man or woman when living as the opposite sex creates difficult
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 oprimal 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. ( $1 \mathrm{I} \oplus \oplus \bigcirc \bigcirc$ )

## 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 $\sim 10$ 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 longacting 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

[^5][^6]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 genderreassignment 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 longterm 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 $14.9( \pm 1.9)$ 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 $16.6( \pm 1.4)$
years for a median duration of 5.8 years ( 3.0 to 8.0 years) in transgender females and from age $16.4( \pm 2.3)$ 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 trearments 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/genderincongruent 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
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 crosssectional 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 furcher 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 dualenergy 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). ( $1 \mathrm{I} \oplus \oplus \bigcirc \bigcirc$ )
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 $\geq 16$ years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. ( 1 Һ○OO)
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 $1 \oplus \oplus \bigcirc 0$ )

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

[^7]
## Table 8. Protocol Induction of Puberty

```
Induction of female puberty with oral 17\beta-estradiol, increasing the dose every }6\textrm{mo
    5 g/kg/d
    10 \mug/kg/d
    15 \mug/kg/d
    20 \mug/kg/d
    Adult dose = 2-6 mg/d
    In postpubertal transgender female adolescents, the dose of 17\beta-estradiol can be increased more rapidly:
        1 mg/d for 6 mo
        2 mg/d
Induction of female puberty with transdermal 17\beta-estradiol, increasing the dose every }6\mathrm{ mo (new patch is placed every 3.5 d):
    6.25-12.5 \mug/24 h (cut 25-\mug patch into quarters, then halves)
    25 \mug/24 h
    37.5 \mug/24 h
    Adult dose = 50-200 \mug/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):
$25 \mathrm{mg} / \mathrm{m}^{2} / 2 \mathrm{wk}$ (or alternatively, half this dose weekly, or double the dose every 4 wk )
$50 \mathrm{mg} / \mathrm{m}^{2} / 2 \mathrm{wk}$
$75 \mathrm{mg} / \mathrm{m}^{2} / 2 \mathrm{wk}$
$100 \mathrm{mg} / \mathrm{m}^{2} / 2 \mathrm{wk}$
Adult dose $=100-200 \mathrm{mg}$ every 2 wk
in postpubertal transgender male adolescents the dose of testosterone esters can be increased more rapidly:
$75 \mathrm{mg} / 2 \mathrm{wk}$ for 6 mo
$125 \mathrm{mg} / 2 \mathrm{wk}$
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, 250 H vitamin D
- In transgender females: prolactin, estradiol, 250 H 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.
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 $17 \beta$-estradiol may be an alternative for oral $17 \beta$-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 initiared 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 trearment 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 restosterone 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 ream 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. ( $1 \mathrm{l} \oplus \oplus \oplus \mathrm{O}$ )
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). ( $1 \mathrm{l} \oplus \oplus \oplus \bigcirc$ )
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. ( $2 \mid \oplus \oplus \bigcirc O$ )

## 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 $1000 \mathrm{ng} / \mathrm{dL}$ ) (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
```

Table 11. Hormone Regimens in Transgender Persons

| Transgender females ${ }^{\text {a }}$ |  |
| :---: | :---: |
| Estrogen |  |
| Oral |  |
| Estradiol | $2.0-6.0 \mathrm{mg} / \mathrm{d}$ |
| Transdermal |  |
| Estradiol transdermal patch | 0.025-0.2 mg/d |
| Parenteral |  |
| Estradiol valerate or cypionate | $5-30 \mathrm{mg} \mid \mathrm{M}$ every 2 wk $2-10 \mathrm{mg}$ IM every week |
| Anti-androgens |  |
| Spironolactone | 100-300 mg/d |
| Cyproterone acetate ${ }^{\text {b }}$ | $25-50 \mathrm{mg} / \mathrm{d}$ |
| GnRH agonist | $3.75 \mathrm{mg} \mathrm{SQ}(\mathrm{SC})$ monthly 11.25 mg SQ (SC) 3-monthly |
| Transgender males |  |
| Testosterone |  |
| Parenteral testosterone |  |
| Testosterone enanthate or cypionate |  |
| Testosterone undecanoate ${ }^{\text {c }}$ | 1000 mg every 12 wk |
| Transdermal testosterone |  |
| Testosterone gel $1.6 \%^{\text {d }}$ | $50-100 \mathrm{mg} / \mathrm{d}$ |
| Testosterone transdermal patch | $2.5-7.5 \mathrm{mg} / \mathrm{d}$ |

Abbreviations: IM, intramuscularly; SQ, sequentially; SC, subcutaneously.
${ }^{\text {a }}$ Estrogens used with or without antiandrogens or GnRH agonist.
${ }^{b}$ Not available in the United States.
${ }^{\text {c }}$ One thousand milligrams initially followed by an injection at 6 wk then at 12 -wk intervals.
${ }^{\sigma}$ 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. $5 \alpha$-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 restosterone 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 $17 \beta$-estradiol, or transdermal $17 \beta$-estradiol. Among estrogen options, the increased risk of thronboembolic 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 estrugen 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-dependenr. Injecrable 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 $200 \mathrm{pg} / \mathrm{mL}$ and $<50 \mathrm{ng} / \mathrm{dL}$, 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 genderaffirming 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 benefirs of gender-affirming hormones prior to initiating therapy. Clinicians should strongly encourage tobacco use cessation in rransgender 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 evidencebased 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. ( $2 \mathrm{I} \oplus \bigcirc O O$ )

## 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.

Alchough 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. <br> Males | Masculinizing Effects in Transgender |  |
| :--- | :---: | :---: |
| Effect | Onset | Maximum |
| Skin oiliness/acne | $1-6 \mathrm{mo}$ | $1-2 \mathrm{y}$ |
| Facial/body hair growth | $6-12 \mathrm{mo}$ | $4-5 \mathrm{y}$ |
| Scalp hair loss | $6-12 \mathrm{mo}$ | -a |
| Increased muscle mass/strength | $6-12 \mathrm{mo}$ | $2-5 \mathrm{y}$ |
| Fat redistribution | $1-6 \mathrm{mo}$ | $2-5 \mathrm{y}$ |
| Cessation of menses | $1-6 \mathrm{mo}$ | $-b$ |
| Clitoral enlargement | $1-6 \mathrm{mo}$ | $1-2 \mathrm{y}$ |
| Vaginal atrophy | $1-6 \mathrm{mo}$ | $1-2 \mathrm{y}$ |
| Deepening of voice | $6-12 \mathrm{mo}$ | $1-2 \mathrm{y}$ |

Estimates represent clinical observations: Toorians et al. (149)، Asscheman et al. (156), Gooren et al. (157), Wierckx et al. (158).
${ }^{\text {a }}$ aprevention and treatment as recommended for biological men,
${ }^{\circ}$ Menorrhagia requires diagnosis and treatment by a gynecologist.

Table 13. Feminizing Effects in Transgender Females

| Effect | Onset | Maximum |
| :--- | :---: | :---: |
| Redistribution of body fat | $3-6 \mathrm{mo}$ | $2-3 \mathrm{y}$ |
| Decrease in muscle mass and strength | $3-6 \mathrm{mo}$ | $1-2 \mathrm{y}$ |
| Softening of skin/decreased oiliness | $3-6 \mathrm{mo}$ | Unknown |
| Decreased sexual desire | $1-3 \mathrm{mo}$ | $3-6 \mathrm{mo}$ |
| Decreased spontaneous erections | $1-3 \mathrm{mo}$ | $3-6 \mathrm{mo}$ |
| Male sexual dysfunction | Variable | Variable |
| Breast growth | $3-6 \mathrm{mo}$ | $2-3 \mathrm{y}$ |
| Decreased testicular volume | $3-6 \mathrm{mo}$ | $2-3 \mathrm{y}$ |
| Decreased sperm production | Unknown | $>3 \mathrm{y}$ |
| Decreased terminal hair growth | $6-12$ mo | $>3 \mathrm{y}^{a}$ |
| Scalp hair | Variable | -6 |
| Voice changes | None | -6 |

Estimates represent clinical observations: Toorians et al. (149), Asscheman et al. (156), Gooren et al. (157).
${ }^{\text {a }}$ Complete removal of male sexual hair requires electrolysis or laser treatment or both.
${ }^{\text {b }}$ 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 trearment 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. $(2 \mid \oplus \oplus \bigcirc \bigcirc)$

## 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 dysfuncrion, 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 syntheric 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: ${ }^{\text {a }}$
a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is $400-700 \mathrm{ng} / \mathrm{dL}$ to $400 \mathrm{ng} / \mathrm{dL}$. 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 $<400 \mathrm{ng} / \mathrm{dL}$, 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.
${ }^{\text {a Adapted from Lapauw et al. (154) and Ott et al. (159). }}$
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 genderaffirming 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 rreated with estrogens. (2 $\mathrm{l} \oplus \oplus \mathrm{O}$ )

## 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 nor 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

[^8]This table presents strong recommendations and does not include lower level recommendations.
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 $1 \oplus \oplus(\mathrm{OO})$

## 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 paramerers 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 $\geq 24$ 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. ( $1 \mid \oplus \oplus \bigcirc O$ )

## 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 assumprion 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. ( $2 \downarrow \oplus \oplus O$ )
4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 $1 \oplus \bigcirc O O$ )

## 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 130 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 fernales 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 toral hysterectomy as part of a genderaffirming 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
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 genderconforming 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 cosmeric 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 masrectomy 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 invoive chest contouring (256). Mastecromy 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. ( $1 \mathrm{l} \oplus \oplus \bigcirc O$ )
5.2. We advise that clinicians approve genital genderaffirming 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 hormonetreated 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 l $\oplus 000$ )
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. ( $2 \oplus \oplus \bigcirc 0$ ).
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. ( $2 \mathrm{l} \oplus \mathrm{O} O \mathrm{O}$ )

## 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 systemaric 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
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 genderaffirming 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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Correspondence and Reprint Requests: The Endocrine Society, 2055 L Street NW, Suite 600, Washington, DC 20036. E-mail: publications@endocrine.org; Phone: 202971-3636.

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## CERTIFICATE OF SERVICE

I certify that I e-filed this appendix on ECF, which will email everyone requiring notice.

Dated: October 13, 2023
Ls/ Mohammad O. Jazil


[^0]:    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.

[^1]:    ${ }^{\text {ccyproterone-based regimen }}$

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[^3]:    Reference: American Psychiatric Association (14),

[^4]:    Reproduced from World Professional Association for Transgender Health (16).

[^5]:    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 $<4 \mathrm{~mL}$
    2. Slight enlargement of penis; enlarged scrotum, pink, texture altered, testes $4-6 \mathrm{~mL}$
    3. Penis longer, testes larger ( $8-12 \mathrm{~mL}$ )
    4. Penis and glans larger, including increase in breadth; testes larger ( $12-15 \mathrm{~mL}$ ), scrotum dark
    5. Penis adult size; testicular volume $>15 \mathrm{ml}$
[^6]:    Adapted from Lawrence (56).

[^7]:    Every 3-6 mo
    Anthropometry: height, weight, sitting height, blood pressure, Tanner stages
    Every 6-12 mo
    Laboratory: LH, FSH, E2/T, 250 H 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;

[^8]:    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 $<50 \mathrm{ng} / \mathrm{dL}$.
    b. Serum estradiol should not exceed the peak physiologic range: $100-200 \mathrm{pg} / \mathrm{mL}$.
    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.
