

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 GnRHs 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-Krishna et al., 2019). Correspondingly, for adolescents who have already completed endogenous puberty and are considering starting GAHT, GnRHs 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.

GnRHs reduce gonadotrophin and sex steroid concentrations in TGD adolescents and thus halt the further development of secondary sex characteristics (Schagen et al., 2016). Their use is generally safe with the development of hypertension being the only short-term adverse event reported in the literature (Delemarre-van de Waal & Cohen-Kettenis, 2006; Klink, Bokenkamp et al., 2015). GnRHs 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 GnRHs 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). GnRHs 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 GnRHs 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 GnRHs in TGD adolescents is considered off-label because they were not initially developed for this purpose. Nonetheless, data from adolescents prescribed GnRHs 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 GnRHs 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 GnRHs 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- β -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 GnRHs for pubertal suppression (also see the Adolescents chapter).

Progestogens may be effective in adolescents whose goal is solely menstrual suppression. Continuous administration of progestin-only oral pills (including the contraceptive and noncontraceptive options), medroxyprogesterone injections, or levonorgestrel intrauterine device can be used for induction of amenorrhea (Pradhan & Gomez-Lobo, 2019). TGD individuals with functioning ovaries who start testosterone therapy may have 1–5 menstrual cycles before amenorrhea is achieved (Taub et al., 2020). Once amenorrhea is achieved, some TGD individuals with functioning ovaries may also choose to continue progestin treatment for birth control if relevant to their sexual practices.

TGD individuals with functioning ovaries and a uterus should be counseled about the potential for breakthrough menstrual bleeding in the first few months after initiating menstrual suppression. With GnRHa therapy, breakthrough bleeding may occur 2–3 weeks after initiation of the medication. For individuals seeking contraception or for those who continue to experience menstrual bleeding on progestin therapy, an estrogen combination with progestin may be considered for the maintenance of amenorrhea, yet they should be counseled on the possible side effect of breast development (Schwartz et al., 2019).

Statement 12.8

We recommend health care providers involve professionals from multiple disciplines who are experts in transgender health and in the management of the care of transgender and gender diverse adolescents.

As with the care of adolescents, we suggest where possible a multidisciplinary expert team of medical and mental health professionals (MHPs) be assembled to manage this treatment. In adolescents who pursue GAHT (given this is a partly irreversible treatment), we suggest initiating treatment using a schedule of gradually increasing doses after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and has established the individual possesses the mental capacity to give informed consent (Hembree et al., 2017). Specific aspects concerning the assessment of adolescents and the involvement of their caregivers and a multidisciplinary team are described in more detail in Chapter 6—Adolescents.

If possible, TGD adolescents should have access to experts in pediatric transgender health from multiple disciplines including primary care, endocrinology, fertility, mental health, voice, social work, spiritual support, and surgery (Chen, Hidalgo et al., 2016; Eisenberg et al., 2020; Keo-Meier & Ehrensaft, 2018). Individual providers are encouraged to form collaborative working relationships with providers from other disciplines to facilitate referrals as needed for the individual youth and their family (Tishelman et al., 2015). However, the lack of available

experts and resources should not constitute a barrier to care (Rider, McMorris et al., 2019). Helpful support for adolescents includes access to accurate, culturally informed information related to gender and sexual identities, transition options, the impact of family support, and connections to others with similar experiences and with TGD adults through online and in person support groups for adolescents and their family members (Rider, McMorris et al., 2019).

Many TGD adolescents have been found to experience mental health disparities and initial mental health screening (e.g., PHQ-2, GAD) can be employed as indicated (Rider, McMorris et al., 2019). Providers should keep in mind being transgender or questioning one's gender does not constitute pathology or a disorder. Therefore, individuals should not be referred for mental health treatment exclusively on the basis of a transgender identity. HCPs and MHPs who treat these youths and make referrals should, at a minimum, be familiar with the impact of trauma, gender dysphoria, and gender minority stressors on any potential mental health symptomatology, such as disordered eating, suicidal ideation, social anxiety. These health care providers should also be knowledgeable about the level of readiness of inpatient mental health services in their region to provide competent, gender-affirming care to TGD youth (Barrow & Apostle, 2018; Kuper, Wright et al., 2018; Kuper, Mathews et al., 2019; Tishelman & Neumann-Mascis, 2018). Statements 6.3, 6.4, and 6.12d in Chapter 6—Adolescents address this in more detail. Because parents of these youth commonly experience high levels of anxiety immediately after learning their youth is TGD, and their response to their child predicts that child's long-term physical and mental health outcomes, appropriate referrals for mental health support of the parents can be of great utility (Coolhart et al., 2017; Pullen Sansfaçon et al., 2015; Taliaferro et al., 2019).

Statement 12.9

We recommend health care professionals organize regular clinical evaluations for physical changes and potential adverse reactions to sex steroid hormones, including laboratory monitoring of sex steroid hormones every 3 months

during the first year of hormone therapy or with dose changes until a stable adult dosing is reached followed by clinical and laboratory testing once or twice a year once an adult maintenance dose is attained.

Sex steroid hormone therapy is associated with a broad array of physical and psychological changes (Irwig, 2017; Tangpricha & den Heijer, 2017) (see Appendix C—Table 1). After sex steroid hormone therapy has been initiated, the HCP should regularly assess the progress and response of the individual to the treatment (also see Chapter 6—Adolescents). This evaluation should assess the presence of any physical changes as well as the impact of treatment on gender dysphoria (if present) and psychological well-being (see Appendix C—Table 1). Clinical visits provide important opportunities for HCPs to educate patients about the typical time course required for physical changes to manifest and encourage realistic expectations. During the first year of hormone therapy, sex steroid hormone doses are often increased. A major factor guiding the dose is the serum level of the corresponding sex steroid hormone. In general, the goal is to target serum levels of the sex steroids to match the levels associated with the individual's gender identity, although optimal target ranges have not been established (Hembree et al., 2017).

In addition to assessing the positive changes associated with sex steroid hormone therapy, the HCP should regularly assess whether the treatment has caused any adverse effects (see Appendix C—Table 2). Examples of adverse signs and symptoms include androgenic acne or bothersome sexual dysfunction (Braun et al., 2021; Kerckhof et al., 2019). GAHT also has the potential to adversely influence several laboratory tests. For example, spironolactone may cause hyperkalemia, although it is an uncommon and transient phenomenon (Millington et al., 2019). Testosterone increases the red blood cell count (hematocrit), which may occasionally cause erythrocytosis (Antun et al., 2020) (see Statement 12.17) (Hembree et al., 2017). Both estrogen and testosterone can alter lipid parameters, such as high-density protein lipoprotein (HDL) cholesterol and triglycerides (Maraka et al., 2017). See Appendix C—Tables 3 and 4.

The frequency of clinical evaluations should be individualized and guided by the individual's response to treatment. We suggest clinical assessments be performed approximately every 3 months during the first year of hormone therapy in patients who are stable and are not experiencing significant adverse effects (Appendix C—Table 5). We suggest rather than recommend testing be carried out every 3 months in the first year to allow some flexibility on the timing of these tests as there is no strong evidence or evidence from published studies supporting specific testing intervals. If an individual does experience an adverse effect, more frequent laboratory testing and/or clinical visits are often needed. Given the potential harm associated with sex hormone levels that exceed expected ranges in humans, we strongly recommend regular testing be performed as a standard practice when initiating GAHT in TGD individuals. Once a person has reached a stable adult dose of sex steroid hormone with no significant adverse effects, the frequency of clinic visits can be reduced to one to two per year (Hembree et al., 2017).

Statement 12.10

We recommend health care professionals inform and counsel all individuals seeking gender-affirming medical treatment about options for fertility preservation prior to initiating puberty suppression and prior to administering hormone therapy.

Pubertal suppression and hormone treatment with sex steroid hormones may have potential adverse effects on a person's future fertility (Cheng et al., 2019) (see also Chapter 6—Adolescents and Chapter 16—Reproductive Health). Although some TGD people may not have given much thought to their future reproductive potential at the time of their initial assessment to begin medical therapy, the potential implications of the treatment and fertility preservation options should be reviewed by the hormone prescriber and discussed with the person seeking these therapies (Ethics Committee of the American Society for Reproductive Medicine et al., 2015; De Roo et al., 2016).

Individuals with testes should be advised prolonged treatment with estrogen often causes

testicular atrophy and a reduction in sperm count and other semen parameters (Adeleye et al., 2018). Nonetheless, there are major gaps in knowledge, and findings regarding the fertility of trans feminine people who take estrogen and antiandrogens are inconsistent (Cheng et al., 2019). In one study, heterogeneity in testicular histology was evident whether patients discontinued or continued therapy prior to orchiectomies (Schneider et al., 2015). For example, the discontinuation of estrogen and antiandrogens for six weeks resulted in complete spermatogenesis in 45% of individuals with the remainder showing meiotic arrest or spermatogonial arrest (Schneider et al., 2015). However, serum testosterone levels confirmed to be within female reference ranges leads to complete suppression of spermatogenesis in most transgender women (Vereecke et al., 2020). The principal fertility preservation option for patients with functioning testes is sperm cryopreservation, also known as sperm banking (Mattawanon et al., 2018). For prepubertal patients, suppression of puberty with GnRHs pauses the maturation of sperm (Finlayson et al., 2016).

Individuals with functioning ovaries should be advised testosterone therapy usually results in the cessation of menses and ovulation, often within a few months of initiation (Taub et al., 2020). There are also major gaps in knowledge regarding the potential effects of testosterone on oocytes and subsequent fertility of TGD patients (Eisenberg et al., 2020; Stuyver et al., 2020). One study found testosterone treatment may be associated with polycystic ovarian morphology, whereas other studies reported no metabolic (Chan et al., 2018) or histologic (De Roo et al., 2017; Grynberg et al., 2010) evidence of polycystic ovary syndrome (PCOS) following treatment with testosterone, and some studies have found a pre-existing higher prevalence of PCOS in transgender patients with ovaries (Baba, 2007; Gezer et al., 2021). TGD patients with an intact uterus and ovaries often regain their fertility potential if testosterone therapy is discontinued (Light et al., 2014). Indeed, a live birth after assisted reproductive technology has been reported following hormone-stimulated egg retrieval from a TGD

individual who did not discontinue testosterone therapy (Greenwald et al., 2021; Safer and Tangpricha, 2019). Other fertility preservation options for TGD patients with ovaries are oocyte cryopreservation and embryo cryopreservation with sperm from a partner or donor. The above options require hormonal stimulation for egg retrieval and the use of assisted reproductive technology.

For early pubertal transgender youth, suppression of puberty with GnRHa's pauses the maturation of germ cells, although a recent report noted ovarian stimulation of a TGD adolescent treated with a GnRHa's in early puberty (and continued during ovarian stimulation) resulted in a small number of mature oocytes that were cryopreserved (Rothenberg et al., 2019). Treating an TGD adolescent with functioning testes in the early stages of puberty with a GnRHa not only pauses maturation of germ cells but will also maintains the penis in a prepubertal size. This will likely impact surgical considerations if that person eventually undergoes a penile-inversion vaginoplasty as there will be less penile tissue to work with. In these cases, there is an increased likelihood a vaginoplasty will require a more complex surgical procedure, e.g., intestinal vaginoplasty (Dy et al., 2021; van de Grift et al., 2020). Such considerations should be included in any discussions with patients and families considering use of pubertal blockers in early pubertal adolescents with functioning testes.

Statement 12.11

We recommend health care professionals evaluate and address medical conditions that can be exacerbated by lowered endogenous sex hormone concentrations and treatment with exogenous sex hormones before beginning treatment in transgender and gender diverse people.

TGD people seeking masculinization must be informed about the possibilities, consequences, limitations, and risks associated with testosterone treatment. Testosterone therapy is contraindicated during pregnancy or while attempting to become pregnant given its potential iatrogenic effects on the fetus. Relative contraindications to testosterone therapy include severe hypertension, sleep apnea, and polycythemia since these conditions

can be exacerbated by testosterone. Monitoring blood pressure and lipid profiles should be performed before and after the onset of testosterone therapy. The increase in blood pressure typically occurs within 2 to 4 months following the initiation of testosterone therapy (Banks et al., 2021). Patients who develop hypercholesterolemia and/or hypertriglyceridemia may require treatment with dietary modifications, medication, or both.

TGD people seeking feminizing treatment with a history of thromboembolic events, such as deep vein thrombosis and pulmonary embolism, should undergo evaluation and treatment prior to the initiation of hormone therapy. This is because estrogen therapy is strongly associated with an increased risk of thromboembolism, a potentially life-threatening complication. In addition, risk factors that can increase the risk of thromboembolic conditions, such as smoking, obesity, and sedentary lifestyle, should be modified. In patients with nonmodifiable risk factors, such as a known history of thrombophilia, a past history of thrombosis, or a strong family history of thromboembolism, treatment with transdermal estrogen concomitant with anticoagulants may decrease the risk of thromboembolism. However, there are limited data to guide treatment decisions. The presence of a disease at baseline such as a hormone sensitive cancer, coronary artery disease, cerebrovascular disease, hyperprolactinemia, hypertriglyceridemia, and cholelithiasis should be evaluated prior to the initiation of gender-affirming hormone therapy as relative risks may be shifted in association with exogenous hormone treatment (Hembree et al., 2017).

Statement 12.12

We recommend health care professionals educate transgender and gender diverse people undergoing gender-affirming treatment about the onset and time course of physical changes induced by sex hormone treatment.

The effects of testosterone treatment are multiple and may include the appearance of increased body and facial hair, male pattern baldness, increased muscle mass and strength, decreased fat mass, deepening of the voice, interruption of

menses (if still present), increased prevalence and severity of acne, clitoral enlargement, and increased sexual desire (Defreyne, Elaut et al., 2020; Fisher, Castellini et al., 2016; Giltay & Gooren, 2000; T'Sjoen et al., 2019; Yeung et al., 2020). Other testosterone-associated changes include increased lean body mass, skin oiliness, (de Blok et al., 2020; Hembree et al., 2017; Kuper, Mathews et al., 2019; Taliaferro et al., 2019; Tishelman & Neumann-Mascis, 2018) (see Appendix C—Table 1).

Estrogen treatment induces breast development. However, fewer than 20% of individuals reach Tanner breast stages 4–5 after 2 years of treatment (de Blok et al., 2021). Additional changes include decreases in testicular volume, lean body mass, skin oiliness, sexual desire, spontaneous erections, facial hair, and body hair along with increased subcutaneous body fat) (see Appendix C—Table 1). In adult patients, estrogen does not alter a person's voice or height (Iwamoto, Defreyne et al., 2019; Wiepjes et al., 2019).

The time course and extent of physical changes vary among individuals and are related to factors such as genetics, age of initiation, and overall state of health (Deutsch, Bhakri et al., 2015; van Dijk et al., 2019). Knowledge of the extent and timing of sex hormone–induced changes, if available, may prevent the potential harm and expense of unnecessary treatment changes, dosage increases, and premature surgical procedures (Dekker et al., 2016).

Statement 12.13

We recommend health care professionals not prescribe ethinyl estradiol for transgender and gender diverse people as part of a gender-affirming hormonal treatment. For supporting text, see Statement 12.15.

Statement 12.14

We suggest health care professionals prescribe transdermal estrogen for eligible* transgender and gender diverse people at higher risk of developing venous thromboembolism based on age >45 years or a previous history of venous thromboembolism, when gender-affirming estrogen treatment is recommended. For supporting text, see Statement 12.15).

Statement 12.15

We suggest health care professionals not prescribe conjugated estrogens in transgender and gender diverse people when estradiol is available as part of a gender-affirming hormonal treatment.

Determining the safest and most efficacious estrogen compound and route of administration for TGD people is an important topic. The recommended estrogen-based regimens are presented in Appendix C—Table 4. The Amsterdam Medical Center (AMC) first reported 45 events of VTE occurring in 816 transgender women, notably an expected incidence ratio of VTE 20-fold higher than that reported in a reference population (van Kesteren et al., 1997). Following this report, the AMC clinic recommended the use of transdermal estradiol for transgender women older than 40 years of age, which subsequently lowered the incidence of VTE (Nota et al., 2019; Toorians et al., 2003). Other studies suggested ethinyl estradiol is associated with a higher risk of blood clotting due to an increased resistance to the anticoagulating effects of activated protein C (APC) and elevated concentrations of the clotting factors protein C and protein S (Toorians et al., 2013). Other studies published within the past 15 years from other clinics reported transgender women taking other forms of estrogen had lower rates of VTE than transgender women taking ethinyl estradiol (Asscheman et al., 2013). Furthermore, a 2019 systematic review concluded ethinyl estradiol administration was associated with the highest risk of VTE in transgender women, while an association between progesterone use and VTE was also identified (Goldstein et al., 2019).

The 2017 Endocrine Society guidelines did not recommend conjugated equine estrogens (CEEs) as a treatment option because blood levels of conjugated estrogens cannot be measured in transgender women making it difficult to prevent supraphysiologic dosing of estrogen and thereby increasing the potential risk of VTE (Hembree et al., 2017). A retrospective study from the UK examined the risks of oral CEE versus oral estradiol valerate versus oral ethinyl estradiol and found up to a 7-fold increase in the percentage of transgender women in the oral CEE group

who developed VTE compared with transgender women using other forms of estrogen (Seal et al., 2012). In a nested, case-control study, over 80,000 cisgender women aged 40–79 who developed a VTE were matched to approximately 390,000 cisgender women without VTE; the results showed oral estradiol use had a lower risk of VTE than conjugated estrogens, and transdermal estrogen was not associated with an increased risk of VTE (Vinogradova et al., 2019).

A systematic review evaluated several formulations of estrogen and identified a retrospective and a cross-sectional study that made head-to-head comparisons of the risks associated with different formulations (Wierckx, Mueller et al., 2012; Wierckx et al., 2013). No identified studies evaluating the risk of different formulations of estrogen employed a prospective interventional design. The retrospective study examined 214 transgender women taking transdermal estradiol (17 β -estradiol gel 1.5 mg/d or estradiol patch 50 mcg/d) or a daily intake of oral estrogens (estradiol 2 mg/d, estriol 2 mg/d, ethinyl estradiol 50 mcg/day, or ethinyl estradiol 30–50 mcg in an oral contraceptive) (Wierckx et al., 2013). Within a 10-year observation period, 5% of the cohort developed a VTE, 1.4% (3 of 214) experienced a myocardial infarction (MI), and 2.3% (5 of 214) a transient ischemic attack or cerebrovascular accident (TIA/CVA). The prevalence of VTE, MI and TIA/CVA was increased following the initiation of estrogen therapy. However, the authors did not report differences between regimens of estrogen in terms of these endpoints.

The same group of investigators conducted a cross-sectional study that examined 50 transgender women (mean age 43 \pm 10) taking oral estrogen (estradiol valerate 2 mg/d, estriol 2 mg/d or ethinyl estradiol 50–120 mcg/day) or using transdermal estradiol (17 β -estradiol 1.5 mg/day or estradiol 50 mcg/day) over a follow-up duration of 9.2 years (Wierckx, Mueller et al., 2012). Twelve percent ($n = 6$) developed either a VTE, MI, or a TIA/CVA. Two of the participants were taking conjugated estrogen 0.625 mg/d (one person in combination with cyproterone acetate), 2 participants were taking ethinyl estradiol 20–50 mcg/d, 1 was taking cyproterone acetate 50 mg/d, while the estrogen regimen used by the

sixth participant was not defined. None of the subjects taking oral estradiol or transdermal estradiol developed a VTE, MI, or TIA/CVA.

One prospective study examined the route of estrogen administration in 53 transgender women in a multicenter study carried out throughout Europe. Transgender women younger than 45 years of age ($n = 40$) received estradiol valerate 4 mg/d in combination with cyproterone acetate (CPA) 50 mg/d and transgender women older than 45 years of age ($n = 13$) received transdermal 17 β -estradiol, also with CPA. No VTE, MI, or TIA/CVA was reported after a 1-year follow-up in either the oral or transdermal estrogen group. An additional retrospective study from Vienna found no occurrences of VTE among 162 transgender women using transdermal estradiol who were followed for a mean of 5 years (Ott et al., 2010).

We are strongly confident in our recommendation against the use of ethinyl estradiol based on historical data from the Amsterdam clinic demonstrating a reduction in the incidence of VTE after discontinuing the use of ethinyl estradiol and the recent systematic review demonstrating an increased risk of VTE in transgender women taking ethinyl estradiol (Weinand & Safer, 2015). We are confident in our recommendation against the use of CEE based on the 2012 study by Seal et al. demonstrating an increased risk of VTE in transgender women taking CEE compared with other formulations of estrogen and with data from cisgender women on hormone replacement therapy (Canonica et al., 2007; Seal et al., 2012). Prospective and retrospective studies in transgender women have reported occurrences of VTE/MI/CVA only in those taking CEE or ethinyl estradiol. Since estradiol is inexpensive, more widely available, and appears safer than CEE in limited studies, the committee recommends against using CEE when estradiol is an available treatment option. The quality of studies may be limited to prospective, cohort or cross-sectional study designs; however, the stronger level of recommendation is based on the consistent evidence supporting the association between the use of ethinyl estradiol and CEE and a greater risk of VTE/MI/CVA in transgender women.

We are also confident in our recommendation for the administration of transdermal preparations of estrogen in older transgender women

(age > 45 years) or those with a previous history of VTE. The confidence in our recommendation is based on the decreased incidence of VTE reported from the Amsterdam clinic when transgender women are switched to using transdermal preparations after age 40 (van Kesteren et al., 1997). Furthermore, the prospective, multicenter cohort study ENIGI found no incidence of VTE/MI/CVA in transgender women who are routinely switched to transdermal estrogen at age 45 (Dekker et al., 2016). In addition, a study by Ott et al. demonstrated no incidence of VTE in 162 transgender women treated with estradiol patches (Ott et al., 2010).

With the exception of cyproterone acetate (note this is not approved for use in the US because of concerns of potential hepatotoxicity), the use of progestins in hormone therapy regimens remains controversial. To date, there have been no quality studies evaluating the role of progestones in hormone therapy for transgender patients.

We are aware some practitioners who prescribe progestins, including micronized progesterone, are under the impression there may be improvements in breast and/or areolar development, mood, libido, and overall shape for those seeking it along with other benefits yet to be demonstrated (Deutsch, 2016a; Wierckx, van Caenegem et al., 2014). However, these improvements remain anecdotal, and there are no quality data to support such progestin use. An attempted systematic review we commissioned for this version of the SOC failed to identify enough data to make a recommendation in favor of any progestins. Instead, existing data suggest harm is associated with extended progestin exposure (Safer, 2021).

For cisgender women who have a uterus, progestins in combination with estrogens are necessary to avoid the endometrial cancer risk associated with the administration of unopposed estrogen. For cisgender women who do not have a uterus, progestins are not used. The best data for the concerns related to progestin use come from comparisons between the above two cisgender populations, which we acknowledge is not necessarily generalizable to this population. Although not definitive of a class effect for all progestins, medroxyprogesterone added to

combined equine estrogens is associated with greater breast cancer and cardiac risks (Chlebowski 2020; Manson, 2013). It is important to note data from the Women's Health Initiative (WHI) studies may not be generalizable to transgender populations. Compared with the cisgender women in the studies, transgender populations seeking hormone therapy tend to be younger, do not use equine estrogen, and hormone therapy in these cases address current mental health and quality of life and not solely risk prevention (Deutsch, 2016a).

Potential adverse effects of progestins include weight gain, depression, and lipid changes. Micronized progesterone may be better tolerated and may have a more favorable impact on the lipid profile than medroxyprogesterone (Fitzpatrick et al., 2000). When paired with estrogens for transgender women, the progestin cyproterone acetate is associated with elevated prolactin, decreased HDL cholesterol, and rare meningiomas—none of which are seen when estrogens are paired with GnRH agonists or spironolactone (Bisson, 2018; Borghei-Razavi, 2014; Defreyne, Nota et al., 2017; Sofer et al., 2020).

Thus, data to date do not include quality evidence supporting a benefit of progestin therapy for transgender women. However, the literature does suggest a potential harm of some progestins, at least in the setting of multi-year exposure. If, after a discussion of the risks and benefits of progesterone treatment, there is a collaborative decision to begin a trial of progesterone therapy, the prescriber should evaluate the patient within a year to review the patient's response to this treatment.

Statement 12.16

We recommend health care professionals prescribe testosterone-lowering medications (either cyproterone acetate, spironolactone, or GnRH agonists) for eligible* transgender and gendered diverse people with testes taking estrogen as part of a hormonal treatment plan if their individual goal is to approximate levels of circulating sex hormone in cisgender women.

Most gender clinics in the US and Europe prescribe estrogen combined with a testosterone-lowering medication (Mamoojee et al., 2017) (see Appendix C—Table 5). In the

US, spironolactone is the most commonly prescribed testosterone-lowering medication, while GnRHAs are commonly used in the UK, and cyproterone acetate are most often prescribed in the rest of Europe (Angus et al., 2021; Kuijpers et al., 2021). The rationale for adding a testosterone-lowering medication is two-fold 1) to lower testosterone levels to within the reference range of cisgender women; and 2) to reduce the amount of estrogen needed to achieve adequate physical effects. Each testosterone-lowering medication has a different side effect profile. Spironolactone is an antihypertensive and potassium-sparing diuretic, and thus may lead to hyperkalemia, increased frequency of urination, and a reduction in blood pressure (Lin et al., 2021). Cyproterone acetate has been associated with the development of meningioma and hyperprolactinemia (Nota et al., 2018). GnRHAs, while very effective in lowering testosterone levels, can result in osteoporosis if doses of estrogen given concurrently are insufficient (Klink, Caris et al., 2015).

One systematic review identified one study that reported findings from a head-to-head comparison of the testosterone-lowering medications cyproterone acetate and leuprolide (Gava et al., 2016). Two studies compared a group of transgender women taking estrogen plus testosterone-lowering medications with a group who received only estrogen. The systematic review did not provide sufficient evidence to suggest any of the three testosterone-lowering medications had a better safety profile in terms of improved outcomes in bone health, testosterone levels, potassium levels, or in the incidence of hyperprolactinemia or meningiomas (Wilson et al., 2020). Therefore, no recommendation can be given. The review did report spironolactone-based regimens were associated with a 45% increase in prolactin levels, whereas cyproterone-based regimens increased prolactin levels by more than 100%. However, the clinical significance of elevated prolactin levels is not clear because the rates of prolactinomas were not significantly elevated in either the spironolactone- or CPA-treated groups (Wilson et al., 2020). One retrospective, cohort study from a single center in the US reported no clinically significant

increases in prolactin levels in 100 transgender women treated with estrogen plus spironolactone (Bisson et al., 2018). A retrospective study from the Netherlands of 2,555 transgender women taking primarily CPA with various formulations of estrogen reported an increased standardized incidence ratio of meningiomas in patients who used cyproterone acetate after gonadectomy for many years when compared with the general Dutch population (Nota et al., 2018). Furthermore, in a shorter study in Belgium, 107 transgender women had transient elevations in prolactin levels following treatment with cyproterone acetate, which declined to normal after discontinuation (Defreyne, Nota et al., 2017). A recent publication, not included in the systematic review, examined 126 transgender women taking spironolactone, GnRHAs, or cyproterone and concluded cyproterone was associated with higher prolactin levels and a worse lipid profile than spironolactone or GnRHAs (Sofer et al., 2020). After balancing the costs and accessibility of measuring prolactin levels against the clinical significance of an elevated level, a decision was made not to make a recommendation for or against monitoring prolactin levels at this time. HCPs should therefore make individualized clinical decisions about the necessity to measure prolactin levels based on the type of hormone regimen and/or the presence of symptoms of hyperprolactinemia or a pituitary tumor (e.g., galactorrhea, visual field changes).

Cyproterone has also been linked to meningiomas. Nine cases of meningioma have been reported in the literature among transgender women primarily taking cyproterone acetate (Mancini et al., 2018). This increased risk has also been identified in cisgender populations. In 2020, the European Medicines Agency published a report recommending cyproterone products with daily doses of 10 mg or more should be restricted because of the risk of developing meningioma (European Medicines Agency, 2020). Most likely this association is a specific effect of cyproterone acetate and has not been extrapolated to include other testosterone-lowering drugs. In the US, where cyproterone acetate is not available, the North American Association of Central Cancer Registries (NAACCRs) database did not identify an increased risk of brain tumors (not specific to

meningiomas) among transgender women (Nash et al., 2018). Furthermore, there was not an increase in the hazard ratio of brain tumors in the Kaiser cohort of 2,791 transgender women compared with cisgender controls (Silverberg et al., 2017). No long-term studies have reported on the risk of meningiomas and prolactinomas in transgender women taking GnRHs.

Our strong recommendation for the use of testosterone-lowering medications as part of a hormone regimen for transgender individuals with testes is based on the global practice of using these medications in addition to estrogen therapies as well as the relatively minimal risk associated with these therapies. However, we are not able to make a recommendation favoring one testosterone-lowering medication over another at this time. The published data thus far raises some concerns about the risk of meningiomas with the prolonged use (>2 years) and higher doses (>10mg daily) of cyproterone acetate (Nota et al., 2018; Ter Wengel et al., 2016; Weill et al., 2021).

Bicalutamide is an antiandrogen that has been used in the treatment of prostate cancer. It competitively binds to the androgen receptor to block the binding of androgens. Data on the use of bicalutamide in trans feminine populations is very sparse and safety data is lacking. One small study looked at the use of bicalutamide 50 mg daily as a puberty blocker in 23 trans feminine adolescents who could not obtain treatment with a GnRH analogue (Neyman et al., 2019). All adolescents experienced breast development which is also commonly seen in men with prostate cancer who are treated with bicalutamide. Although rare, fulminant hepatotoxicity resulting in death has been described with bicalutamide (O'Bryant et al., 2008). Given that bicalutamide has not been adequately studied in trans feminine populations, we do not recommend its routine use.

The administration of 5 α -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 α -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 α -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 α -reductase inhibitors in transgender populations.

Statement 12.17

We recommend health care professionals monitor hematocrit (or hemoglobin) levels in transgender and gender diverse people treated with testosterone.

There are good quality data suggesting a rise in hematocrit (or hemoglobin) is associated with TGD persons treated with testosterone (Defreyne et al., 2018). The testosterone regimens in the systematic review included testosterone esters ranging from the equivalent of 25–250 mg SC/IM weekly, testosterone undecanoate 1000 mg every 12 weeks, or testosterone gel 50 mg applied daily to the skin (Defreyne et al., 2018; Gava et al., 2018; Giltay et al., 2000; Meriggiola et al., 2008; Pelusi et al., 2014; T'Sjoen et al., 2005; Wierckx, van Caenegem et al., 2014; Wierckx, van de Peer et al., 2014). The expected rise should be consistent with reference ranges in cisgender males.

Statement 12.18

We suggest health care professionals collaborate with surgeons regarding hormone use before and after gender-affirmation surgery. For supporting text, see Statement 12.19.

Statement 12.19

We suggest health care professionals counsel eligible* transgender and gender diverse people about the various options for gender-affirmation surgery unless surgery is either not indicated or is medically contraindicated.

Despite the absence of evidence, perioperative clinical standards for gender-affirmation surgeries have included cessation of hormone therapy for 1–4 weeks before and after surgery, most commonly genital surgeries (Hembree et al., 2009). Such practice was meant to mitigate the risk of VTE associated with exogenous estrogen administration (Hembree et al., 2009). Estrogen and testosterone could then be resumed at some point postoperatively.

After careful examination, investigators have found no perioperative increase in the rate of VTE among transgender individuals undergoing surgery, while being maintained on sex steroid treatment throughout when compared with that among patients whose sex steroid treatment was discontinued preoperatively (Gaither et al., 2018; Hembree et al., 2009; Kozato et al., 2021; Prince & Safer, 2020). Sex steroid treatment is especially important after gonadectomy to avoid the sequelae of hypogonadism, the risk of developing osteoporosis, and for the maintenance of mental health and quality of life (Fisher, Castellini et al., 2016; Rosen et al., 2019). Thus, hormone providers and surgeons should educate patients about the necessity for continuous exogenous hormone therapy after gonadectomy.

To be able to educate patients and serve as clinical advocates, HCPs should be knowledgeable about the risks and benefits of gender-affirmation surgeries and should also be cognizant of the performance measures and surgical outcomes of the surgeons to whom they might refer patients (Beek, Kreukels et al., 2015; Colebunders et al., 2017; Wiepjes et al., 2018). In general, most medically necessary surgeries can be thought of as involving three regions: the face, chest/breasts, and genitalia (internal and external). Additional medically necessary procedures include body contouring and voice surgery. See medical necessity statement in Chapter 2—Global Applicability, Statement 2.1).

Multiple procedures are available for facial gender-affirming surgeries including, but not limited to chondrolaryngoplasty, rhinoplasty, contouring or augmentation of the jaw, chin, and forehead, facelift, hair removal and hair transplantation (see Chapter 13—Surgery and Postoperative Care). Procedures available for

chest/breast surgery include breast augmentation, double mastectomy with nipple grafts, periareolar mastectomy, and liposuction. The most common gender-affirmation surgery for TGD individuals with endogenous breast development is masculinizing chest surgery (mastectomy) (Horbach et al., 2015; Kailas et al., 2017).

Internal genital surgery procedures include but are not limited to orchiectomy, hysterectomy, salpingo-oophorectomy, vaginoplasty, and colpectomy/vaginectomy (Horbach et al., 2015; Jiang et al., 2018). The inner lining in vaginoplasty is typically constructed from penile skin, skin grafts, a combination of both, or a bowel segment. Removal of the uterus/ovaries can be performed individually or all at once (hysterectomy, salpingo-oophorectomy, and colpectomy). If colpectomy is performed, a hysterectomy must also be performed. The ovaries may remain in situ, upon patient request. A potential benefit of leaving one or both ovaries is fertility preservation, while the downside is the potential for the development of ovarian pathology, including cancer (De Roo et al., 2017).

External genital surgery procedures include but are not limited to vulvoplasty, metoidioplasty, and phalloplasty (Djordjevic et al., 2008; Frey et al., 2016). Hair removal is generally necessary before performing external genital procedures (Marks et al., 2019). Vulvoplasty can include the creation of the mons, labia, clitoris, and urethral opening. Urethral lengthening is an option for both metoidioplasty and phalloplasty, but is associated with a greatly increased complication rate (Schechter & Safa, 2018). Wound care and physical therapy are necessary for managing wounds resulting from the donor sites for phalloplasty (van Caenegem, Verhaeghe et al., 2013). Pelvic physical therapy can also be an important adjunct intervention after surgery for managing voiding and sexual function (Jiang et al., 2019). Dialogue, mutual understanding, and clear communication in a common language between patients, HCPs, and surgeons will contribute to well-considered decisions about the available surgical procedures.

Statement 12.20

We recommend health care professionals initiate and continue gender-affirming hormone

therapy for eligible* transgender and gender diverse people who wish this treatment due to demonstrated improvement in psychosocial functioning and quality of life. For supporting text, see Statement 12.21.

Statement 12.21

We recommend health care professionals maintain existing hormone therapy if the transgender and gender diverse individual's mental health deteriorates and assess the reason for the deterioration, unless contraindicated.

Several mental health disparities have been documented in the transgender population including depression, suicidality, anxiety, decreased self-esteem, and post-traumatic stress disorder (Arcelus et al., 2016; Becerra-Culqui et al., 2018; Bouman et al., 2017; Eisenberg et al., 2017; Heylens, Elaut et al., 2014; Witcomb et al., 2018). The gender minority stress model provides evidence of several mediators and moderators of these disparities (Hendricks & Testa, 2012; Meyer, 2003). Mediators and moderators of mental health disparities unique to transgender people include experiences of discrimination, victimization, misgendering, family rejection, and internalized transphobia (Hendricks & Testa, 2012). Factors that have a positive effect on mental health include family acceptance, supportive social and romantic relationships, transgender community connectedness, protection by affirming and inclusive policies, policies of affirmation and inclusion, possession of updated legal name/gender documentation, and achievement of physical gender transition based on individualized embodiment goals (Bauer et al., 2015; Bockting et al., 2013; Bouman et al., 2016; Davey et al., 2014; de Vries et al., 2014; Du Bois et al., 2018; Gower, Rider, Brown et al., 2018; Hendricks & Testa, 2012; Keo-Meier et al., 2015; Meier et al., 2013; Pflum et al., 2015; Ryan et al., 2010; Smith et al., 2018).

Hormone therapy has been found to positively impact the mental health and quality of life of TGD youth and adults who embark on this treatment (Aldridge et al., 2020; Allen et al., 2019; Bauer et al., 2015; Nobili et al., 2018; Russell et al., 2018; Ryan, 2009). In many cases, hormone

therapy is considered a lifesaving intervention (Allen et al., 2019; Grossman & D'Augelli, 2006; Moody et al., 2015). Several studies have found associations between the initiation of hormone therapy and improved mental health in youth and adults (Aldridge et al., 2020; Costa et al., 2016; de Vries et al., 2014; Kuper et al., 2020; Nguyen et al., 2018; White Hughto & Reisner, 2016), including improvements in quality of life (Gorin-Lazard et al., 2012; Gorin-Lazard et al., 2013; Murad et al., 2010; Newfield et al., 2006; Nobili et al., 2018; White Hughto & Reisner, 2016), a reduction in anxiety and depression (Aldridge et al., 2020; Colizzi et al., 2014; Davis & Meier, 2014; de Vries, Steensma et al., 2011; Gómez-Gil et al., 2012; Rowniak et al., 2019), decreased stress, and decreased paranoia (Keo-Meier & Fitzgerald, 2017). A prospective, controlled trial using the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) demonstrated significant improvement in multiple domains of psychological functioning in transgender men after only 3 months of testosterone treatment (Keo-Meier et al., 2015). Although there are higher rates of autism symptoms in the transgender population, these symptoms have not been found to increase after the initiation of hormone therapy (Nobili et al., 2020).

As a reduction in depressive symptoms may correlate with a decrease in the risk of suicide, withholding hormone therapy based on the presence of depression or suicidality may cause harm (Keo-Meier et al., 2015; Levy et al., 2003). Turban, King et al. (2020) found a decrease in the odds of lifetime suicidal ideation in adolescents who required pubertal suppression and had access to this treatment compared with those with a similar desire with no such access (Turban, King et al., 2020). A recent systematic review found pubertal suppression in TGD adolescents was associated with an improved social life, decreased suicidality in adulthood, improved psychological functioning and quality of life (Rew et al., 2020). Because evidence suggests hormone therapy is directly linked to decreased symptoms of depression and anxiety, the practice of withholding hormone therapy until these symptoms are treated with traditional psychiatry is considered to have iatrogenic effects

(Keo-Meier et al., 2015). If psychiatric treatment is indicated, it can be started or adjusted concurrently without discontinuing hormone therapy.

**For eligibility criteria for adolescents and adults, please refer to Chapter 5—Assessment for Adults and Chapter 6—Adolescents as well as Appendix D.*

CHAPTER 13 Surgery and Postoperative Care

Medically necessary gender-affirmation surgery (GAS) refers to a constellation of procedures designed to align a person's body with their gender identity (see Chapter 2—Global Applicability for medical necessity, Statement 2.1). This chapter describes surgery and postoperative care recommendations for TGD adults and adolescents. Please refer to Chapter 5—Assessment of Adults and Chapter 6—Adolescents for the assessment criteria related to surgery for adults and adolescents, respectively. A summary of the recommendations and assessment criteria can be found in [Appendix D](#).

Recognizing the diverse and heterogeneous community of individuals who identify as transgender and gender diverse (TGD), gender-affirming surgical interventions may be categorized along a spectrum of procedures for individuals assigned male at birth (AMAB) and assigned female at birth (AFAB).

In appropriately selected TGD individuals, the current literature supports the benefits of GAS. While complications following GAS occur, many are either minor or can be treated with local care on an outpatient basis (Canner et al., 2018; Gaither et al., 2018; Morrison et al., 2016). In addition, complication rates are consistent with those of similar procedures performed for different diagnoses (i.e., non-gender-affirming procedures).

In individuals AFAB, gender-affirming chest surgery or “top surgery” (i.e. “subcutaneous mastectomy”) has been studied in prospective (Agarwal et al., 2018; Frederick et al., 2017; Top & Balta, 2017; van de Grift, Elaut et al., 2017; van de Grift et al., 2016), retrospective (Bertrand et al., 2017; Claes et al., 2018; Esmonde et al., 2019; Lo Russo et al., 2017; Marinkovic & Newfield, 2017; Poudrier et al., 2019; Wolter et al., 2015; Wolter et al., 2018), and cross-sectional cohort studies (Olson-Kennedy, Warus et al., 2018; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018; van de Grift, Elfering et al., 2018). The efficacy of top surgery has been demonstrated in multiple domains, including a consistent and direct increase in health-related quality of life, a significant decrease in gender dysphoria, and a consistent increase in satisfaction with body and appearance. Additionally, rates of regret

remain very low, varying from 0 to 4%. While the effect of top surgery on additional outcome measures such as depression, anxiety, and sexual function also demonstrated a benefit, the studies were of insufficient strength to draw definitive conclusions. Although further investigation is needed to draw more robust conclusions, the evidence demonstrates top surgery to be a safe and effective intervention.

In individuals AMAB, fewer studies have been published regarding gender-affirming breast surgery (“breast augmentation”) and include 2 prospective (Weigert et al., 2013; Zavlin et al., 2018), 1 retrospective cohort (Fakin et al., 2019), and 3 cross-sectional cohort studies (Kanhai et al., 2000; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018). All the studies reported a consistent and direct improvement in patient satisfaction, including general satisfaction, body image satisfaction, and body image following surgery. Owen-Smith et al. (2018) demonstrated a positive trend toward improvement in both depression and anxiety scores with increasing levels of gender-affirming interventions. However, there was no statistical comparison between individuals who underwent top surgery and any other group.

Gender-affirming vaginoplasty is one of the most frequently reported gender-affirming surgical interventions; 8 prospective (Buncamper et al., 2017; Cardoso da Silva et al., 2016; Kanhai, 2016; Manero Vazquez et al., 2018; Papadopulos, Zavlin et al., 2017; Tavakkoli Tabassi et al., 2015; Wei et al., 2018; Zavlin et al., 2018), 15 retrospective cohort (Bouman, van der Sluis et al., 2016; Buncamper et al., 2015; Hess et al., 2016; Jiang et al., 2018; LeBreton et al., 2017; Manrique et al., 2018; Massie et al., 2018; Morrison et al., 2015; Papadopulos, Lelle et al., 2017; Raigosa et al., 2015; Salgado et al., 2018; Seyed-Forootan et al., 2018; Sigurjonsson et al., 2017; Simonsen et al., 2016; Thalaivirithan et al., 2018), and 3 cross-sectional cohort studies have recently been reported (Castellano et al., 2015; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018).

Although different assessment measurements were used, the results from all studies consistently reported both a high level of patient satisfaction (78–100%) as well as satisfaction with sexual function (75–100%). This was especially evident

Statements of Recommendations

13.1- We recommend surgeons who perform gender-affirming surgical procedures have the following credentials:

13.1.a- Training and documented supervision in gender-affirming procedures;

13.1.b- Maintenance of an active practice in gender-affirming surgical procedures;

13.1.c- Knowledge about gender diverse identities and expressions;

13.1.d- Continuing education in the field of gender-affirmation surgery

13.1.e- Tracking of surgical outcomes.

13.2- We recommend surgeons assess transgender and gender diverse people for risk factors associated with breast cancer prior to breast augmentation or mastectomy.

13.3- We recommend surgeons inform transgender and gender diverse people undergoing gender-affirming surgical procedures about aftercare requirements, travel and accommodations, and the importance of postoperative follow-up during the preoperative process.

13.4- We recommend surgeons confirm reproductive options have been discussed prior to gonadectomy in transgender and gender diverse people.

13.5- We suggest surgeons consider offering gonadectomy to eligible* transgender and gender diverse adults when there is evidence they have tolerated a minimum of 6 months of hormone therapy (unless hormone replacement therapy or gonadal suppression is not clinically indicated or the procedure is inconsistent with the patient's desires, goals, or expressions of individual gender identity).

13.6- We suggest health care professionals consider gender-affirming genital procedures for eligible* transgender and gender diverse adults seeking these interventions when there is evidence the individual has been stable on their current treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).

13.7- We recommend surgeons consider gender-affirming surgical interventions for eligible* transgender and gender diverse adolescents when there is evidence a multidisciplinary approach that includes mental health and medical professionals has been involved in the decision-making process.

13.8- We recommend surgeons consult a comprehensive, multidisciplinary team of professionals in the field of transgender health when eligible* transgender and gender diverse people request individually customized (previously termed "non-standard") surgeries as part of a gender-affirming surgical intervention.

13.9- We suggest surgeons caring for transgender men and gender diverse people who have undergone metoidioplasty/phalloplasty encourage lifelong urological follow-up.

13.10- We recommend surgeons caring for transgender women and gender diverse people who have undergone vaginoplasty encourage follow-up with their primary surgeon, primary care physician, or gynecologist.

13.11- We recommend patients who regret their gender-related surgical intervention be managed by an expert multidisciplinary team.

* For eligibility criteria for adolescents and adults, please refer to the *Assessment for Adults and Adolescents* chapters and *Appendix D*.

when using more recent surgical techniques. Gender-affirming vaginoplasty was also associated with a low rate of complications and a low incidence of regret (0–8%).

Recent literature reflects the increased clinical interest in metoidioplasty and phalloplasty as reflected by 3 prospective cohort (Garaffa et al., 2010; Stojanovic et al., 2017; Vukadinovic et al., 2014), 6 retrospective cohort (Cohanzad, 2016; Garcia et al., 2014; Simonsen et al., 2016; van de Grift, Pigot et al., 2017; van der Sluis et al., 2017; Zhang et al., 2015), and 4 cross-sectional studies (Castellano et al., 2015; Owen-Smith et al., 2018; van de Grift, Elaut et al., 2018; Wierckx, Van Caenegem et al., 2011), which reviewed the risks and benefits of these procedures.

In terms of urinary function, between 75 and 100% of study participants were able to void while standing. In terms of sexual function,

between 77 and 95% of study participants reported satisfaction with their sexual function. Most of these studies report high overall levels of postoperative satisfaction (range 83–100%), with higher rates of satisfaction in studies involving newer surgical techniques. Two prospective and two retrospective cohort studies specifically assessed regret following surgery and found no transgender men experienced regret. While study limitations were identified, the reported results were consistent and direct.

In recent years, facial GAS (FGAS) has received increased attention, and current literature supports its benefits. Eight recent publications include 1 prospective cohort (Morrison et al., 2020), 5 retrospective cohort (Bellinga et al., 2017; Capitán et al., 2014; Noureai et al., 2007; Raffaini et al., 2016; Simon et al., 2022), and 2 cross-sectional studies (Ainsworth & Spiegel, 2010; van de Grift, Elaut

et al., 2018). All 8 studies clearly demonstrated individuals were very satisfied with their surgical results (between 72% and 100% of individuals). Additionally, individuals were significantly more satisfied with the appearance of their face compared with individuals who had not undergone surgery. One prospective, international, multicenter, cohort study found facial GAS significantly improves both mid- and long-term quality of life (Morrison et al., 2020). The results were direct and consistent, but somewhat imprecise because of certain study limitations. While gender-affirming facial surgery for AFAB individuals is an emerging field, current limited data points toward equal benefits in select patients. Future studies are recommended.

Additional procedures and/or interventions such as hair removal (prior to facial and/or genital surgery) may be required as part of the preoperative process. See Chapter 15—Primary Care. Furthermore, consultation with pelvic floor physical therapy may be important (or required) both before and after surgery.

Representative surgical interventions include (for complete list, see appendix E and the end of this chapter):

AMAB: facial feminization surgery (including chondrolaryngoplasty/vocal cord surgery), gender-affirming breast surgery, body contouring procedures, orchiectomy, vagino/vulvoplasty (with/without depth), aesthetic procedures, and procedures designed to prepare individuals for surgery (i.e., hair removal).

AFAB: facial masculinization surgery, gender-affirming chest surgery, hysterectomy/oophorectomy, metoidioplasty (including placement of testicular prosthesis), phalloplasty (including placement of testicular/penile prostheses), body contouring procedures, aesthetic procedures, and procedures designed to prepare individuals for surgery (i.e., hair removal).

It is important surgeons understand the indication(s) and the timing for GAS. This is especially important when caring for adolescents (see Chapter 6—Adolescents).

It is important the surgeon and the patient participate in a shared decision-making approach that includes 1) a multidisciplinary approach; 2) an understanding of the patient's goals and

expectations; 3) a discussion regarding the surgical options and associated risks and benefits; and 4) an informed plan for aftercare (see Chapter 5—Assessment for Adults). These recommendations are designed to facilitate an individualized approach to care.

Appropriate aftercare is essential for optimizing outcomes (Buncamper et al., 2015; Lawrence, 2003), and it is important patients are informed about postoperative needs (including local wound care, activity restrictions, time off from work or school, etc.). In addition, it is important the surgeon is available to provide and facilitate postoperative care, refer to specialty services, or both as needed. This may include the need for ongoing support (i.e., both from the caregiver as well as the primary care provider, mental health professionals (MHPs), or both), as well as the need for routine primary care (i.e., breast/chest cancer screening, urologic/gynecologic care, etc.).

With the increase both in public interest and in the number of gender-affirming surgical procedures (Canner et al., 2018; Ross, 2017; Shen et al., 2019), additional training, tracking of outcomes, and continuing medical education for surgeons are necessary (Schechter et al., 2017).

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

Statement 13.1

We recommend surgeons who perform gender-affirming surgical procedures have the following credentials:

- a. **Training and documented supervision in gender-affirming procedures;**
- b. **Maintenance of an active practice in gender-affirming surgical procedures;**
- c. **Knowledge about gender diverse identities and expressions;**
- d. **Continuing education in the field of gender-affirmation surgery;**
- e. **Tracking of surgical outcomes.**

Surgeons offering GAS may have a variety of surgical specialty training and backgrounds. The most common surgical specialties include plastic surgery, urology, gynecology, otolaryngology and oro-maxillofacial surgery (Jazayeri et al., 2021). Consistent with other surgical domains, we recommend only surgeons who are certified or eligible to be certified by their respective national professional boards offer GAS. Furthermore, it is recommended surgeons offering care for TGD people have received documented training in gender-affirming procedures and principles of gender-affirming care (Schechter et al., 2017; Schechter & Schechter, 2019). The latter includes, but is not limited, to knowledge about gender diverse identities and expressions, and how those affect patient goals, expectations, and outcomes. It is important surgeons offering GAS be familiar with the available procedures and can provide informed consent. If surgeons do not offer a requested procedure, they may offer a referral for a second opinion. Surgeons offering GAS are expected to participate in continuing education activities in the field of GAS (i.e., meetings, conferences, seminars, etc.) to maintain current knowledge. We further recommend surgical outcomes be tracked and communicated to the patients as part of the informed consent (Schechter et al., 2017).

In addition, hospitals, institutions, and physician offices that offer GAS need to be knowledgeable regarding cultural competencies (i.e., language, terminology, etc.). This may require ongoing and regular staff education.

Statement 13.2

We recommend surgeons assess transgender and gender diverse people for risk factors associated with breast cancer prior to breast augmentation or mastectomy.

Prior to breast augmentation or mastectomy, individuals need to be informed about and assessed for breast cancer risk factors, including genetic mutations (i.e., BRCA1, BRCA2), family history, age, radiation, exposure to estrogen, and the amount of breast tissue anticipated to remain after surgery (Brown, Lourenco et al., 2021; Brown & Jones, 2015; Colebunders et al., 2014; Gooren et al., 2013; Salibian et al., 2021; Weyers et al., 2010). Breast cancer screening balances the

identification of cancer with the selection of appropriate imaging, tests, and procedures. Currently, evidence-based screening guidelines specific for TGD individuals do not exist (Salibian et al., 2021), however, recent guidelines have been proposed by the American College of Radiology (Brown, Lourenco et al., 2021). Because the risk of cancer in individuals seeking gender-affirming breast augmentation or mastectomy is similar to that in the general population (even in the setting of hormone use), existing cancer screening guidelines need to be followed (Brown & Jones, 2015; Gooren et al., 2013; Salibian et al., 2021; Weyers et al., 2010). Professionals need to be familiar with updates to these guidelines as they are subject to change. Individuals who undergo gender-affirming surgery of the chest should have ongoing breast cancer surveillance, which should be overseen by their primary care providers.

Statement 13.3

We recommend surgeons inform transgender and gender diverse people undergoing gender-affirming surgical procedures about aftercare requirements, travel and accommodations, and the importance of postoperative follow-up during the preoperative process.

Details about the timing, technique, and duration of the aftercare requirements are shared with patients in the preoperative period such that appropriate planning may be undertaken. This includes a discussion regarding the anticipated staging of surgical procedures (and associated travel requirements). Given the small number of surgeons who specialize in GAS, it is common for patients to travel for their procedures. Prior to surgery, surgeons should provide patients with a postoperative follow-up schedule. The surgeon should discuss the duration of the patient's travel dates, the anticipated inpatient versus outpatient stay, and the potential need for flexibility in travel arrangements (especially if complications occur). Given the complexity and cost of travel and lodging, changes in the care plan should be shared with the patient as early as possible. Surgeons should facilitate continuity of care with a local provider upon returning home.

Aftercare and postsurgical follow-up are important. Gender-affirming surgical procedures

often have specific aftercare requirements, such as postsurgery resources (stable, safe housing; resources for travel and follow-up care), instructions in health-positive habits (e.g., personal hygiene, healthy living, prevention of urinary tract infections (UTIs) and sexually-transmitted infections (STIs) (Wierckx, Van Caenegem et al., 2011)), postsurgery precautions or limitations on activities of daily life (e.g., bathing, physical activity, exercise, nutritional guidance, resumption of sexual activity) (Capitán et al., 2020), postsurgery resumption of medications (i.e., anticoagulants, hormones, etc.), and detailed postsurgery self-care activities (e.g., postvaginoplasty dilation and douching regimens, activation of a penile prosthesis, strategies to optimize postphalloplasty urination, recommendations for hair transplant care) (Capitán et al., 2017; Falcone et al., 2018; Garcia, 2018; Hoebeke et al., 2005). Some aspects of postsurgery self-care activities may be introduced prior to surgery and are reinforced after surgery (Falcone et al., 2018). As issues such as wound disruptions, difficulty with dilation, and UTIs may occur (Dy et al., 2019), the follow-up period provides an opportunity to intervene, mitigate, and prevent complications (Buncamper et al., 2016; Garcia, 2021).

Statement 13.4

We recommend surgeons confirm reproductive options have been discussed prior to gonadectomy in transgender and gender diverse people.

Infertility is often a consequence of both gender-affirming hormone therapy (temporary) and GAS (permanent), and fertility preservation is discussed prior to medical interventions, surgical interventions, or both (Defreyne, van Schuylenbergh et al., 2020; Jahromi et al., 2021; Jones et al., 2021). Surgical interventions that alter reproductive anatomy or function may limit future reproductive options to varying degrees (Nahata et al., 2019). It is thus critical to discuss infertility risk and fertility preservation (FP) options with transgender individuals and their families prior to initiating any of these interventions and on an ongoing basis thereafter (Hembree et al., 2017).

For specific recommendations regarding reproductive options, see Chapter 16—Reproductive Health.

Statement 13.5

We suggest surgeons consider offering gonadectomy to eligible* transgender and gender diverse adults when there is evidence they have tolerated a minimum of 6 months of hormone therapy (unless hormone replacement therapy or gonadal suppression is not clinically indicated or the procedure is inconsistent with the patient's desires, goals, or expressions of individual gender identity). For supporting text, see Statement 13.6.

Statement 13.6

We suggest health care professionals consider gender-affirming genital procedures in eligible* transgender and gender diverse adults seeking these interventions when there is evidence the individual has been stable on their current treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result unless hormone therapy is either not desired or is medically contraindicated).

GAHT leads to anatomical, physiological, and psychological changes. The onset of the anatomic effects (e.g., clitoral growth, vaginal mucosal atrophy) may begin early after the initiation of therapy, and the peak effect is expected at 1–2 years (T'Sjoen et al., 2019). Depending upon the surgical result required, a period of hormone treatment may be required (e.g., sufficient clitoral virilization prior to metoidioplasty/phalloplasty) or preferred for psychological reasons, anatomical reasons, or both (breast growth and skin expansion prior to breast augmentation, softening of skin and changes in facial fat distribution prior to facial GAS) (de Blok et al., 2021).

For individuals who are not taking hormones prior to surgical interventions, it is important surgeons review the impact of this on the proposed surgery.

For individuals undergoing gonadectomy who are not taking hormones, a plan for hormone replacement can be developed with their prescribing professional prior to surgery.

Statement 13.7

We recommend surgeons consider gender-affirming surgical interventions for eligible* transgender and gender diverse adolescents when there is evidence a multidisciplinary approach that includes mental health and medical professionals has been involved in the decision-making process.

Substantial evidence (i.e., observational studies (Monstrey et al., 2001; Stojanovic et al., 2017), literature reviews and expert opinions (Esteve 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 pre-surgical assessment in adolescents, see Chapter 6—Adolescents.

Statement 13.8

We recommend surgeons consult a comprehensive, multidisciplinary team of professionals in the field of transgender health when eligible* transgender and gender diverse people request individually customized (previously termed “non-standard”) surgeries as part of a gender-affirming surgical intervention.

Gender identities may present along a spectrum, and the expression of a person’s identity may vary quite widely amongst individuals (Beek et al., 2015; Koehler et al., 2018). While the overall goal of a particular procedure usually includes

reduction of gender dysphoria (van de Grift, Elaut et al., 2017) or achieving gender congruence, gender diverse presentations may lead to individually customized surgical requests some may consider “non-standard” (Beek et al., 2015; Bizic et al., 2018). Individually customized surgical requests can be defined as 1) a procedure that alters an individual’s gender expression without necessarily aiming to express an alternative, binary gender; 2) the “non-standard” combination of well-established procedures; or 3) both.

This is designed to help counsel and inform the patient as well as to ensure their goals can be achieved. The patient and their surgeon need to work together to ensure the patient’s expectations are realistic and achievable, and the proposed interventions are safe and technically feasible. The patient and their surgical team need to engage in a shared decision-making process (Cavanaugh et al., 2016). This informed consent process needs to address the irreversibility of some procedures, the newer nature of some procedures, and the limited information available about the long-term outcomes of some procedures.

Statement 13.9

We suggest surgeons caring for transgender men and gender diverse people who have undergone metoidioplasty/phalloplasty encourage life-long 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 post-void 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 Cuyper & Vercruysse, 2009; Defreyne, Motmans et al., 2017; Hadj-Moussa et al., 2019; Hadj-Moussa, Agarwal et al., 2018; Hadj-Moussa, Ohl et al., 2018; Landén et al., 1998; Narayan et al., 2021; van de Grift, Elaut et al., 2018; Wiepjes et al., 2018). The highest incidence of

regret was reported at a time when surgical techniques were less refined, the role of multidisciplinary care was less established, and the *Standards of Care* did not exist or were not widely known (Landén et al., 1998). Regret can be temporarily or permanent and may be classified as (Narayan et al., 2021) social regret (caused by difficulties in familial, religious, social, or professional life), medical regret (due to long-term medical complications, disappointment in surgical results or inadequate preoperative decision-making), and true gender-related regret (mostly based on patient experienced misdiagnosis, insufficient exploration of gender identity, or both). This classification is in accordance with previously discussed positive and negative

predictive factors (De Cuypere & Vercruyse, 2009; Gils & Brewaeys, 2007; Pfäfflin & Junge, 1998).

A multidisciplinary team can help identify the etiology of regret as well as the temporal stability of the surgical request (Narayan et al., 2021). Following this evaluation and in consideration of the individual's circumstances, medical and/or surgical interventions with the intent of either continuing transition or performing surgical procedures to return anatomy to that of the sex assigned at birth may be indicated. For further information see Chapter 5—Assessment of Adults.

**For eligibility criteria for adolescents and adults, please refer to the Assessment for Adults and Adolescent chapters and Appendix D*

GENDER-AFFIRMING SURGICAL PROCEDURES

As the field's understanding of the many facets of gender incongruence expands, and as technology develops which allows for additional treatments, it is imperative to understand this list is

not intended to be exhaustive. This is particularly important given the often lengthy time periods between updates to the SOC, during which evolutions in understanding and treatment modalities may occur.

FACIAL SURGERY

Brow	<ul style="list-style-type: none"> • Brow reduction • Brow augmentation • Brow lift
Hair line advancement and/or hair transplant	
Facelift/mid-face lift (following alteration of the underlying skeletal structures)	
Facelift/mid-face lift (following alteration of the underlying skeletal structures)	• Platysmaplasty
Blepharoplasty	• Lipofilling
Rhinoplasty (+/- fillers)	
Cheek	<ul style="list-style-type: none"> • Implant • Lipofilling
Lip	<ul style="list-style-type: none"> • Upper lip shortening • Lip augmentation (includes autologous and non-autologous)
Lower jaw	<ul style="list-style-type: none"> • Reduction of mandibular angle • Augmentation
Chin reshaping	<ul style="list-style-type: none"> • Osteoplastic • Alloplastic (implant-based) • Vocal cord surgery (see voice chapter)
Chondrolaryngoplasty	
BREAST/CHEST SURGERY	
Mastectomy	<ul style="list-style-type: none"> • Mastectomy with nipple-areola preservation/reconstruction as determined medically necessary for the specific patient • Mastectomy without nipple-areola preservation/reconstruction as determined medically necessary for the specific patient
Liposuction	
Breast reconstruction (augmentation)	<ul style="list-style-type: none"> • Implant and/or tissue expander • Autologous (includes flap-based and lipofilling)
GENITAL SURGERY	
Phalloplasty (with/without scrotoplasty)	<ul style="list-style-type: none"> • With/without urethral lengthening • With/without prosthesis (penile and/or testicular) • With/without colpectomy/colpocleisis
Metoidioplasty (with/without scrotoplasty)	<ul style="list-style-type: none"> • With/without urethral lengthening • With/without prosthesis (penile and/or testicular) • With/without colpectomy/colpocleisis
Vaginoplasty (inversion, peritoneal, intestinal)	<ul style="list-style-type: none"> • May include retention of penis and/or testicle • May include procedures described as "flat front"
Vulvoplasty	
GONALECTOMY	
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)	<ul style="list-style-type: none"> • Electrolysis • Laser epilation
Tattoo (i.e., nipple-areola)	
Uterine transplantation	
Penile transplantation	

CHAPTER 14 Voice and Communication

Human beings engage in communication practices not only to exchange ideas about the outside world, but also to present themselves as socio-cultural 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 sub-population, 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, socio-cultural meaning-making, and external material forces (Azul & Hancock, 2020). This specialist is capable of conducting appropriate assessments to inform the TGD person’s choice and support the exploration of goals and intervention options by providing guidance in a culturally responsive, person-centered approach. This specialist has knowledge and skills in behavioral voice and communication intervention approaches.

Practices amenable to behavioral change include: speaking and singing voice, mindfulness, relaxation, respiration, pitch and pitch range, voice quality, resonance/timbre, loudness, projection, facial expression, gesture, posture, movement, introducing self to others, describing identifications and requesting culturally responsive treatment and forms of address by others, assertive and resilient responses to misattributions, practicing implementation of voice use and communication practices with different people and in different everyday settings (e.g., Hancock & Siegfriedt, 2020; Mills & Stoneham, 2017).

Voice and communication services are offered as part of a complete and coordinated approach to health, including support for medical, psychological, and social needs (Södersten et al., 2015); however, there are no prerequisites (e.g., hormone use, pursuit of surgeries, or duration living in a gender role). The overall purposes of voice and communication support for TGD people are:

- To educate clients about the factors that influence functional voice and communication practices and the communication of the speaker’s identity (speaker, listener, professional practices, external material, biophysiological, and sociocultural factors);
- To enable clients to communicate their sense of sociocultural belonging (e.g., in terms of gender) in everyday encounters in a manner that matches the client’s desired

self-presentation and to develop, maintain and habituate voices, vocal qualities, and communication practices that support the clients’ goals in a manner that does not harm the voice production mechanism;

- To provide training in functional voice production for clients who present with restrictions of voice function (e.g., as a result of overextending their voice production mechanism);
- To support clients with developing the capacity to assertively negotiate desired forms of address and referral from others (e.g., names, pronouns, titles) and to respond to misattributions in a skillful manner that contributes to increasing and maintaining the client’s well-being;
- To support clients to develop the problem-solving skills needed to manage anxiety, stress, and dysphoria in collaboration with mental health providers; and to navigate barriers to practice or real-life use of one’s preferred voice and communication.
- To provide, or refer clients to, supportive resources that facilitate developing voice and communication skills, vocal awareness, and well-being.
- To refer clients to, or collaborate with, other specialists such as mental health practitioners, laryngeal surgeons, and endocrinologists, who may be more equipped to meet the specific needs of that client. This may be especially relevant in cases where clients face unique challenges due to multiple barriers to their health and well-being or when the client wishes to pursue laryngeal surgery or hormone therapy.

Two types of laryngeal surgeries are relevant for TGD populations: those for raising voice pitch (e.g., glottoplasty with retro-displacement of the anterior commissure, cricothyroid approximation (CTA), feminization laryngoplasty, laser-assisted voice adjustment (LAVA)) (Anderson, 2007; Anderson, 2014; Brown, 2000; Casado, 2017; Geneid, 2015; Gross, 1999; Kelly et al., 2018; Kanagalingam, 2005; Kim, 2017; Kim, 2020; Kocak, 2010; Kunachak, 2000; Mastronikolis, 2013; Mastronikolis et al., 2013; Matai, 2003; Meister,

Statements of Recommendations

14.1- We recommend voice and communication specialists assess current and desired vocal and communication function of transgender and gender diverse people and develop appropriate intervention plans for those dissatisfied with their voice and communication.

14.2- We recommend voice and communication specialists working with transgender and gender diverse people receive specific education to develop expertise in supporting vocal functioning, communication, and well-being in this population.

14.3- We recommend health care professionals in transgender health working with transgender and gender diverse people who are dissatisfied with their voice or communication consider offering a referral to voice and communication specialists for voice-related support, assessment, and training.

14.4- We recommend health care professionals consider working with transgender and gender diverse people who are considering undergoing voice surgery consider offering a referral to a voice and communication specialist who can provide pre- and/or postoperative support.

14.5- We recommend health care professionals in transgender health inform transgender and gender diverse people commencing testosterone therapy of the potential and variable effects of this treatment on voice and communication.

2017; Mora, 2018; Neumann, 2004; Nuyen et al., 2022; Orloff, 2006; Pickuth, 2000; Remacle, 2011; Thomas & MacMillan, 2013; Tschan, 2016; Van Borsel, 2008; Wagner, 2003; Wendler, 1990; Yang, 2002) and for lowering voice pitch (e.g., thyroplasty type III, vocal fold injection augmentation) (Bultynck et al., 2020; Isshiki et al., 1983; Kojima, et al. 2008; Webb et al., 2021). Reported acoustic benefits of pitch-raising surgery include increased voice pitch (average frequency (f_o)) and increased $\text{Min } f_o$ (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 $\text{Max } f_o$, in the physiological voice range), hoarseness, vocal instability, and lowering of frequency values over time (Kelly et al., 2018; Song & Jiang, 2017), although the rate of these outcomes is inconsistent.

Research on pitch-lowering surgeries is limited. However, studies including eight TGD people who elected to undergo thyroplasty type III after continued dissatisfaction with hormonal treatment (Bultynck et al., 2020) and one person who received injection augmentation after testosterone therapy and voice training (Webb

et al., 2020), reported statistically significant lowering of fundamental frequency, perceived as pitch.

Estrogen treatment in TGD people has not been associated with measurable voice changes (Mészáros et al., 2005), while testosterone treatment in TGD people has been found to result in both desired and undesired changes in gender- and function-related aspects of voice production (Azul, 2015; Azul et al., 2017, 2018, 2020; Azul & Neuschaefer-Rube, 2019; Cosyns et al., 2014; Damrose, 2008; Deuster, Di Vincenzo 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 socio-cultural 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 TGD persons across all settings can share a standard set of expectations of the knowledge,

skills, and cultural competence required for the care of TGD persons.

Due to the unique medical, surgical, and social conditions faced by TGD people, PCPs need distinct competencies in the care of TGD persons, apart from what is expected of all PCP’s who may otherwise care for a diverse population that includes ethnic, racial, or sexual minorities. Professional bodies from a range of generalist disciplines have issued position statements and guidelines specific to the care of TGD people (American College of Obstetricians and Gynecology, 2021; Italian Society of Gender, Identity and Health (SIGIS); the Italian Society of Andrology and Sexual Medicine (SIAMS); the Italian Society of Endocrinology (SIE), 2021; Polish Sexological Society, 2021; the Southern African HIV Clinicians’ Society, 2021). Wylie et al. (2016) state “For the most part, the general health and well-being of transgender people should be attended to within the primary care setting, without differentiation from services offered to cisgender (non-transgender) people for physical, psychological, and sexual health issues. Specific care for gender transition is also possible in primary care.” There are many examples of these services being provided safely and effectively outside of specialist care in diverse cities such as Toronto and Vancouver in Canada, New York and Boston in the US, and in Sydney, Australia, (Radix & Einfeld, 2014; Reisner, Radix et al., 2016; Spanos et al., 2021).

Hormone therapy

Whether TGD patients receive medically necessary gender-affirming hormone therapy (GAHT) from a specialist, e.g., an endocrinologist, or a PCP may depend on the availability of knowledgeable and welcoming providers and country-level factors, such as health care regulations and health services funding (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1). In much of the world, specialty services for TGD people are partly or wholly unavailable, which reinforces the need for all health providers to undertake

training in the provision of gender-affirming care. In some countries, PCPs may be required to refer TGD patients to specialist services (e.g., gender identity clinics) resulting in unacceptable delays to access GAHT (Royal College of General Practitioners, 2019).

Hormone-related therapy encompasses a range of interventions, such as puberty suppression and hormone initiation or hormone maintenance. With training, gender-affirming hormone therapy can be managed by most PCPs. Regardless of whether they serve as the primary hormone prescriber, all PCPs should be familiar with the medications, suggested monitoring, and potential side effects associated with GAHT (see Chapter 12—Hormone Therapy). PCPs should be able to make appropriate referrals to appropriate providers for all transition-related services they do not themselves provide.

This chapter supports the argument GAHT can be prescribed by PCPs or other non-specialists—“Considering barriers to health care access and the importance of GAHT to this population, it is imperative that PCPs are able and willing to provide GAHT for TGD patients.” (Shires, 2017).

PCPs are commonly called upon to provide care for a broad range of conditions and needs, including those with which they may have had limited or no prior experience. Often this involves accessing commonly used and readily available reference sources, such as professional society guidelines or obtaining a subscription to online knowledge bases. PCPs are advised to use a similar approach when asked to provide basic GAHT care by using the Standards of Care as well as other readily accessed resources (Cheung et al., 2019; Hembree et al., 2017; Oliphant et al., 2018; T’Sjoen et al., 2020). It should be noted most of the commonly used medications in gender-affirming regimens are familiar to everyday primary care practice, including, but not limited to, testosterone, estradiol, progesterone and other progestagens, and spironolactone.

Mental health

PCPs should be able and willing to assess and provide mental health support for TGD

people and GAHT that can alleviate gender dysphoria and allow gender expression. At the very least, they should be aware of these needs and consult additional specialty support if needed.

Preventive care

General practitioners are versed to provide comprehensive primary and secondary cancer prevention as a part of routine primary care. Evidence-based cancer prevention guidelines vary globally due to differences in national guidelines and levels of access to screening modalities at the local level. To date, research on the long-term impact of GAHT on cancer risk is limited (Blondeel et al., 2016; Braun et al., 2017). We have insufficient evidence to estimate the prevalence of cancer of the breast or reproductive organs among TGD populations (Joint et al., 2018). However, cancer screening should commence, in general, according to local guidelines. Several modifications are discussed in detail, below, depending on the type and duration of hormone use, surgical intervention, or both. In caring for transgender patients, the PCP should maintain an updated record of which organs are present in TGD patients so that appropriate, routine screening can be offered.

This organ inventory should be updated based on the surgical history or any development that has occurred due to taking gender-affirming hormones. Not all PCPs provide care across the lifespan. However, if providers routinely care for children, adolescents, or elder cisgender persons, they should develop competency in transgender care that is applicable to these age groups. If they are unable to do so, then PCPs should be able to make appropriate referrals to other HCPs who care for these populations.

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

Statements of Recommendations

15.1- We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people that includes past and present use of hormones, gonadal surgeries, as well as the presence of traditional cardiovascular and cerebrovascular risk factors with the aim of providing regular cardiovascular risk assessment according to established, locally used guidelines.

15.2- We recommend health care professionals assess and manage cardiovascular health in transgender and gender diverse people using a tailored risk factor assessment and cardiovascular/cerebrovascular management methods.

15.3- We recommend health care professionals tailor sex-based risk calculators used for assessing medical conditions to the needs of transgender and gender diverse people, taking into consideration the length of hormone use, dosing, serum hormone levels, current age, and the age at which hormone therapy was initiated.

15.4- We recommend health care professionals counsel transgender and gender diverse people about their tobacco use and advise tobacco/nicotine abstinence prior to gender-affirming surgery.

15.5- We recommend health care professionals discuss and address aging-related psychological, medical, and social concerns with transgender and gender diverse people.

15.6- We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people who have received estrogens, taking into consideration the length of time of hormone use, dosing, current age, and the age at which hormones were initiated.

15.7- We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people with breasts from natal puberty who have not had gender-affirming chest surgery.

15.8- We recommend health care professionals apply the same respective local screening guidelines (including the recommendation not to screen) developed for cisgender women at average and elevated risk for developing ovarian or endometrial cancer in their care of transgender and gender diverse people who have the same risks.

15.9- We recommend against routine oophorectomy or hysterectomy solely for the purpose of preventing ovarian or uterine cancer for transgender and gender diverse people undergoing testosterone treatment and who have an otherwise average risk of malignancy.

15.10- We recommend health care professionals offer cervical cancer screening to transgender and gender diverse people who currently have or previously had a cervix following local guidelines for cisgender women.

15.11- We recommend health care professionals counsel transgender and gender diverse people that the use of antiretroviral medications is not a contraindication to gender-affirming hormone therapy.

15.12- We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people that includes past and present use of hormones, gonadal surgeries as well as the presence of traditional osteoporosis risk factors to assess the optimal age and necessity for osteoporosis screening.

15.13- We recommend health care professionals discuss bone health with transgender and gender diverse people including the need for active weight bearing exercise, healthy diet, calcium, and vitamin D supplementation.

15.14- We recommend health care professionals offer transgender and gender diverse people referrals for hair removal from the face, body, and genital areas for gender-affirmation or as part of a preoperative preparation process.

Statement 15.1

We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people, that includes past and present use of hormones, gonadal surgeries, as well as the presence of traditional cardiovascular and cerebrovascular risk factors with the aim of providing regular cardiovascular risk assessment according to established, locally used guidelines. For supporting text, see Statement 15.3.

Statement 15.2

We recommend health care professionals assess and manage cardiovascular health in transgender and gender diverse people using a tailored risk factor assessment and cardiovascular/cerebrovascular management methods. For supporting text, see Statement 15.3.

Statement 15.3

We recommend health care professionals tailor sex-based risk calculators used for assessing

medical conditions to the needs of transgender and gender diverse people, taking into consideration the length of hormone use, dosing, serum hormone levels, current age, and the age at which hormone therapy was initiated.

Cardiovascular disease (CVD) and stroke are the leading causes of mortality worldwide (World Health Organization, 2018). Extensive data among racial, ethnic, and sexual minorities in multiple settings demonstrate significant disparities in the prevalence of CVD and its risk factors as well as in the outcomes to medical interventions. Structural factors such as access to care, socio-economic status, and allostatic load related to minority stress contribute to these disparities (Flentje et al., 2020; Havranek et al., 2015; Streed et al., 2021). TGD people often experience social, economic, and discriminatory conditions similar to other minority populations with known increased cardiovascular risk (Carpenter et al., 2020; James et al., 2016; Reisner, Radix et al., 2016). TGD persons of racial, ethnic, and sexual

minorities have been shown to experience increased impact related to intersectional stress. Conversely, access to gender-affirming care, including GAHT, may buffer against the elevation of CVD risk due to the improvement in quality of life and reduction in gender dysphoria and incongruence (Defreyne et al., 2019; Martinez et al., 2018). PCPs can significantly improve TGD health through screening and prevention of CVD and its associated risk conditions—such as tobacco use, diabetes mellitus, hypertension, dyslipidemia, and obesity.

The few, primarily US based, studies evaluating the prevalence of CVD, stroke, or CVD risk in TGD persons independent of GAHT indicate an elevated CV risk, including high rates of undiagnosed and untreated CV risk factors with inadequate CV prevention when compared with cisgender populations (Denby et al., 2021; Malhotra et al., 2022; Nokoff et al., 2018). In one population-based study, TGD people had greater odds of discrimination, psychological distress, and adverse childhood experience, and these were associated with increased odds of having a cardiovascular condition (Poteat et al., 2021).

In US studies that are based on data from the Behavioral Risk Factor Surveillance System, both transgender men and transgender women show a higher prevalence of myocardial infarction (MI), stroke, or any CVD compared with cisgender men, cisgender women or both. Results vary based on the adjustment of data for additional variables, including race, income, or cardiovascular risk factors (Alzahrani et al., 2019; Caceres et al., 2020; Nokoff et al., 2018). Gender nonbinary persons also have higher odds of CVD (Downing & Przedworski, 2018). Data on hormone use was not collected in these studies, which are also limited by the use of self-reported health histories. In the US, TGD individuals presenting for GAHT may have higher rates of undiagnosed and untreated CVD risk factors compared with the cisgender population (Denby et al., 2021), although this may not be applicable globally.

A large 2018 case control study from several US centers that used 10:1 cisgender matched controls found no statistically significant difference in rates of MI or stroke between transgender women and cisgender men, and no difference in

rates of MI, stroke, or venous thromboembolism (VTE) between transgender men and cisgender men or women. There was a statistically significant hazard ratio of 1.9 for VTE among transgender women when compared with cisgender men. A subcohort of transgender women who initiated GAHT during (versus prior to) the 6-year study window did show an increased risk of stroke. Increases in rates of VTE in the overall cohort of transgender women and in rates of stroke in the initiation subcohort of transgender women demonstrated calculated numbers-needed-to-harm (not reported in the paper) between 71-123 (Getahun et al., 2018). Other studies have demonstrated no increase in CV events or stroke among transgender men undergoing testosterone therapy, although studies are limited by their small sample size, relatively short follow-up, and the younger age of the sample population (Martinez et al., 2020; Nota et al., 2019).

European and US studies in transgender women who have accessed feminizing GAHT increasingly indicate a higher risk of CVD, stroke, or both, compared with cisgender women and, in some studies, cisgender men (Getahun et al., 2018; Nota et al., 2019; Wierckx et al., 2013). Many of these studies had significant limitations, such as variably adjusting for CV-related risk factors, small sample sizes—especially involving older transgender women—and variable duration and types of GAHT (Connelly et al., 2019; Defreyne et al., 2019; Martinez et al., 2020). Furthermore, the overall increased risk was small. In many of these studies, the majority of transgender women who experienced cardiac events or stroke were over 50 years old, had one or more CVD risk factors, and were taking a variety of hormone regimens, including, but not limited, to ethinyl estradiol, a synthetic estrogen that confers significant elevations in thrombotic risk and is not recommended for use in feminizing regimens (Gooren et al., 2014; Martinez et al., 2020). Current limited evidence suggests estrogen-based GAHT is associated with an increased risk of myocardial infarction and stroke, but whether this small risk is a result of GAHT or an effect of pre-existing CV risk is unclear. There are no known studies that specifically address CVD and

related conditions in nonbinary individuals, individuals who use subphysiologic doses of gender-affirming hormones, or in adults previously treated with puberty suppression.

PCPs can best address CVD risk during GAHT by assessing TGD people for CVD and modifiable CVD risk factors, such as diabetes mellitus, hypertension, hyperlipidemia, obesity, and smoking, as well as by addressing the impact of minority stress on cardiovascular risk (Streed et al., 2021). In addition, PCPs can mitigate transgender cardiovascular health disparities by providing a timely diagnosis and treatment of risk conditions and by tailoring their management in a way that supports ongoing gender-affirming interventions.

Risk assessment guidelines vary based on the national or international context and scientific affiliation of guideline developers. CVD prevention guidelines also vary in terms of the nature and frequency of the risk assessment for otherwise healthy adults under age 40 (Arnett et al., 2019; Piepoli et al., 2020; Précoma et al., 2019; Streed et al., 2021; WHO, 2007). Over age 40, when cardiovascular risk increases, guidelines clearly recommend scheduled risk assessments using a calculated prediction of ten-year total CVD risk based on risk prediction equations from large population samples. Examples of risk calculators include SCORE (recommended by the European Guidelines on CVD Prevention), Pooled Cohort Studies Equations (2013 AHA ACC Guideline on the Assessment of CVD risk), Framingham Risk scores, and the World Health Organization (WHO) Risk Prediction Charts. The WHO charts were developed based on information from the countries in each WHO subregion. In many low resource settings, facilities are not available to measure cholesterol or serum glucose, and alternative predication charts are available without these measures.

Of note, all current cardiovascular risk calculators are gendered, using sex as a significant risk variable. There is currently insufficient data on cardiovascular risk interventions across the lifespan in TGD persons with medical and surgical interventions to adjust these predictive equations. Nonetheless, it is clear both sex assigned at birth and medical transition can affect the parameters used to calculate cardiovascular risk (Connelly

et al., 2019; Defreyne et al., 2019; Maraka et al., 2017; Martinez et al., 2020). Providers can take a variety of approaches to using cardiovascular risk calculators in TGD persons, including employing the risk calculator for the sex assigned at birth, affirmed gender, or a weighted average of the two, taking into consideration total lifetime exposure to GAHT. Although data are lacking, using the affirmed gender for transgender adults with a history of pubertal-age GAHT initiations is likely to be most appropriate. Patients with a history of submaximal GAHT use or prolonged periods of time postgonadectomy without hormone replacement before roughly age 50 may require an even more nuanced approach. Providers should be aware of the characteristics and limitations of the risk calculator in use and should engage patients in shared decision-making regarding these specific considerations.

There are currently no studies comparing the prevalence of dyslipidemia between transgender and cisgender samples, while controlling for hormone use. As noted previously, data in other populations demonstrate the presence of psychosocial stress during childhood and remote adulthood favor adiposity and abnormal lipid metabolism. Both testosterone- and estrogen-based GAHT affect lipid metabolism, although evidence is limited by the variety of hormone regimens and additional variables (Connelly et al., 2019; Defreyne et al., 2019; Deutsch, Glidden et al., 2015; Maraka et al., 2017; Martinez et al., 2020;). On balance, estrogen tends to increase high-density lipoprotein (HDL) cholesterol and triglycerides with variable effects on low density lipoprotein (LDL) cholesterol, while testosterone variably affects triglycerides, decreases HDL cholesterol and increases LDL cholesterol. The method of administration may also affect this pattern, particularly in relation to oral versus transdermal estrogen and their impact on triglycerides (Maraka et al., 2017). In general, the effect sizes of these differences are minimal, and the overall impact on cardio- and cerebrovascular outcomes is unclear. There are no studies examining hormone effects in TGD people with pre-existing dyslipidemia with hormone use starting over age 50, or investigating effects beyond 2-5 years of therapy.

Studies comparing the prevalence of hypertension between TGD and cisgender samples that controlled for hormone use are lacking. Data in other populations demonstrate chronic and acute psychosocial stress, including experiences of discrimination can mediate hypertension (Din-Dzietham et al., 2004; Spruill, 2010). In US studies that were based on the Behavioral Risk Factor Surveillance System, a large national US health survey, there were no differences in reported hypertension between transgender men or women compared with cisgender samples (Alzahrani et al., 2019; Nokoff et al., 2018).

Studies of testosterone—and estrogen-based GAHT have shown inconsistent effects on systolic and diastolic blood pressure. A retrospective study of the effects of estrogen- and testosterone-based GAHT regimens on blood pressure found a slight reduction in systolic blood pressure with the initiation of estrogen-based regimens; while there was a slight elevation (4 mm Hg) in mean systolic blood pressure on long term follow-up of testosterone-based regimens, this difference was at the margin of statistical significance and of limited clinical relevance (Banks et al., 2021). A systematic review concluded, given the limited quality of the studies, there is insufficient data to reach conclusions on the effects of gender-affirming hormone therapy on blood pressure (Connelly et al., 2021). Spironolactone, often used as an androgen blocker in feminizing GAHT, is a potassium sparing diuretic and may increase potassium when used in conjunction with ACE inhibitors or angiotensin receptor blocker medications, as well as salt substitutes. There are no studies examining hormone effects in TGD people with pre-existing hypertension with hormone use starting over age 50, or investigating effects beyond 2–5 years of therapy. Transgender persons receiving GAHT should undergo any additional blood pressure screening or monitoring indicated by WPATH guidelines for GAHT.

There are limited data comparing the prevalence of diabetes mellitus between TGD and cisgender samples independent of hormone use. Recent data from the STRONG cohort study (Islam et al., 2021) found the prevalence and incidence of type 2 diabetes was more common in the trans feminine cohort compared with cisgender females but

not cisgender male controls. No significant differences in the prevalence or incidence of type 2 diabetes were observed in the trans masculine cohort and in TGD persons overall after starting hormone therapy. However, the mean follow-up for both cohorts was 2.8 and 3.1 years, respectively (Islam et al., 2021). Data in other populations, including sexual minorities, indicates chronic and acute psychosocial stress can mediate the development and control of type 2 diabetes (Beach et al., 2018; Kelly & Mubarak, 2015).

US studies based on the Behavioral Risk Factor Surveillance System found no differences in reported diabetes between transgender men, transgender women and nonbinary persons compared with cisgender persons (Alzahrani et al., 2019; Caceres et al., 2020; Nokoff et al., 2018). Several small studies have shown a higher-than-expected prevalence of polycystic ovarian syndrome or hyperandrogenemia among transgender men (Feldman et al., 2016), conditions associated with insulin resistance and diabetes risk. While studies of both testosterone- and estrogen-based GAHT show varying effects on weight/body fat, glucose metabolism, and insulin resistance (Defreyne et al., 2019), most do not demonstrate any increase in prediabetes or diabetes (Chan et al., 2018; Connelly et al., 2019). There are no studies examining hormone effects in TGD people with pre-existing diabetes, with hormone use starting over age 50, or investigating effects beyond 2–5 years of therapy. There are currently no studies specifically addressing diabetes in adults previously treated with puberty suppression.

While intermediate-outcome studies of the effects of GAHT on blood pressure and lipids are helpful for hypothesis generation and for studying etiology, future studies should focus on cardiovascular outcomes of interest, with a specific focus on individual predictors such as age, route and dose of hormones used, and total lifetime exposure to GAHT. Interpretation of data should always consider whether cisgender controls were of the same natal sex or identified gender.

Statement 15.4

We recommend health care professionals counsel transgender and gender diverse people about

their tobacco use and advise tobacco/nicotine abstinence prior to gender-affirming surgery.

Tobacco use is a leading contributor to cardiovascular disease, pulmonary disease, and cancer worldwide (World Health Organization, 2020). TGD persons have a higher prevalence of tobacco use compared with cisgender individuals, which varies across the gender spectrum (Azagba et al., 2019; Buchting et al., 2017). This pattern is consistent with other populations experiencing minority stress (Gordon et al., 2021). PCPs can promote protective factors against tobacco use, including reducing exposure to personal or structural discrimination, having gender-affirming identification, and having health insurance (Kidd et al., 2018; Shires & Jafee, 2016).

The health risks of tobacco use affect TGD persons disproportionately, primarily due to decreased access to culturally competent, affordable screening, and treatment of tobacco-related diseases (Shires & Jafee, 2016). Smoking may further increase cardiovascular and VTE risk for TGD individuals taking feminizing GAHT (Hontscharuk, Alba, Manno et al., 2021). Smoking also doubles or triples the risk of general surgery complications, such as wound healing, scarring, and infection (Yoong et al., 2020) and increases these risks for those accessing gender-affirming surgeries. Data in cisgender populations show quitting smoking prior to surgery and maintaining abstinence for six weeks postoperatively significantly reduces complications (Yoong et al., 2020).

There are currently few studies of smoking cessation programs specifically focused on TGD persons (Berger & Mooney-Somers, 2017). However, limited evidence suggests PCPs can enhance smoking cessation efforts by addressing the effects of minority stress (Gamarel et al., 2015) and incorporating gender-affirming interventions, such as GAHT (Myers & Safer, 2016).

HCPs should take into consideration the significant barriers people habituated to nicotine encounter when attempting cessation. Nicotine replacement therapy and/or other cessation adjuncts should be made available, with an emphasis on individual preferences and a recognition of underlying behavioral health factors that contribute to continued nicotine use. Decision-making

regarding approaches to GAHT or surgery should include consideration of the “first do no harm” principle of medical practice, with the realities of an individual patient’s abilities and needs.

Statement 15.5

We recommend health care professionals discuss and address aging-related psychological, medical, and social concerns with transgender and gender diverse people.

Aging presents specific social, physical, and mental health challenges for TGD persons. While the literature on aging and transgender elders is limited, many older TGD adults have experienced a lifetime of stigma, discrimination, and repression of identified gender (Fabbre & Gaveras, 2020; Witten, 2017). This experience affects TGD elders’ interactions with health care systems (Fredriksen-Goldsen et al., 2014; Kattari & Hasche, 2016; Walker et al., 2017). Transgender elders are more likely than cisgender LGB peers to report poor physical health, even when controlling for socio-demographic factors (Fredriksen-Goldsen 2011; Fredriksen-Goldsen et al., 2014). Reduced access to culturally competent care and the sequelae of minority stress often result in delayed care, potentially exacerbating chronic conditions common with aging (Bakko & Kattari, 2021; Fredriksen-Goldsen et al., 2014).

Although there are few studies on gender-affirming medical interventions among TGD elders, evidence suggests older adults experience a significantly higher quality of life with medical transition even when compared with younger TGD adults (Cai et al., 2019). Although age itself is not an absolute contraindication or limitation to gender-affirming medical or surgical interventions, TGD elders may not be aware of the current range of social, medical or surgical options available that can help them meet their individual needs (Hardacker et al., 2019; Houlberg, 2019).

While studies on mental health among TGD elders are limited, those over age fifty experience significantly higher rates of depressive symptoms and perceived stress compared with cisgender LGB and heterosexual older adults (Fredriksen-Goldsen 2011, Fredriksen-

Goldsen et al., 2014). Risk factors specific to TGD elders include gender- and age-related discrimination, general stress, identity concealment, victimization, and internalized stigma, while social support and community belonging appear protective (Fredriksen-Goldsen et al., 2014; Hoy-Ellis & Fredriksen-Goldsen, 2017; White Hughto & Reisner, 2018). PCPs can assist patients by encouraging spirituality, self-acceptance and self-advocacy, and an active healthy lifestyle, all of which are associated with resilience and successful aging (McFadden et al., 2013; Witten, 2014).

TGD elders often face social isolation, loss of support systems, and disconnection from close friends and children (Fredriksen-Goldsen 2011; Witten, 2017). The most common aging concerns among TGD persons are losing the ability to care for themselves followed by having to go into a nursing home or assisted living facility (Henry et al., 2020). While long-term care settings offer the helpful needed assistance, they also have the potential for physical or emotional abuse, for denial of GAHT and routine care, for being “outed,” and being prevented from living and dressing according to one’s affirmed gender (Auldridge et al., 2012; Pang et al., 2019; Porter et al., 2016). TGD elders identify senior housing, transportation, social events, support groups as being the most needed services (Auldridge et al., 2012; Witten, 2014).

Despite barriers, most TGD persons engage in successful aging strengthened by self-acceptance, caring relationships, and advocacy (Fredriksen-Goldsen 2011; Witten, 2014). PCPs should address core health issues facing TGD elders, including mental health, gender-affirming medical interventions, social support, and end of life/long-term care.

Beyond the independent impact of factors such as minority stress and social determinants of health in later years, data are lacking on specific health issues facing transgender people who use GAHT later in life, individuals who began GAHT at a younger age, and those seeking to continue or begin GAHT in their sixth, seventh, eighth, or later decades. With an increasing proportion of transgender people beginning GAHT at younger ages, including some who begin at the time of puberty, studies to examine the impact of decades of such treatment on long-term health are ever more important.

Statement 15.6

We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people who have received estrogens, taking into consideration length of time of hormone use, dosing, current age, and the age at which hormones were initiated.

TGD individuals taking estrogen-based GAHT will develop breasts, and therefore warrant consideration for breast cancer screening. Exogenous estrogen may be one of multiple factors that contribute to breast cancer risk in cisgender people. Two cohort studies have been published evaluating breast cancer prevalence among transgender women in the Netherlands (Gooren et al., 2013) and the US (Brown & Jones, 2015). Both were retrospective cohorts of clinical samples using a diagnosis of breast cancer as the outcome of interest and cisgender controls as a comparison group. Neither study involved prospective screening for breast cancer, and both had significant methodological limitations. Numerous guidelines have been published (Deutsch, 2016a) recommending some combination of “age plus length of estrogen exposure” as the determinant of need to commence screening. These recommendations are based on expert consensus only and are evidentially weak.

BRCA1 and 2 mutations increase the risk of breast cancer, however the role sex hormone exposure plays, if any, in this increased risk is unclear (Rebbeck et al., 2005) The degree of increase in risk, if any, from gender-affirming estrogen therapy is unknown. Patients with a known BRCA1 mutation should be counseled about the unknowns and shared decision-making with informed consent should occur between the patient and provider, recognizing the numerous benefits of GAHT.

Breast cancer screening among transgender women should also take into consideration the likelihood that a transgender woman’s breasts may be denser on mammography. Dense breasts, a history of injecting breasts with fillers such as silicone, and breast implants may complicate the interpretation of mammographic findings (Sonnenblick et al., 2018). Therefore, special

techniques should be used accordingly. People who have injected particles such as silicone or other fillers for breast augmentation may also develop complications, such as sclerosing lipogranulomas, which obscure normal tissue on mammography or ultrasound.

Statement 15.7

We recommend health care professionals follow local breast cancer screening guidelines developed for cisgender women in their care of transgender and gender diverse people with breasts from natal puberty who have not had gender-affirming chest surgery.

For TGD people assigned female at birth and who developed breasts via natal puberty, there are theoretical concerns about whether direct exposure to testosterone and exposure to aromatized estrogen resulting from testosterone therapy are risk factors for the development of breast cancer. Limited retrospective data has not demonstrated increased risk for breast cancer among transgender men (Gooren et al., 2013; Grynberg et al., 2010), however prospective and comparison data are lacking. Most people in this group will have some breast tissue remaining, and therefore it is important for providers to be aware breast cancer risk is not zero in this population. The timing and approach to breast cancer screening in this group who have had chest surgery is currently not established, and, similar to cisgender men with significant family history or BRCA gene mutation, screening via MRI or ultrasound may be appropriate. Because the utility and performance of these approaches have not been studied and because self- and HCP-led chest/breast screening exams are not recommended in cisgender women due to potential harms of both false-positive results and over-detection (detection of a cancer which would have regressed on its own with no need for intervention), any approach to screening in this group should occur in the context of shared decision-making between patients and providers regarding the potential harms, benefits, and unknowns of these approaches.

Statement 15.8

We recommend health care professionals apply the same respective local screening guidelines

(including the recommendation not to screen) developed for cisgender women at average and elevated risk for developing ovarian or endometrial cancer in their care of transgender and gender diverse people who have the same risks.

Current consensus guidelines do not recommend routine ovarian cancer screening for cisgender women. Case reports of ovarian cancer among transgender men have been reported (Dizon et al., 2006; Hage et al., 2000). There is currently no evidence testosterone therapy leads to an increased risk of ovarian cancer, although long-term prospective studies are lacking (Joint et al., 2018).

Statement 15.9

We recommend against routine oophorectomy or hysterectomy solely for the purpose of preventing ovarian or uterine cancer for transgender and gender diverse people undergoing testosterone treatment and who have an otherwise average risk of malignancy.

TGD people with ovaries who are taking testosterone-based GAHT are often in an oligo- or anovulatory state, or otherwise experience shifts in luteal phase function and progesterone production. This condition combined with the possible increased estrogen exposure from aromatization of exogenous testosterone raises the concern for excessive or unopposed endometrial estrogen exposure, although the clinical significance is unknown. Histologic studies of the endometrium in TGD people taking testosterone have found atrophy rather than hyperplasia (Grimstad et al., 2018; Grynberg et al., 2010; Perrone et al., 2009). In a large cohort of trans masculine people who underwent a hysterectomy with oophorectomy, benign ovarian histopathology was noted in all cases (n = 85) (Grimstad et al., 2020). While prospective outcome data are lacking, there is insufficient evidence at this time to support a recommendation transgender men undergo routine hysterectomy or oophorectomy solely to prevent endometrial or ovarian cancer. Certainly, unexplained signs/symptoms of endometrial or ovarian cancer should be evaluated appropriately.

Statement 15.10

We recommend health care professionals offer cervical cancer screening to transgender and

gender diverse people who currently have or previously had a cervix, following local guidelines for cisgender women.

Individuals with a cervix should undergo routine cervical cancer screening and prevention according to age-based regional practices and guidelines. This includes vaccination against the human papilloma virus (HPV) and screening according to local guidelines, including cytologic, high-HPV co-testing if available. It is important HCPs be mindful of performing pelvic speculum examinations in a manner that minimizes pain and distress for transgender masculine people.

TGD people with a cervix are less likely to have had conventional cervical cancer screening, either because the exam can cause worsening of dysphoria and/or because general practitioners and patients are misinformed about the need for this screening (Agenor et al., 2016; Potter et al., 2015). In addition, testosterone therapy can result in atrophic changes of the genital tract, and the duration of testosterone use has been associated with a greater likelihood of obtaining an inadequate sample for cytologic screening of cervical cancer (Peitzmeier et al., 2014). Alternatives to speculum exams and cervical cytology, such as provider- or self-collected high-risk HPV swabs, may be of particular benefit for screening people with a cervix. Research underway in the US is investigating the use of self-collected vaginal high-risk HPV testing among transgender masculine populations. HPV swabs were found to be highly acceptable among transgender men with a sensitivity to high-risk HPV of 71.4% (negative predictive value of 94.7%) and a specificity of 98.2% (Reisner et al., 2018). Further study is needed to evaluate the harms of HPV primary screening in transgender men in terms of the potential increased harms associated with invasive examinations and colposcopies.

Statement 15.11

We recommend health care professionals counsel transgender and gender diverse people that the use of antiretroviral medications is not a contraindication to gender-affirming hormone therapy.

Human immunodeficiency virus (HIV) prevalence is disproportionately high in TGD

populations. A recent large metanalysis found a global odds ratio for HIV infection of sixty-six for trans feminine individuals and 6.8 for trans masculine individuals (Stutterheim et al., 2021). PCPs have unique opportunities to provide crucial education and implement prevention strategies, especially related to decreasing HIV burden among TGD people. Mistrust of health care providers due to past experiences of discrimination and transphobia impacts HIV prevention and disrupts the linkage to care efforts (Sevelius et al., 2016). Stigma, lack of adequate training, and innate power hierarchies within medical establishments, all contribute to ambivalence and uncertainty among HCPs when caring for TGD people (Poteat et al., 2013). Finally, a lack of inclusiveness and gender-affirming practices in the health care setting may lead to TGD people feeling unsafe discussing sensitive topics, such as HIV diagnosis and avoiding care out of fear (Bauer et al., 2014; Gibson et al., 2016; Seelman et al., 2017).

HCPs should be aware of this broader context within which many TGD people are seeking care for either gender-affirming hormones, HIV pre-exposure chemoprophylaxis/treatment (PrEP), or both. There may be various misconceptions about the safety of taking gender-affirming hormones concurrently with antiretroviral therapy for HIV chemoprophylaxis or treatment.

Direct study of antiretroviral/gender-affirming hormone therapy (ART/GAHT) interactions has been limited. A subanalysis of transgender women and trans feminine persons in the multinational iPrEx trial found poor effectiveness in this group in the intention-to-treat analysis, although effectiveness was similar to that in cisgender gay men among those transgender participants who adhered to the medication as prescribed, suggesting that uptake and adherence to PrEP remain challenging in this population. Two studies of the effects of GAHT on tenofovir diphosphate (Grant et al., 2021) and tenofovir diphosphate and emtricitabine (Shieh et al., 2019) found the significantly lowered ART drug levels were unlikely to be of clinical significance. Overall, data on the interactions between hormonal contraceptives and antiretrovirals are reassuring in terms of the impact of hormones on ART (Nanda

et al., 2017). Because estradiol is partially metabolized by cytochrome P450 (CYP) 3A4 and 1A2 enzymes, potential drug interactions with other medications that induce or inhibit these pathways, such as non-nucleoside reverse transcriptase inhibitors (NNRTIs, e.g., efavirenz (EFV) and nevirapine (NVP)), may exist (Badowski et al., 2021). However, the preferred first-line ART regimens in most countries include integrase inhibitors, which have minimal to no drug interactions with gender-affirming hormones and can be used safely (Badowski, 2021; Department of Health and Human Services. Panel on Antiretroviral Guidelines for Adults and Adolescents, 2021). If concerns exist about potential interactions, HCPs should monitor blood hormone levels as needed. Therefore, TGD people living with HIV and taking antiretroviral medications should be counseled that taking antiretrovirals alongside GAHT is safe.

Statement 15.12

We recommend health care professionals obtain a detailed medical history from transgender and gender diverse people that includes past and present use of hormones, gonadal surgeries as well as the presence of traditional osteoporosis risk factors, to assess the optimal age and necessity for osteoporosis screening. For supporting text, see Statement 15.13.

Statement 15.13

We recommend health care professionals discuss bone health with transgender and gender diverse people including the need for active weight bearing exercise, healthy diet, calcium, and vitamin D supplementation.

Estrogen and testosterone both support bone formation and turnover. Decreased sex hormone levels are associated with a greater risk of osteoporosis in older age (Almeida et al., 2017). TGD individuals may receive medical and/or surgical interventions that have the potential to influence bone health, such as sex hormone treatment, androgen blockade, and gonadectomy. Therefore, a detailed medical history, including past and present use of hormones along with gonadal surgeries, is necessary to establish the need for osteoporosis screening.

Several observational studies have compared bone mineral density (BMD) of TGD adults before and after gender-affirming hormone therapy along with in TGD individuals compared with sex-at-birth matched cisgender controls.

Low BMD may exist before the initiation of hormones. One study showed a lower mean areal BMD at the femoral neck, total hip, and spine in transgender women than in age-matched cisgender male controls (Van Caenegem, Taes et al., 2013). Another study revealed a high prevalence of low BMD scores among TGD youth before starting puberty blockers (Lee, Finlayson et al., 2020). The authors of both studies concluded low rates of physical activity may be an important contributor to these findings.

Acceleration of bone loss can occur after gonadectomy if hormones are stopped or if hormones levels are suboptimal. In one study, thirty percent of transgender women who had undergone gonadectomy had low bone mass, and this correlated with lower 17- β estradiol levels and adherence to GAHT (Motta et al., 2020).

Investigation of the effects of GAHT on BMD have revealed TGD women receiving estrogen therapy show improvements in BMD. A systematic review and meta-analysis on the impact of sex hormones on bone health of transgender individuals included 9 eligible studies in transgender women (n=392) and 8 eligible studies in transgender men (n=247) published between 2008 and 2015. The meta-analysis revealed transgender women showed a statistically significant increase in lumbar spine BMD (but not femoral neck BMD) compared with baseline measures. Among transgender men, there were no statistically significant changes in the lumbar spine, femoral neck, and total hip BMD at 12 and 24 months after starting testosterone compared with baseline measures (Singh-Ospina et al., 2017). Since the publication of this study, the European Network for Investigation of Gender Incongruence (ENIGI) study, a multicenter prospective observational study (Belgium, Norway, Italy, and the Netherlands) published results on BMD outcomes for 231 transgender women and 199 transgender men one year after initiating GAH (Wiepjes et al., 2017). Transgender women had an increase in BMD of the lumbar spine, total hip and

femoral neck, and increased BMD of the total hip occurred in transgender men. One study reported no fractures in transgender individuals at 12 months following initiation of hormones in 53 transgender men and 53 transgender women (Wierckx, van Caenegem et al., 2014). No studies suggest GAHT should be an indication for enhanced osteoporosis screening. Rather, gaps in GAHT in those who have undergone prior gonadectomy would be a consideration for such screening.

Clinical practice guidelines include recommendations for osteoporosis screening in TGD individuals (Deutsch, 2016a; Hembree et al., 2017; Rosen et al., 2019). For TGD people, both the International Society for Clinical Densitometry and the Endocrine Society suggest consideration of baseline BMD screening before initiation of hormones. Further recommendations for BMD screening are based on several factors including sex reported at birth and age along with the presence of traditional risk factors for osteoporosis, such as prior fracture, high risk medication use, conditions associated with bone loss, and low body weight (Rosen et al., 2019). Specifically, the ISCD guidelines state BMD testing is indicated for TGD individuals if they have a history of gonadectomy or therapy that lowers endogenous gonadal steroid levels prior to the initiation of GAHT, hypogonadism with no plan to take GAHT or known indications for BMD testing (Rosen et al., 2019). However, the evidentiary basis for these recommendations is weak.

The recommended screening modality for osteoporosis is dual energy x-ray absorptiometry (DXA) of the lumbar spine, total hip, and femoral neck (Kanis, 1994). However in many low- and middle-income countries, BMD tests using DXA are not available, and routine DXA-based screening is conducted in few countries, the US being an exception.

PCPs should discuss ways to optimize bone health with TGD people. In addition, PCPs should provide information about the importance of nutrition and exercise on maintaining bone health. TGD individuals with (or at risk) for osteoporosis should be informed about the benefits of weight bearing exercise along with strength and resistance exercises in limiting bone loss

(Benedetti et al., 2018). Nutrition is integral to bone health. Nutritional deficiencies, including insufficient calcium intake and low vitamin D, can result in low bone mineralization. Vitamin D and calcium supplementation have been shown to reduce hip as well as total fracture incidence (Weaver et al., 2016). Although relevant to all populations, this discussion is pertinent as a high prevalence of hypovitaminosis D has been observed in TGD populations (Motta et al., 2020; Van Caenegem, Taes et al., 2013).

Statement 15.14

We recommend health care professionals offer transgender and gender diverse people referrals for hair removal from the face, body, and genital areas for gender-affirmation or as part of a preoperative preparation process.

Hair removal is necessary both for the elimination of facial hair (Marks et al., 2019) as well as in preparation for certain gender-affirming surgeries (GAS) such as vaginoplasty, phalloplasty, and metoidioplasty (Zhang et al., 2016). Preoperative permanent hair removal is required for any skin area that will either be brought into contact with urine (e.g., used to construct a neourethra) or be moved to reside within a partially closed cavity within the body (e.g., used to line the neovagina) (Zhang et al., 2016). Hair removal techniques used in gender-affirming care are electrolysis hair removal (EHR) and laser hair removal (LHR) (Fernandez et al., 2013). EHR is currently the only US Food and Drug Administration–approved method of permanent hair removal, whereas LHR is approved for permanent hair reduction (Thoreson et al., 2020).

EHR involves the use of an electric current with a very fine probe that is manually inserted sequentially into individual hair follicles (Martin et al., 2018). Since this method uses direct mechanical destruction of the blood supply to the hair, it can be used on all hair colors and skin types (Martin et al., 2018). EHR is time consuming and costly as it requires each hair follicle to be treated individually, but is effective for permanent hair removal. For genital permanent hair removal prior to GAS, this treatment needs to be performed by a practitioner competent in genital hair removal as this method differs

from that of the face and body. EHR is more painful than LHR, with possible side effects of erythema, crusting, and swelling (Harris et al., 2014). Postinflammatory hyperpigmentation is a risk for dark-skinned individuals (Richards & Meharg, 1995). Pain can be controlled with topical local anesthetic and cooling techniques, and tolerance to EHR does develop to some degree with many persons able to tolerate longer sessions (Richards & Meharg, 1995).

LHR uses laser energy to target hair follicles. It is beneficial for larger surface areas. The mechanism is photo-thermolysis, whereby light from a laser selectively targets melanin in the hair shaft (Gao et al., 2018). This energy is converted to heat, which damages the follicles within the skin that produce hairs and results in the destruction of hair growth. Further treatments are needed to achieve best results and are typically spaced six weeks apart to allow for hair cycling (Zhang et al., 2016). Because LHR targets melanin, results may be limited for those with grey, blonde, or red hair.

There are specific considerations for using LHR in dark-skinned individuals (Fitzpatrick skin types IV to VI) (Fayne et al., 2018)). The higher melanin content of the epidermis can compete with the target chromophore of the light or laser, which is the melanin in the hair shaft of the hair follicle. For selective thermolysis to occur, heat

diffuses from the hair shaft to the follicular stem cells to cause damage. In darker skin types, rather than reaching the target melanin in the hair shaft, light is absorbed in the epidermis where it is then converted to heat. This may result in poorer clinical outcomes and a higher rate of thermally induced adverse effects, such as hypo- or hyperpigmentation, blistering, and crust formation (Fayne et al., 2018). The selection of laser wavelength is critical in reducing this risk, with longer wavelength recommended to minimize the absorption of light in epidermal melanin and thus maximize efficacy and minimize adverse effects in patients with dark skin (Zhang et al., 2016). Side effects from LHR can include the feeling of sunburnt after treatment, as well as inflammation, redness, hyperpigmentation, and swelling. Flashing lights have been known to induce seizures in susceptible patients, so patients should be screened for this risk. Pain and discomfort during the procedure can also represent a significant barrier, and PCPs should be prepared to prescribe topical or systemic analgesics, such as a eutectic mixture of local anesthetics (EMLA) or a low dose systemic opioid. For genital GAS, some have recommended a 3-month wait after the last planned hair removal treatment before proceeding with surgery to confirm that no further hair regrowth will occur (Zhang et al., 2016).

CHAPTER 16 Reproductive Health

All humans, including transgender individuals, have the reproductive right to decide whether or not to have children (United Nations Population Fund, 2014). Medically necessary gender-affirming hormonal treatments (GAHTs) and surgical interventions (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1) that alter reproductive anatomy or function may limit future reproductive options to varying degrees (Hembree et al., 2017; Nahata et al., 2019). It is thus critical to discuss infertility risk and fertility preservation (FP) options with transgender individuals and their families prior to initiating any of these treatments and to continue these conversations on an ongoing basis thereafter (Hembree et al., 2017). Established FP options, such as embryo, oocyte, and sperm cryopreservation, may be available for postpubertal transgender individuals (Nahata et al., 2019). Research protocols for ovarian and testicular tissue cryopreservation have also been developed and studied (Borgström et al., 2020; Nahata et al., 2019; Rodriguez-Wallberg, et al., 2019). Whereas the use of embryos, mature oocytes, and sperm have all proven to be efficacious when employed within clinical treatments, cryopreserved gonadal tissues would require either future retransplantation aimed at obtaining fully functional gametes or the application of laboratory methods for culture, which are still under development in basic science research settings. Of note, recent American Society for Reproductive Medicine guidelines have lifted the experimental label on ovarian tissue cryopreservation, but evidence remains limited in prepubertal children (Practice Committee of the American Society for Reproductive Medicine, 2019).

Individualized care should be provided in the context of each person's parenthood goals. Some research suggests transgender and gender diverse (TGD) people may be less likely to desire genetically related children or children at all when compared with cisgender peers (Defreyne, van Schuylenbergh 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 (Armuan, 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 (Armuan, Dhejne, et al., 2017; Baram et al., 2019). When available, a multidisciplinary team approach, where both medical and mental health providers collaborate with gender-affirming fertility specialists, can help overcome some of these barriers (Tishelman et al., 2019). TGD individuals should be educated about the distinction between fertility (utilizing one's own gametes/reproductive tissues) and pregnancy. In addition to fertility considerations, efforts to ensure equitable high-quality care for all forms of family planning and building throughout the full reproductive continuum must be maintained. This includes procreative options such as perinatal care, pregnancy, delivery, and postpartum care, as well as family planning and contraceptive options to prevent unplanned pregnancies, and pregnancy termination if sanctioned (Bonnington et al., 2020; Cipres et al., 2017; Krempasky et al., 2020; Light et al., 2018; Moseson, Fix et al., 2020). TGD people who wish to carry a pregnancy should undergo standard of care preconception care and prenatal counseling and should receive counseling about breast/chest feeding in environments supportive of people with diverse gender identities and experiences (MacDonald et al., 2016; Obedin-Maliver & Makadon, 2016).

All the statements in this chapter have been recommended based on a thorough review of evidence, an assessment of the benefits and

Statements of Recommendations

16.1- We recommend health care professionals who are treating transgender and gender diverse people and prescribing or referring patients for hormone therapies/surgeries advise their patients about:

16.1.a- Known effects of hormone therapies/surgery on future fertility;

16.1.b- Potential effects of therapies that are not well studied and are of unknown reversibility;

16.1.c- Fertility preservation (FP) options (both established and experimental);

16.1.d- Psychosocial implications of infertility.

16.2- We recommend health care professionals refer transgender and gender diverse people interested in fertility preservation to providers with expertise in fertility preservation for further discussion.

16.3- We recommend transgender care teams partner with local reproductive specialists and facilities to provide specific and timely information and fertility preservation services prior to offering medical and surgical interventions that may impact fertility.

16.4- We recommend health care professionals counsel pre- or early-pubertal transgender and gender diverse youth seeking gender-affirming therapy and their families that currently evidence-based/established fertility preservation options are limited.

16.5- We recommend transgender and gender diverse people with a uterus who wish to carry a pregnancy undergo preconception care, prenatal counseling regarding use and cessation of gender-affirming hormones, pregnancy care, labor and delivery, chest/breast feeding supportive services, and postpartum support according to local standards of care in a gender-affirming way.

16.6- We recommend medical providers discuss contraception methods with transgender and gender diverse people who engage in sexual activity that can result in pregnancy.

16.7- We recommend providers who offer pregnancy termination services ensure procedural options are gender-affirming and serve transgender people and those of diverse genders.

harms, values and preferences of providers and patients, and resource use and feasibility. In some cases, we recognize evidence is limited and/or services may not be accessible or desirable.

Statement 16.1

We recommend health care professionals who are treating transgender and gender diverse people and prescribing or referring patients for hormone therapies/surgeries advise their patients about:

- a. Known effects of hormone therapies/surgeries on future fertility;**
- b. Potential effects of therapies that are not well studied and are of unknown reversibility;**
- c. Fertility preservation (FP) options (both established and experimental);**
- d. Psychosocial implications of infertility.**

TGD individuals assigned female at birth

GAHT may negatively impact future reproductive capacity (Hembree et al., 2017). Based on current evidence in transgender men and gender diverse people assigned female at birth, these risks are as follows:

Gonadotropin-releasing hormone agonists (GnRHAs) may be used for pubertal suppression to prevent further pubertal progression until adolescents are ready for masculinizing treatment. GnRHAs may also be used for menstrual

suppression. GnRHAs impact the maturation of gametes but do not cause permanent damage to gonadal function. Thus, if GnRHAs are discontinued, oocyte maturation would be expected to resume.

There are few studies detailing the effects of testosterone therapy on reproductive function in transgender men (Moravek et al., 2020). Restoration of normal ovarian function with oocyte maturation after testosterone interruption has been demonstrated in transgender men who have achieved natural conception. A retrospective study on oocyte cryopreservation showed no differences in the total number of oocytes retrieved or in the number of mature oocytes between transgender men and age- and BMI-matched cisgender women (Adeleye et al., 2018, 2019). The first results have recently been published evaluating live birth rates after controlled ovarian stimulation in transgender men compared with cisgender women (Leung et al., 2019). Testosterone was discontinued prior to ovarian stimulation. Overall, the results concerning the influence of testosterone on reproductive organs and their function appear to be reassuring. However, there have been no prospective studies to date evaluating the effect of long-term hormone therapy on fertility (i.e., started in adolescence) or in those treated with GnRHAs in early puberty followed by testosterone therapy. It is important to take into consideration that required medications and procedures for cryopreserving oocytes (a

pelvic examination, vaginal ultrasound monitoring, and oocyte retrievals) may lead to increasing gender dysphoria in transgender men (Armuaud, 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:

GnRHs 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 (Armuaud, Dhejne et al., 2017; De Sutter et al., 2002; James-Abra et al., 2015).

In other patient populations, fertility referrals and formal fertility programs have been shown to increase FP rates and improve patient satisfaction (Kelvin et al., 2016; Klosky, Anderson et al., 2017; Klosky, Wang et al., 2017;

Shnorhavorian et al., 2012) Physician attitudes have been investigated, and recent studies indicate both an awareness and a desire to provide fertility-related information to children and their families (Armuand et al., 2020). However, barriers have also been identified, including lack of knowledge, comfort, and resources (Armuand, Nilsson et al., 2017; Frederick et al., 2018). Thus, the need for appropriate training of health care providers has been highlighted, with emphasis placed on fertility counseling and offering FP options to all at-risk individuals in an unbiased way (Armuand, Nilsson et al., 2017). Parents' recommendations have also been shown to significantly influence FP rates in adolescent and young adult males with cancer (Klosky, Flynn et al., 2017). While there are clear clinical differences in these populations, these findings can help inform best practices for fertility counseling and FP referrals for transgender individuals.

Statement 16.3

We recommend transgender care teams partner with local reproductive specialists and facilities to provide specific and timely information and fertility preservation services prior to offering medical and surgical interventions that may impact fertility.

Cryopreservation of sperm and oocytes are established FP techniques and can be offered to pubertal, late pubertal, and adult birth assigned males and birth assigned females, respectively, preferably prior to the initiation of GAHT (Hembree et al., 2017; Practice Committee of the American Society for Reproductive Medicine, 2019). Cryopreservation of embryos can be offered to adult (post-pubertal) TGD people who wish to have a child and have an available partner. The future use of cryopreserved gametes is also dependent on the gametes and reproductive organs of the future partner (Fischer, 2021; Maxwell et al., 2017)

Although semen parameters have been shown to be compromised when FP is performed after initiation of GAH medication (Adeleye et al., 2019), one small study showed when the treatment was discontinued, semen parameters were comparable to those in TGD patients who had

never undergone GAH treatment. With regard to ovarian stimulation, oocyte vitrification yield and subsequent use of the oocytes in in-vitro fertilization (IVF), there is no reason to anticipate a different outcome in assisted reproductive technology (ART) treatments for TGD patients than that obtained in cisgender patients undergoing ART—other than individual confounding factors related to (in)fertility—when gametes are banked prior to any medical treatment (Adeleye et al., 2019). The use of oocytes in ART treatment resulted in similarly successful outcomes in TGD compared with controlled, matched cisgender patients (Adeleye et al., 2019; Leung et al., 2019; Maxwell et al., 2017).

Although these are established options, few pubertal, late pubertal or adult TGD people undergo FP (Nahata et al., 2017), and many experience challenges while undergoing FP interventions. Not only is access and cost of these methods a barrier (particularly in regions without insurance coverage), but these procedures are often physically and emotionally uncomfortable, and many express concerns about postponing the transitioning process (Chen et al., 2017; De Sutter et al., 2002; Nahata et al., 2017; Wierckx, Stuyver et al., 2012). Especially for the birth assigned females, the invasiveness of endovaginal ultrasound follow-up of the ovarian stimulation and oocyte retrieval procedures (and associated psychological distress) have been cited as a barrier (Armuand, Dhejne et al., 2017; Chen et al., 2017). There is also the concern young adults going through transitioning may not have a clear vision of parenting and are therefore likely to decline the opportunity to use FP at that time—while as adults, they may have different opinions about parenthood (Cauffman & Steinberg, 2000). The reduction of gender dysphoria during transitioning could also influence the decision-making process surrounding FP (Nahata et al., 2017). Based on research showing TGD youths' fertility perspectives may change over time (Nahata et al., 2019; Strang, Jarin et al., 2018), FP options should be discussed on an ongoing basis.

Statement 16.4

We recommend health care professionals counsel pre- or early-pubertal transgender and

gender diverse youth seeking gender-affirming therapy and their families that currently evidence-based/established fertility preservation options are limited.

For prepubertal and early-pubertal children, FP options are limited to the storage of gonadal tissue. Although this option is available for TGD children in the same way that it is available for cisgender prepubertal and early-pubertal oncological patients, there is no literature describing the utilization of this approach in the transgender population. Ovarian tissue autotransplantation has resulted in over 130 live births in cisgender women. Most of these patients conceived naturally without ART (Donnez & Dolmans, 2015; Jadoul et al., 2017), and the majority stored their ovarian tissue either as adults or during puberty. Although the recent American Society for Reproductive Medicine guideline has lifted the experimental label from ovarian tissue cryopreservation (Practice Committee of the American Society for Reproductive Medicine, 2019), there are very few case reports describing a successful pregnancy in a woman following the transplantation of ovarian tissue cryopreserved before puberty. Demeestere et al. (2015) and Rodriguez-Wallberg, Milenkovic et al. (2021) described cases of successful pregnancies following transplantation of tissue procured at the age of 14, and recently Matthews et al. (2018) described the case of a girl diagnosed with thalassemia who had ovarian tissue stored at the age of 9 and transplantation 14 years later. She subsequently conceived through IVF and delivered a healthy baby.

Currently, the only future clinical application for storing ovarian tissue is autotransplantation, which might be undesirable in a transgender man (due to the potentially undesirable effects of estrogen). A laboratory procedure that would make it possible to mature oocytes *in vitro* starting with ovarian tissue would be the ideal future application of stored ovarian tissue for transgender people, but this technique is currently only being investigated and optimized in basic science research settings (Ladanyi et al., 2017; Oktay et al., 2010).

Prepubertal procurement of testicular tissue has been documented as a low-risk procedure (Borgström et al., 2020; Ming et al., 2018). Some

authors have also described this approach as a theoretical option in transgender people (De Roo et al., 2016; Martinez et al., 2017; Nahata, Curci et al., 2018). However, there are no reports in the literature describing the clinical or investigational utilization of this FP option for TGD patients. Moreover, the viability of the clinical application of autotransplantation of testicular tissue remains unknown in humans, and *in vitro* maturation techniques are still in the realm of basic science research. Thus, specialists currently consider this technique experimental (Picton et al., 2015). The possibility of storing gonadal tissue should be discussed prior to any genital surgery that would result in sterilization, although the probability of being able to use this tissue must be clearly addressed.

Statement 16.5

We recommend transgender and gender diverse people with a uterus who wish to carry a pregnancy undergo preconception care and prenatal counseling regarding the use and cessation of gender-affirming hormones, pregnancy care, labor and delivery, chest/breast feeding supportive services, and postpartum support according to local standards of care in a gender-affirming way.

Most transgender men and gender diverse people (AFAB) retain their uterus and ovaries and thus can conceive and carry a pregnancy even after long-term testosterone use (Light et al., 2014). Many transgender men desire children (Light et al., 2018; Wierckx, van Caenegem et al., 2012) and are willing to carry a pregnancy (Moseson, Fix, Hastings et al., 2021; Moseson, Fix, Ragosta et al., 2021). ART has expanded the opportunity for many transgender men to conceive and fulfill their family planning wishes (De Roo et al., 2017; Ellis et al., 2015; Maxwell et al., 2017). Some transgender men report psychological isolation, dysphoria related to the gravid uterus and chest changes, and depression (Charter, 2018; Ellis et al., 2015; Hoffkling et al., 2017; Obedin-Maliver & Makadon, 2016). Conversely, other studies have reported some positive experiences during pregnancy as well (Fischer, 2021; Light et al., 2014). Mental health providers should be involved to provide support, and counseling should be

provided addressing when to stop and when to resume gender-affirming hormones, what options are available for the mode of delivery and for chest/breast feeding (Hoffkling et al., 2017). Finally, system-level and interpersonal-level interventions should be implemented to ensure person-centered reproductive health care for all people (Hahn et al., 2019; Hoffkling et al., 2017; Moseson, Zazanis et al., 2020; Snowden et al., 2018).

Given the potential harmful effects of testosterone on the developing embryo, discontinuing testosterone or masculinizing hormone therapy prior to conception and during the entire pregnancy is recommended. However, the optimal time for both the discontinuation of testosterone prior to pregnancy and its resumption after pregnancy is unknown. Since stopping gender-affirming hormones may cause distress and exacerbate dysphoria in transgender men, when and how to stop this therapy should be discussed during prenatal counseling (Hahn et al., 2019). Because information about the duration of testosterone exposure and the risk of teratogenicity is lacking, testosterone use should be discontinued prior to attempting pregnancy and before stopping contraception. Moreover, there is limited information regarding health outcomes of infants born to transgender men. Small case series attempting to evaluate this question have revealed no adverse physical or psychosocial differences between infants born to transgender men and infants in the general population (Chiland et al., 2013).

Chest/Breast feeding

In the limited studies evaluating lactation and chest/breast feeding, the majority of transgender men and TGD individuals AFAB who chose to chest/breast feed postpartum were successful, with research suggesting induction of lactation is in part dependent on preconception counseling and experienced lactation nursing support (MacDonald et al., 2016; Wolfe-Roubatis & Spatz, 2015). Specifically, transgender men and TGD people who use testosterone should be informed 1) although quantities are small, testosterone does pass through chest/breast milk; and 2) the impact on the developing neonate/child is unknown, and therefore gender-affirming testosterone use is not recommended during lactation but may be resumed after discontinuation of

chest/breast feeding (Glaser et al., 2009). Transgender men and other TGD individuals AFAB should be made aware some patients who carry a pregnancy may experience undesired chest growth and/or lactation even after chest reconstruction and should therefore be supported if they desire to suppress lactation (MacDonald et al., 2016).

There is limited information concerning lactation in transgender women as well as other TGD AMAB but many also express the desire to chest/breast feed. While there is a case report of a transgender woman successfully lactating and chest/breast feeding her infant after hormonal support using a combination of estrogen, progesterone, domperidone, and breast pumping (Reisman & Goldstein, 2018), the nutritional and immunological profile of chest/breast milk under these conditions has not been studied. Therefore, patients need to be informed about the risks and benefits of this approach to child feeding (Reisman & Goldstein, 2018).

Statement 16.6

We recommend medical providers discuss contraception methods with transgender and gender diverse people who engage in sexual activity that can result in pregnancy.

Many TGD individuals may retain reproductive capacity, and they (if they retain a uterus, ovaries, and tubes) or their sexual partners (for sperm producing individuals) may experience unplanned pregnancies (James et al., 2016; Light et al., 2014; Moseson, Fix et al., 2020). Therefore, intentional family planning counseling, including contraception and abortion conducted in gender-expansive ways is needed (Klein, Berry-Bibee et al., 2018; Obedin-Maliver, 2015; Stroumsa & Wu, 2018). TGD people AFAB may not use contraception due to an erroneous assumption that testosterone is a reliable form of contraception (Abern & Maguire, 2018; Ingraham et al., 2018; Jones, Wood et al., 2017; Potter et al., 2015). However, based on current understanding, testosterone should not be considered a reliable form of contraception because of its incomplete suppression of the hypothalamic-pituitary-adrenal axis (Krempasky et al., 2020). Furthermore, pregnancies have occurred while individuals are amenorrheic due

to testosterone use, which may outlast active periods of administration (Light et al., 2014). Pregnancy can also occur in TGD people after long-term testosterone use (at least up to 10 years), although the effect on oocytes and baseline fertility is still unknown (Light et al., 2014).

TGD people AFAB may use a variety of contraceptive methods (Abern & Maguire, 2018; Bentsianov et al., 2018; Bonnington et al., 2020; Chrisler et al., 2016; Cipres et al., 2017; Jones, Wood et al., 2017; Krempasky et al., 2020; Light et al., 2018). These methods may be used explicitly for pregnancy prevention, menstrual suppression, abnormal bleeding, or other gynecological needs (Bonnington et al., 2020; Chrisler et al., 2016; Krempasky et al., 2020; Schwartz et al., 2019). Contraceptive research gaps within this population are profound. No studies have examined how the use of exogenous androgens (e.g., testosterone) may modify the efficacy or safety profile of hormonal contraceptive methods (e.g., combined estrogen and progestin hormonal contraceptives, progestin-only based contraceptives) or non-hormonal and barrier contraceptive methods (e.g., internal and external condoms, non-hormonal intrauterine devices, diaphragms, sponges, etc.).

Gender diverse individuals who currently have a penis and testicles may engage in sexual activity with individuals who have a uterus, ovaries, and tubes of any gender. Gender diverse people who have a penis and testicles can produce sperm even while on gender-affirming hormones (i.e., estrogen), and although semen parameters are diminished among those who are currently using or who have previously used gender-affirming hormones, azoospermia is not complete and sperm activity is not totally suppressed (Adeleye et al., 2019; Jindarak et al., 2018; Kent et al.,

2018). Therefore, contraception needs to be considered if pregnancy is to be avoided in penis-in-vagina sexual activity between a person with a uterus, ovaries, and tubes and one with a penis and testicles, irrespective of the use of gender-affirming hormones by either partner. Currently, contraceptive methods available for use by the sperm-producing partner are primarily mechanical barriers (i.e., external condoms, internal condoms), permanent sterilization (i.e., vasectomy), and gender-affirming surgery (e.g., orchiectomy, which also results in sterilization). Contraceptive counseling that considers sperm producing, egg producing, and gestating partners (as relevant) is recommended.

Statement 16.7

We recommend providers who offer pregnancy termination services ensure procedural approaches are gender-affirming and serve transgender people and those of diverse genders.

Unplanned pregnancies and abortions have been reported among TGD individuals with a uterus (Abern & Maguire, 2018; Light et al., 2014; Light et al., 2018; Moseson, Fix et al., 2020) and documented through surveys of abortion-providing facilities (Jones et al., 2020). However, the population-based epidemiology of abortion provision and the experiences and preferences of TGD individuals AFAB undergoing abortion still represents a critical gap in research (Fix et al., 2020; Moseson, Fix et al., 2020; Moseson, Lunn et al., 2020). Nonetheless, given that pregnancy capacity exists among many TGD people and pregnancies may not always be planned or desired, access to safe, legal, and gender-affirming pregnancy medical and surgical termination services is necessary.

CHAPTER 17 Sexual Health

Sexual health has a profound impact on physical and psychological well-being, regardless of one's sex, gender, or sexual orientation. However, stigma about sex, gender and sexual orientation influences individual's opportunities to live out their sexuality and to receive appropriate sexual health care. Specifically, in most societies, cisnormativity and heteronormativity lead to the assumption that all people are cisgender and heterosexual (Bauer et al., 2009), and that this combination is superior to all other genders and sexual orientations (Nieder, Güldenring et al., 2020; Rider, Vencill et al., 2019). Hetero-cisnormativity negates the complexity of gender, sexual orientation, and sexuality and disregards diversity and fluidity. This is all the more important since sexual identities, orientations, and practices of transgender and gender diverse (TGD) people are characterized by an enormous diversity (Galupo et al., 2016; Jessen et al., 2021; Thurston & Allan, 2018; T'Sjoen et al., 2020). Likewise, a strong cross-cultural tendency toward allonormativity—the assumption that all people experience sexual attraction or interest in sexual activity—negates the diverse experiences of TGD people, especially those who locate themselves on the asexual spectrum (McInroy et al., 2021; Mollet, 2021; Rothblum et al., 2020).

The World Health Organization (WHO, 2010) emphasizes sexual health depends on respect for the sexual rights of all people, including the right to express diverse sexualities and to be treated respectfully, safely, and with freedom from discrimination and violence. Sexual health discourses have focused on agency and body autonomy, which include consent, sexual pleasure, sexual satisfaction, partnerships, and family life (Cornwall & Jolly, 2006; Lindley et al., 2021). In light of this, the WHO defines sexual health as “a state of physical, emotional, mental, and social well-being in relation to sexuality and not merely the absence of disease, dysfunction, or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination, and violence. For sexual health to be

attained and maintained, the sexual rights of all persons must be respected, protected, and fulfilled” (WHO, 2006, p. 5). This includes individuals on the asexual spectrum, who may not experience sexual attraction to others but may still choose to be sexual at times (e.g., via self-stimulation) and/or experience interest in forming and building romantic relationships (de Oliveira et al., 2021).

Scientific attention to the sexual experiences and behaviors of TGD people has grown in recent years (Gieles et al., 2022; Holmberg et al., 2019; Klein & Gorzalka, 2009; Kloer et al., 2021; Mattawanon et al., 2021; Stephenson et al., 2017; Tirapegui et al., 2020; Thurston & Allan, 2018). This expansion within the literature reflects a sex-positive framework (Harden, 2014), a framework that recognizes both the positive aspects such as sexual pleasure (Laan et al., 2021) and potential risks associated with sexuality (Goldhammer et al., 2022; Mujugira et al., 2021). Studies of TGD people's sexuality, however, often lack validated measures, an appropriate control group, or a prospective design (Holmberg et al., 2019). Additionally, most focus exclusively on sexual functioning (Kennis et al., 2022), and thus neglecting sexual satisfaction and broader operationalizations of sexual pleasure beyond functioning. The effects of current TGD-related medical treatments on sexuality are heterogeneous (Özer et al., 2022; T'Sjoen et al., 2020), and there has been little research on the sexuality of TGD adolescents (Bungener et al., 2017; Maheux et al., 2021; Ristori et al., 2021; Stübler & Becker-Hebly, 2019; Warwick et al., 2022). While sex-positive approaches to counseling and treatment for sexual difficulties experienced by TGD individuals have been proposed (Fielding, 2021; Jacobson et al., 2019; Richards, 2021), to date there is insufficient research on the effectiveness of such interventions. Focusing on the promotion of sexual health, the World Association for Sexual Health (WAS) asserts the importance of sexual pleasure and considers self-determination, consent, safety, privacy, confidence, and the ability to communicate and negotiate sexual relations as major facilitators (Kismödi et al., 2017). WAS asserts sexual pleasure is integral to sexual rights and human rights (Kismödi et al., 2017). To contribute to

Statements of Recommendations

17.1- We recommend health care professionals who provide care to transgender and gender diverse people acquire the knowledge and skills needed to address sexual health issues (relevant to their care provision).

17.2- We recommend health care professionals who provide care to transgender and gender diverse people discuss the impact of gender-affirming treatments on sexual function, pleasure, and satisfaction.

17.3- We recommend health care professionals who provide care to transgender and gender diverse people offer the possibility of including the partner(s) in sexuality-related care, if appropriate.

17.4- We recommend health care professionals counsel transgender and gender diverse people about the potential impact of stigma and trauma on sexual risk behavior, sexual avoidance, and sexual functioning.

17.5- We recommend any health care professional who offers care that may impact sexual health provide information, ask about the expectations of the transgender and gender diverse individual and assess their level of understanding of possible changes.

17.6- We recommend health care professionals who provide care to transgender and gender diverse people counsel adolescents and adults regarding prevention of sexually transmitted infections.

17.7- We recommend health care professionals who provide care to transgender and gender diverse people follow local and World Health Organization guidelines for human immunodeficiency virus/sexual transmitted infections (HIV/STIs) screening, prevention, and treatment.

17.8- We recommend health care professionals who provide care to transgender and gender diverse people address concerns about potential interactions between antiretroviral medications and hormones.

the sexual health of TGD people, health care professionals (HCPs) need both transgender-related expertise and sensitivity (Nieder, Gldenring 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, Gldenring 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, HCPs 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., non-binary, 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, Guldenring et al., 2020). Some level of disconnect or dissociation may at times be present, particularly in the case of acute trauma symptoms (Colizzi et al., 2015). It is important HCPs be aware of these potential impacts on sexual health, functioning, pleasure, and satisfaction, so they may refer patients as needed to trauma-informed sexual counselors, mental health providers, or both, who may be of further assistance and may also normalize and validate TGD patients exploring multiple diverse pathways of healing and accessing sexual pleasure.

Statement 17.5

We recommend any health care professional who offers care that may impact sexual health provide information, ask about the expectation of the transgender and gender diverse individual, and assess their level of understanding of possible changes.

Transition-related care can affect sexual function, pleasure, and satisfaction, both in positive and negative ways (Holmberg et al., 2018; Kerckhof et al., 2019; Thurston & Allan, 2018; Tirapegui et al., 2020). On the positive side, gender-affirming care can help TGD people improve their sexual functioning and increase their sexual pleasure and satisfaction (Kloer et al., 2021; Özer et al., 2022; T'Sjoen et al., 2020). On the negative side, however, data indicate problematic sexual health outcomes due to hormonal and surgical treatments (Holmberg et al., 2018; Kerckhof et al., 2019; Stephenson et al., 2017; Weyers et al., 2009). Transition-related hormones may affect mood, sexual desire, the ability to have an erection and ejaculation, and genital tissue health, which in turn can impact sexual function, pleasure and sexual self-expression (Defreyne, Elaut et al., 2020; Garcia & Zaliznyak, 2020; Kerckhof et al., 2019; Klein & Gorzalka, 2009; Wierckx, Elaut et al., 2014). TGD people who wish to use their original genital anatomy for penetrative sex may benefit from medications that address sexual health side effects of hormone therapy, such as erectile dysfunction, medications for TGD persons taking estrogen or antiandrogens, and topical estrogen and/or moisturizers for TGD persons experiencing vaginal atrophy or dryness due to testosterone therapy.

Sexual desire, arousal, and function may also be affected by the use of psychotropic drugs (Montejo et al., 2015). As some TGD people are prescribed medication to treat depression (Heylens, Elaut et al., 2014), anxiety (Millet et al., 2017) or other mental health concerns (Dhejne et al., 2016), their potential side effects on sexual health should be considered.

Many gender-affirming surgeries can have significant effects on erogenous sensation, sexual desire and arousal as well as sexual function and pleasure. The impact of these changes for patients may be mixed (Holmberg et al., 2018). Chest surgeries (breast reduction, mastectomy, and breast augmentation) and body contouring surgeries, for example, may offer desired changes in form and appearance thereby reducing psychological distress that can disrupt sexual functioning but may adversely affect erogenous sensation (Bekeny et al., 2020; Claes et al., 2018; Rochlin

et al., 2020). Genital surgeries in particular can potentially affect sexual function and pleasure in adverse ways, although they are likely to be experienced positively as the patient's body becomes more aligned with their gender, potentially opening new avenues for sexual pleasure and satisfaction (Hess et al., 2018; Holmberg et al., 2018; Kerckhof et al., 2019).

There are numerous examples of this in the extant literature:

- Surgery may result in a decrease, a total loss, or a possible increase in erogenous stimulation and/or experienced sensation compared with the patient's presurgery anatomy (Garcia, 2018; Sigurjónsson et al., 2017).
- A particular surgical option may be associated with specific limitations to sexual function that may manifest immediately, in the future, or at both timepoints, and which patients should consider before finalizing their choice when considering different surgical options (Frey et al., 2016; Garcia, 2018; Isaacson et al., 2017).
- Postsurgical complications can adversely affect sexual function by either decreasing the quality of sexual function (e.g., discomfort or pain with sexual activity) or by precluding satisfactory intercourse (Kerckhof et al., 2019; Schardein et al., 2019).

In general, satisfaction with any medical treatment is heavily influenced by the patient's expectations (Padilla et al., 2019). Furthermore, when patients have unrealistic expectations before treatment, they are much more likely to be dissatisfied with the outcome, their care, and with their HCP (Padilla et al., 2019). Therefore, it is important to both provide patients with adequate information about their treatment options and to understand and consider what is important to the patient with regard to outcomes (Garcia, 2021). Finally, it is important the HCP ensure patients understand the potential adverse effects of a treatment on their sexual function and pleasure so that a well-informed decision can be made. This is relevant for both meeting the standard of informed consent (i.e.,

discussion and understanding) and for providing an opportunity to offer further clarification to patients and, if desired, to their partners (Glaser et al., 2020).

Statement 17.6

We recommend health care professionals who provide care to transgender and gender diverse people counsel adolescents and adults regarding prevention of sexually transmitted infections.

The WHO (2015) recommends HCPs implement brief sexuality-related communication in primary care for all adolescents and adults. Therefore, TGD persons who are sexually active or considering sexual activity may benefit from sexuality-related communication or counseling for the purpose of HIV/STI prevention. These conversations are particularly important as TGD persons are disproportionately impacted by human immunodeficiency virus (HIV) and other sexually transmitted infections (STIs) relative to cisgender persons (Baral et al., 2013; Becasen et al., 2018; Poteat et al., 2016). However, few data are available for non-HIV STIs, such as chlamydia, gonorrhea, syphilis, viral hepatitis, and herpes simplex virus (Tomson et al., 2021). The United Nations Joint Programme on HIV/AIDS estimates transgender women are 12 times more likely than other adults to be living with HIV (UNAIDS, 2019). A meta-analysis estimated a pooled global HIV prevalence of 19% among transgender women who have sex with men (Baral et al., 2013). HIV/STI risk is concentrated among TGD subgroups at the confluence of multiple biological, psychological, interpersonal, and structural vulnerabilities. In particular, transfeminine persons who have sex with cisgender men, belong to minoritized racial/ethnic groups, live in poverty, and engage in survival sex work are at elevated HIV/STI risk (Becasen et al., 2018; Poteat et al., 2015; Poteat et al., 2016). Less is known about HIV/STI risk among transgender men or gender diverse persons AFAB. Small studies in high-income countries indicate a laboratory-confirmed HIV prevalence of 0-4% among transmasculine people (Becasen et al., 2018; Reisner & Murchison, 2016). Almost no research has been conducted with transmasculine people who have sex with cisgender men in

high-HIV-prevalence countries. Despite limited epidemiologic data, transmasculine persons who have sex with cisgender men frequently report HIV/STI risk related to receptive vaginal and/or anal sex (Golub et al., 2019; Reisner et al., 2019; Scheim et al., 2017) and may be more susceptible to HIV acquisition from vaginal intercourse than (pre-menopausal) cisgender women due to hormone-related vaginal atrophy.

HCPs will need to supplement general guidelines by developing the knowledge and skills needed for discussing sexual health issues with TGD people, such as the use of gender-affirming language (see Statement 17.1 in this chapter). It is critical HCPs avoid assumptions about HIV/STI risk based solely on a patient's gender identity or anatomy. For example, many transgender people are not sexually active, and TGD persons may use prosthetics or toys for sex. To provide appropriate prevention counseling, HCPs should inquire about the specific sexual activities TGD people engage in, and the body parts (or prosthetics) involved in those activities (ACON, 2022). Well-prepared HCPs (including, but not limited to mental health providers) may also engage in in-depth counseling with their patients to address the underlying drivers of HIV/STI risk (see Statement 17.3 in this chapter).

In all cases, HCPs should be sensitive to the collective and individual histories of TGD people (e.g., stereotypes and stigma about trans sexualities and gender dysphoria) and should explain to patients the reasons for sexuality-related inquiries and the voluntary nature of such inquiries. In discussing HIV/STI prevention, HCPs should refer to the full range of prevention options including barrier methods, post-exposure prophylaxis, pre-exposure prophylaxis, and HIV treatment to prevent onwards transmission (WHO, 2021). Trans-specific considerations for pre-exposure prophylaxis are addressed in Statement 17.8.

Statement 17.7

We recommend health care professionals who provide care to transgender and gender diverse people follow local and World Health Organization guidelines for human immunodeficiency virus/sexual transmitted infections (HIV/STIs) screening, prevention, and treatment.

Like cisgender patients, TGD adolescents and adults should be offered screening for HIV/STIs in accordance with existing guidelines and based on their individual risk of HIV/STI acquisition, considering anatomy and behavior rather than gender identity alone. Where local or national guidelines are unavailable, WHO (2019a) offers global recommendations; more frequent screening is recommended for transgender people who have sex with cisgender men as a key population affected by HIV.

Gender-affirming genital surgeries and surgical techniques have implications for STI risks and screening needs, as outlined in recent guidelines from the US Centers for Disease Control (Workowski et al., 2021). For instance, transfeminine persons who have had penile inversion vaginoplasty using only penile and scrotal skin to line the vaginal canal are likely at lower risk of urogenital *Chlamydia trachomatis* (*C. trachomatis*) and *Neisseria gonorrhoeae* (*N. gonorrhoeae*), but newer surgical techniques that employ buccal or urethral mucosa or peritoneum flaps could in theory increase susceptibility to bacterial STIs relative to the use of penile/scrotal skin alone (Van Gerwen et al., 2021). Routine STI screening of the neovagina (if exposed) is recommended for all transfeminine persons who have had vaginoplasty (Workowski et al., 2021). For transmasculine persons who have had metoidioplasty with urethral lengthening, but not vaginectomy, testing for bacterial urogenital STIs should include a cervical swab because infections may not be detected in urine (Workowski et al., 2021).

Further, it is important for HCPs to offer testing at multiple anatomical sites as STIs in transgender patients are often extragenital (Hiransuthikul et al., 2019; Pitasi et al., 2019). Consistent with WHO (2020) recommendations, self-collection of samples for STI testing should be offered as an option, particularly if patients are uncomfortable or unwilling to undergo provider-collected sampling due to gender dysphoria, trauma histories, or both. Where relevant, integration of HIV/STI testing with regular serology used to monitor hormone therapy may better facilitate access to care (Reisner, Radix et al., 2016; Scheim & Travers, 2017).

Statement 17.8

We recommend health care professionals who provide care to transgender and gender diverse people address concerns about potential interactions between antiretroviral medications and hormones.

For TGD adolescents and adults at substantial risk of HIV infection (generally defined as an ongoing serodiscordant relationship or condomless sex outside of a mutually monogamous relationship with a known HIV-negative partner; WHO, 2017), pre-exposure prophylaxis (PrEP) is an important HIV prevention option (Golub et al., 2019; Sevelius et al., 2016; WHO, 2021). To encourage uptake of PrEP, in 2021 the US Centers for Disease Control recommended all sexually active adolescents and adults be informed about PrEP and offered it if requested (CDC, 2021). For treatment among people living with HIV, transgender-specific guidelines are available in some settings (e.g., Panel on Antiretroviral Guidelines for Adults and Adolescents, 2019).

For both HIV prevention and treatment, there are antiretroviral dosing and administration considerations specific to TGD persons. For oral PrEP, only daily dosing is currently recommended for TGD persons as studies demonstrating the effectiveness of event-driven PrEP with emtricitabine/tenofovir disoproxil fumarate (TDF) have been limited to cisgender men (WHO, 2019c). In addition, while emtricitabine/tenofovir alafenamide (TAF) is a new oral PrEP option, as of early 2022 it is not recommended for people at risk of HIV acquisition through receptive vaginal sex due to a lack of evidence (CDC, 2021). Finally, long-acting injectable formulations of both PrEP and HIV treatment are increasingly available (e.g., cabotegravir for PrEP), and while they are recommended for all patients who might benefit from injectable options, indicated injection sites (i.e., the gluteal muscle) may be unsuitable for individuals who have used soft tissue fillers (Rael et al., 2020).

There is little evidence supporting the occurrence of drug-drug interactions between gender-affirming hormones and PrEP medications. A few small studies, primarily relying on self-reported PrEP use, have shown reduced PrEP drug concentrations in transgender women undergoing hormone therapy, although

concentrations remained in the protective range (Yager & Anderson, 2020). A subsequent drug-drug interaction study using directly observed PrEP therapy failed to detect an impact of hormone therapy on PrEP drug concentrations in transgender women and found transgender women and men taking hormone therapy achieved high levels of protection against HIV infection (Grant et al., 2020). Most importantly, for many TGD people, no impact of PrEP on hormone concentrations has been detected. With regard to HIV treatment, specific antiretroviral medications may impact hormone concentrations; however, these can be managed by selecting alternative agents, monitoring and adjusting hormone dosing, or both (Cirrincione et al., 2020) as detailed in guidelines from the US Department of Health and Human Services (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2019). Nevertheless, concerns

about drug-drug interactions, particularly interactions that may limit hormone concentrations, represent a barrier to the implementation and adherence to antiretroviral therapy for HIV prevention or treatment (Radix et al., 2020; Sevelius et al., 2016). Therefore, it is advisable for HCPs to proactively address such concerns with those who are candidates for PrEP or HIV treatment. Integration of PrEP or HIV treatment with hormone therapy may further reduce barriers to implementation and adherence (Reisner, Radix et al., 2016). Integration may be achieved through colocation or through coordination with an HIV specialist if the primary care provider does not have the necessary expertise. Some TGD persons may benefit from standalone PrEP or sexual health services that provide greater privacy and flexibility, and thus differentiated service delivery models are needed (Wilson et al., 2021).

CHAPTER 18 Mental Health

This chapter is intended to provide guidance to health care professionals (HCPs) and mental health professionals (MHPs) who offer mental health care to transgender and gender diverse (TGD) adults. It is not meant to be a substitute for chapters on the assessment or evaluation of people for hormonal or surgical interventions. Many TGD people will not require therapy or other forms of mental health care as part of their transition, while others may benefit from the support of mental health providers and systems (Dhejne et al., 2016).

Some studies have shown a higher prevalence of depression (Witcomb et al., 2018), anxiety (Bouman et al., 2017), and suicidality (Arcelus et al., 2016; Bränström & Pachankis, 2022; Davey et al., 2016; Dhejne, 2011; Herman et al., 2019) among TGD people (Jones et al., 2019; Thorne, Witcomb et al., 2019) than in the general population, particularly in those requiring medically necessary gender-affirming medical treatment (see medically necessary statement in Chapter 2—Global Applicability, Statement 2.1). However, transgender identity is not a mental illness, and these elevated rates have been linked to complex trauma, societal stigma, violence, and discrimination (Nuttbrock

et al., 2014; Peterson et al., 2021). In addition, psychiatric symptoms lessen with appropriate gender-affirming medical and surgical care (Aldridge et al., 2020; Almazan and Keuroghlian, 2021; Bauer et al., 2015; Grannis et al., 2021) and with interventions that lessen discrimination and minority stress (Bauer et al., 2015; Heylens, Verroken et al., 2014; McDowell et al., 2020).

Mental health treatment needs to be provided by staff and implemented through the use of systems that respect patient autonomy and recognize gender diversity. MHPs working with transgender people should use active listening as a method to encourage exploration in individuals who are uncertain about their gender identity. Rather than impose their own narratives or preconceptions, MHPs should assist their clients in determining their own paths. While many transgender people require medical or surgical interventions or seek mental health care, others do not (Margulies et al., 2021). Therefore, findings from research involving clinical populations should not be extrapolated to the entire transgender population.

Addressing mental illness and substance use disorders is important but should not be a barrier to transition-related care. Rather, these interventions to address mental health and substance use disorders can facilitate successful outcomes from

Statements of Recommendations

18.1- We recommend mental health professionals address mental health symptoms that interfere with a person's capacity to consent to gender-affirming treatment before gender-affirming treatment is initiated.

18.2- We recommend mental health professionals offer care and support to transgender and gender diverse people to address mental health symptoms that interfere with a person's capacity to participate in essential perioperative care before gender-affirmation surgery.

18.3- We recommend when significant mental health symptoms or substance abuse exists, mental health professionals assess the potential negative impact that mental health symptoms may have on outcomes based on the nature of the specific gender-affirming surgical procedure.

18.4- We recommend health care professionals assess the need for psychosocial and practical support of transgender and gender diverse people in the perioperative period surrounding gender-affirmation surgery.

18.5- We recommend health care professionals counsel and assist transgender and gender diverse people in becoming abstinent from tobacco/nicotine prior to gender-affirmation surgery.

18.6- We recommend health care professionals maintain existing hormone treatment if a transgender and gender diverse individual requires admission to a psychiatric or medical inpatient unit, unless contraindicated.

18.7- We recommend health care professionals ensure if transgender and gender diverse people need in-patient or residential mental health, substance abuse or medical care, all staff use the correct name and pronouns (as provided by the patient), as well as provide access to bathroom and sleeping arrangements that are aligned with the person's gender identity.

18.8- We recommend mental health professionals encourage, support, and empower transgender and gender diverse people to develop and maintain social support systems, including peers, friends, and families.

18.9- We recommend health care professionals should not make it mandatory for transgender and gender diverse people to undergo psychotherapy prior to the initiation of gender-affirming treatment, while acknowledging psychotherapy may be helpful for some transgender and gender diverse people.

18.10- We recommend "reparative" and "conversion" therapy aimed at trying to change a person's gender identity and lived gender expression to become more congruent with the sex assigned at birth should not be offered.

transition-related care, which can improve quality of life (Nobili et al., 2018).

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

Statement 18.1

We recommend mental health professionals address mental health symptoms that interfere with a person's capacity to consent to gender-affirming treatment before gender-affirming treatment is initiated.

Because patients generally are assumed to be capable of providing consent for care, whether the presence of cognitive impairment, psychosis, or other mental illness impairs the ability to give informed consent is subject to individual examination (Applebaum, 2007). Informed consent is central to the provision of health care. The health care provider must educate the patient about the risks, benefits, and alternatives to any care that is offered so the patient can make an informed, voluntary choice (Berg et al., 2001). Both the primary care provider or endocrinologist prescribing hormones and the surgeon performing surgery must obtain informed consent. Similarly, MHPs obtain informed consent for mental health treatment and may consult on a patient's capacity to give informed consent when this is in question. Psychiatric illness and substance use disorders, in particular cognitive impairment and psychosis, may impair an individual's ability to understand the risks and benefits of the treatment (Hostiuc et al., 2018). Conversely, a patient may also have significant mental illness, yet still be able to understand the risks and benefits of a particular treatment (Carpenter et al., 2000). Multidisciplinary communication is important in challenging cases, and expert consultation should be utilized as needed (Karasic & Fraser, 2018). For many patients, difficulty understanding the risks and benefits of a particular treatment can be overcome with time and careful explanation. For some patients, treatment of the underlying condition that is interfering with the capacity to

give informed consent—for example treating an underlying psychosis—will allow the patient to gain the capacity to consent to the required treatment. However, mental health symptoms such as anxiety or depressive symptoms that do not affect the capacity to give consent should not be a barrier for gender-affirming medical treatment, particularly as this treatment has been found to reduce mental health symptomatology (Aldridge et al., 2020).

Statement 18.2

We recommend mental health professionals offer care and support to transgender and gender diverse people to address mental health symptoms that interfere with a person's capacity to participate in essential perioperative care before gender-affirmation surgery.

The inability to adequately participate in perioperative care due to mental illness or substance use should not be viewed as an obstacle to needed transition care, but should be seen as an indication mental health care and social support be provided (Karasic, 2020). Mental illness and substance use disorders may impair the ability of the patient to participate in perioperative care (Barnhill, 2014). Visits to health care providers, wound care, and other aftercare procedures (e.g., dilation after vaginoplasty) may be necessary for a good outcome. A patient with a substance use disorder might have difficulty keeping necessary appointments to the primary care provider and the surgeon. A patient with psychosis or severe depression might neglect their wound or not be attentive to infection or signs of dehiscence (Lee, Marsh et al., 2016). Active mental illness is associated with a greater need for further acute medical and surgical care after the initial surgery (Wimalawansa et al., 2014).

In these cases, treatment of the mental illness or substance use disorder may assist in achieving successful outcomes. Arranging more support for the patient from family and friends or a home health care worker may help the patient participate sufficiently in perioperative care for surgery to proceed. The benefits of mental health treatments that may delay surgery should be weighed against the risks of delaying surgery and should

include an assessment of the impact on the patients' mental health delays may cause in addressing gender dysphoria (Byne et al., 2018).

Statement 18.3

We recommend when significant mental health symptoms or substance abuse exists, mental health professionals assess the potential negative impact mental health symptoms may have on outcomes based on the nature of the specific gender-affirming surgical procedure.

Gender-affirming surgical procedures vary in terms of their impact on the patient. Some procedures require a greater ability to follow preoperative planning as well as engage in peri- and postoperative care to achieve the best outcomes (Tollinche et al., 2018). Mental health symptoms can influence a patient's ability to participate in the planning and perioperative care necessary for any surgical procedure (Paredes et al., 2020). The mental health assessment can provide an opportunity to develop strategies to address the potential negative impact mental health symptoms may have on outcomes and to plan support for the patient's ability to participate in the planning and care. Gender-affirming surgical procedures have been shown to relieve symptoms of gender dysphoria and improve mental health (Owen-Smith et al., 2018; van de Grift, Elaut et al., 2017). These benefits are weighed against the risks of each procedure when the patient and provider are deciding whether to proceed with the treatment. HCPs can assist TGD people in reviewing preplanning and perioperative care instructions for each surgical procedure (Karasic, 2020). Provider and patient can collaboratively determine the necessary support or resources needed to assist with keeping appointments for perioperative care, obtaining necessary supplies, addressing financial issues, and handling other preoperative coordination and planning. In addition, issues surrounding appearance-related and functional expectations, including the impact of these various factors on gender dysphoria, can be explored.

Statement 18.4

We recommend health care professionals assess the need for psychosocial and practical support

of transgender and gender diverse people in the perioperative period surrounding gender-affirmation surgery.

Regardless of specialty, all HCPs have a responsibility to support patients in accessing medically necessary care. When HCPs are working with TGD people as they prepare for gender-affirming surgical procedures, they should assess the levels of psychosocial and practical support required (Deutsch, 2016b). Assessment is the first step in recognizing where additional support may be needed and enhancing the ability to work collaboratively with the individual to successfully navigate the pre-, peri-, and postsurgical periods (Tollinche et al., 2018). In the perioperative period, it is important to help patients optimize functioning, secure stable housing, when possible, build social and family supports by assessing their unique situation, plan ways of responding to medical complications, navigate the potential impact on work/income, and overcome additional hurdles some patients may encounter, such as coping with electrolysis and tobacco cessation (Berli et al., 2017). In a complex medical system, not all patients will be able to independently navigate the procedures required to obtain care, and HCPs and peer navigators can support patients through this process (Deutsch, 2016a).

Statement 18.5

We recommend health care professionals counsel and assist transgender and gender diverse people in becoming abstinent from tobacco/nicotine prior to gender-affirmation surgery.

Transgender populations have higher rates of tobacco and nicotine use (Kidd et al., 2018). However, many are unaware of the well-documented smoking-associated health risks (Bryant et al., 2014). Tobacco consumption increases the risk of developing health problems (e.g., thrombosis) in individuals receiving gender-affirming hormone treatment, particularly estrogens (Chipkin & Kim, 2017).

Tobacco use has been associated with worse outcomes in plastic surgery, including overall complications, tissue necrosis, and the need for surgical revision (Coon et al., 2013). Smoking also increases the risk for postoperative infection (Kaoutzanis et al., 2019). Tobacco use has been shown to affect

the healing process following any surgery, including gender-related surgeries (e.g., chest reconstructive surgery, genital surgery) (Pluvy, Garrido et al., 2015). Tobacco users have a higher risk of cutaneous necrosis, delayed wound healing, and scarring disorders due to hypoxia and tissue ischemia (Pluvy, Panouilleres et al., 2015). In view of this, surgeons recommend stopping the use of tobacco/nicotine prior to gender-affirmation surgery and abstaining from smoking up to several weeks post-operatively until the wound has completely healed (Matei & Danino, 2015). Despite the risks, cessation may be difficult. Tobacco smoking and nicotine use is addictive and is also used as a coping mechanism (Matei et al., 2015). HCPs who see patients longitudinally before surgery, including mental health and primary care providers, should address the use of tobacco/nicotine with individuals in their care, and either assist TGD people in accessing smoking cessation programs or provide treatment directly (e.g., varenicline or bupropion).

Statement 18.6

We recommend health care professionals maintain existing hormone treatment if a transgender and gender diverse individual requires admission to a psychiatric or medical inpatient unit, unless contraindicated.

TGD people entering inpatient psychiatric, substance use treatment, or medical units should be maintained on their current hormone regimens. There is an absence of evidence supporting routine cessation of hormones prior to medical or psychiatric admissions. Rarely, a newly admitted patient may be diagnosed with a medical complication necessitating suspension of hormone treatment, for example an acute venous thromboembolism (Deutsch, 2016a). There is no strong evidence for routinely stopping hormone treatment prior to surgery, and the risks and benefits for each individual patient should be assessed before doing so (Boskey et al., 2018).

Hormone treatment has been shown to improve quality of life and to decrease depression and anxiety (Aldridge et al., 2020; Nguyen et al., 2018; Nobili et al., 2018; Owen-Smith et al., 2018; Rowniak et al., 2019). Access to gender-affirming medical treatment is associated with a substantial reduction in the risk of suicide attempt (Bauer

et al., 2015). Halting a patient's regularly prescribed hormones denies the patient of these salutary effects, and therefore may be counter to the goals of hospitalization.

Some providers may be unaware of the low risk of harm and the high potential benefit of continuing transition-related treatment in the inpatient setting. A study of US and Canadian medical schools revealed that students received an average of 5 hours of LGBT-related course content over their entire four years of education (Obedin-Maliver et al., 2011). According to a survey of Emergency Medicine physicians, who are often responsible for making quick decisions about medications as patients are being admitted, while 88% reported caring for transgender patients, only 17.5% had received any formal training about this population (Chisolm-Straker et al., 2018). As education about transgender topics increases, more providers will become aware of the importance of maintaining transgender patients on their hormone regimens during hospitalization.

Statement 18.7

We recommend health care professionals ensure if transgender and gender diverse people need inpatient or residential mental health, substance abuse, or medical care, all staff use the correct name and pronouns (as provided by the patient), as well as provide access to bathroom and sleeping arrangements that are aligned with the person's gender identity.

Many TGD patients encounter discrimination in a wide range of health settings, including hospitals, mental health treatment settings, and drug treatment programs (Grant et al., 2011). When health systems fail to accommodate TGD individuals, they reinforce the longstanding societal exclusion many have experienced (Karasic, 2016). Experiences of discrimination in health settings lead to avoidance of needed health care due to anticipated discrimination (Kcomt et al., 2020).

The experience of discrimination experienced by TGD individuals is predictive of suicidal ideation (Rood et al., 2015; Williams et al., 2021). Gender minority stress associated with rejection and nonaffirmation has also been associated with suicidality (Testa et al., 2017). Denial of access to gender appropriate bathrooms has been

associated with increased suicidality (Seelman, 2016). However, the use of chosen names for TGD people has been associated with lower depression and suicidality (Russell et al., 2018). Structural as well as internalized transphobia must be addressed to reduce the incidence of suicide attempts in TGD people (Brumer et al., 2015). To successfully provide care, health settings must minimize the harm done to patients because of transphobia by respecting and accommodating TGD identities.

Statement 18.8

We recommend mental health professionals encourage, support, and empower transgender and gender diverse people to develop and maintain social support systems, including peers, friends, and families.

While minority stress and the direct effects of discriminatory societal discrimination can be harmful to the mental health of TGD people, strong social support can help lessen this harm (Trujillo et al., 2017). TGD children often internalize rejection from family and peers as well as the transphobia that surrounds them (Amodeo et al., 2015). Furthermore, exposure to transphobic abuse may be impactful across a person's lifespan and may be particularly acute during the adolescent years (Nuttbrock et al., 2010).

The development of affirming social support is protective of mental health. Social support can act as a buffer against the adverse mental health consequences of violence, stigma, and discrimination (Bockting et al., 2013), can assist in navigating health systems (Jackson Levin et al., 2020), and can contribute to psychological resilience in TGD people (Bariola et al., 2015; Başar and Öz, 2016). Diverse sources of social support, especially LGBTQ+ peers and family, have been found to be associated with better mental health outcomes, well-being, and quality of life (Bariola et al., 2015; Başar et al., 2016; Kuper, Adams et al., 2018; Puckett et al., 2019). Social support has been proposed to facilitate the development of coping mechanisms and lead to positive emotional experiences throughout the transition process (Budge et al., 2013).

HCPs can support patients in developing social support systems that allow them to be recognized

and accepted as their authentic identity and help them cope with symptoms of gender dysphoria. Interpersonal problems and lack of social support have been associated with a greater incidence of mental health difficulties in TGD people (Bouman, Davey et al., 2016; Davey et al., 2015) and have been shown to be an outcome predictor of gender-affirming medical treatment (Aldridge et al., 2020). Therefore, HCPs should encourage, support, and empower TGD people to develop and maintain social support systems. These experiences can foster the development of interpersonal skills and help with coping with societal discrimination, potentially reducing suicidality and improving mental health (Pflum et al., 2015).

Statement 18.9

We recommend health care professionals should not make it mandatory for transgender and gender diverse people to undergo psychotherapy prior to the initiation of gender-affirming treatment, while acknowledging psychotherapy may be helpful for some transgender and gender diverse people.

Psychotherapy has a long history of being used in clinical work with TGD people (Fraser, 2009b). The aims, requirements, methods and principles of psychotherapy have been an evolving component of the Standards of Care from the initial versions (Fraser, 2009a). At present, psychotherapeutic assistance and counseling with adult TGD people may be sought to address common psychological concerns related to coping with gender dysphoria and may also help some individuals with the coming-out process (Hunt, 2014). Psychological interventions, including psychotherapy, offer effective tools and provide context for the individual, such as exploring gender identity and its expression, enhancing self-acceptance and hope, and improving resilience in hostile and disabling environments (Matsuno and Israel, 2018). Psychotherapy is an established alternative therapeutic approach for addressing mental health symptoms that may be revealed during the initial assessment or later during the follow-up for gender-affirming medical interventions. Recent research shows, although mental health symptoms are reduced following gender-affirming medical treatment, levels of anxiety remain high (Aldridge et al., 2020) suggesting psychological therapy can play a role in helping

individuals suffering from anxiety symptoms following gender-affirming treatment.

In recent years, the uses and potential benefits of specific psychotherapeutic modalities have been reported (Austin et al., 2017; Budge, 2013; Budge et al., 2021; Embaye, 2006; Fraser, 2009b; Heck et al., 2015). Specific models of psychotherapy have been proposed for adult transgender and nonbinary individuals (Matsuno & Israel, 2018). However, more empiric data is needed on the comparative benefits of different psychotherapeutic models (Catelan et al., 2017). Psychotherapy can be experienced by transgender persons as a fearful as well as a beneficial experience (Applegarth & Nuttall, 2016) and presents challenges to the therapist and to alliance formation when it is associated with gatekeeping for medical interventions (Budge, 2015).

Experience suggests many transgender and nonbinary individuals decide to undergo gender-affirming medical treatment with little or no use of psychotherapy (Spanos et al., 2021). Although various modalities of psychotherapy may be beneficial for different reasons before, during, and after gender-affirming medical treatments and varying rates of desire for psychotherapy have been reported during different stages of transition (Mayer et al., 2019), a requirement for psychotherapy for initiating gender-affirming medical procedures has not been shown to be beneficial and may be a harmful barrier to care for those who do not need this type of treatment or who lack access to it.

Statement 18.10

We recommend “reparative” and “conversion” therapy aimed at trying to change a person’s gender identity and lived gender expression to become more congruent with the sex assigned at birth should not be offered.

The use of “reparative” or “conversion” therapy or gender identity “change” efforts is opposed

by many major medical and mental health organizations across the world, including the World Psychiatric Association, Pan American Health Organization, American Psychiatric and American Psychological Associations, Royal College of Psychiatrists, and British Psychological Society. Many states in the US have instituted bans on practicing conversion therapy with minors. Gender identity change efforts refers to interventions by MHPs or others that attempt to change gender identity or expression to be more in line with those typically associated with the person’s sex assigned at birth (American Psychological Association, 2021).

Advocates of “conversion therapy” have suggested it could potentially allow a person to fit better into their social world. They also point out some clients specifically ask for help changing their gender identities or expressions and therapists should be allowed to help clients achieve their goals. However, “conversion therapy” has not been shown to be effective (APA, 2009; Przeworski et al., 2020). In addition, there are numerous potential harms. In retrospective studies, a history of having undergone conversion therapy is linked to increased levels of depression, substance abuse, suicidal thoughts, and suicide attempts, as well as lower educational attainment and less weekly income (Ryan et al., 2020; Salway et al., 2020; Turban, Beckwith et al., 2020). In 2021, the American Psychological Association resolutions states that “scientific evidence and clinical experience indicate that GICEs [gender identity change efforts] put individuals at significant risk of harm” (APA, 2021).

While there are barriers to ending gender identity “change” efforts, education about the lack of benefit and the potential harm of these practices may lead to fewer providers offering “conversion therapy” and fewer individuals and families choosing this option.

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Conflict of Interest

Conflict of interests were reviewed as part of the selection process for committee members and at the end of the process before publication. No conflicts of interest were deemed significant or consequential.

Ethical Approval

This manuscript does not contain any studies with human participants performed by any of the authors.

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