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

Values and preferences

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

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

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

Evidence

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

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

Values and preferences

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

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

Remarks

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

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

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

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

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

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

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

2.0 Treatment of Adolescents

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

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

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

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

Evidence

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

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

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

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

Values and preferences

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

Remarks

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

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

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

Evidence

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

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

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

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

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

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

Adapted from Lawrence (56).

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

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

Side effects

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

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

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

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

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

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

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

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

Values and preferences

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

Remarks

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

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

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

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

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

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

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

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

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

Table 8. Protocol Induction of Puberty

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

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

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

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

Abbreviations: IM, intramuscularly; SC, subcutaneously.

Evidence

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Values and preferences

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

Remarks

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

3.0 Hormonal Therapy for Transgender Adults

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

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

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

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

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

Evidence

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

Transgender males

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

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

Table 10. Medical Risks Associated With Sex Hormone Therapy

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

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Table 11. Hormone Regimens in Transgender Persons

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

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

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

[b]Not available in the United States.

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

[d]Avoid cutaneous transfer to other individuals.

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

Transgender females

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

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

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

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

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

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

Values

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

Remarks

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

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

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

Evidence

Transgender males

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

Transgender females

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

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

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

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

Table 12. Masculinizing Effects in Transgender Males

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

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

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

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

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Table 13. Feminizing Effects in Transgender Females

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

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

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

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

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

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

Values and preferences

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

4.0 Adverse Outcome Prevention and Long-Term Care

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

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

Evidence

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

Transgender males

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

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

Transgender females

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

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

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

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

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

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

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

Evidence

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

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

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

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

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

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

Evidence

Transgender males

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

Transgender females

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

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

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

Evidence

Transgender males

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

Transgender females

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

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

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

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

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

Evidence

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

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

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

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

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

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

Evidence

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

Values

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

Remarks

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

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

5.0 Surgery for Sex Reassignment and Gender Confirmation

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Evidence

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

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

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

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

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

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Long-Term Follow-Up of Transsexual Persons Undergoing Sex Reassignment Surgery: Cohort Study in Sweden

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Abstract

Context: The treatment for transsexualism is sex reassignment, including hormonal treatment and surgery aimed at making the person's body as congruent with the opposite sex as possible. There is a dearth of long term, follow-up studies after sex reassignment.

Objective: To estimate mortality, morbidity, and criminal rate after surgical sex reassignment of transsexual persons.

Design: A population-based matched cohort study.

Setting: Sweden, 1973-2003.

Participants: All 324 sex-reassigned persons (191 male-to-females, 133 female-to-males) in Sweden, 1973–2003. Random population controls (10:1) were matched by birth year and birth sex or reassigned (final) sex, respectively.

Main Outcome Measures: Hazard ratios (HR) with 95% confidence intervals (CI) for mortality and psychiatric morbidity were obtained with Cox regression models, which were adjusted for immigrant status and psychiatric morbidity prior to sex reassignment (adjusted HR [aHR]).

Results: The overall mortality for sex-reassigned persons was higher during follow-up (aHR 2.8; 95% CI 1.8–4.3) than for controls of the same birth sex, particularly death from suicide (aHR 19.1; 95% CI 5.8–62.9). Sex-reassigned persons also had an increased risk for suicide attempts (aHR 4.9; 95% CI 2.9–8.5) and psychiatric inpatient care (aHR 2.8; 95% CI 2.0–3.9). Comparisons with controls matched on reassigned sex yielded similar results. Female-to-males, but not male-to-females, had a higher risk for criminal convictions than their respective birth sex controls.

Conclusions: Persons with transsexualism, after sex reassignment, have considerably higher risks for mortality, suicidal behaviour, and psychiatric morbidity than the general population. Our findings suggest that sex reassignment, although alleviating gender dysphoria, may not suffice as treatment for transsexualism, and should inspire improved psychiatric and somatic care after sex reassignment for this patient group.

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Introduction

Transsexualism (ICD-10),[1] or gender identity disorder (DSM-IV),[2] is a condition in which a person's gender identity - the sense of being a man or a woman - contradicts his or her bodily sex characteristics. The individual experiences gender dysphoria and desires to live and be accepted as a member of the opposite sex.

The treatment for transsexualism includes removal of body hair, vocal training, and cross-sex hormonal treatment aimed at making the person's body as congruent with the opposite sex as possible to alleviate the gender dysphoria. Sex reassignment also involves the surgical removal of body parts to make external sexual characteristics resemble those of the opposite sex, so called sex reassignment/confirmation surgery (SRS). This is a unique

intervention not only in psychiatry but in all of medicine. The present form of sex reassignment has been practised for more than half a century and is the internationally recognized treatment to ease gender dysphoria in transsexual persons.[3,4]

Despite the long history of this treatment, however, outcome data regarding mortality and psychiatric morbidity are scant. With respect to suicide and deaths from other causes after sex reassignment, an early Swedish study followed 24 transsexual persons for an average of six years and reported one suicide.[5] A subsequent Swedish study recorded three suicides after sex reassignment surgery of 175 patients.[6] A recent Swedish follow-up study reported no suicides in 60 transsexual patients, but one death due to complications after the sex reassignment surgery.[7] A Danish study reported death by suicide in 3 out of 29 operated male-to-female transsexual persons followed for an average of six years.[8] By contrast, a Belgian study of 107 transsexual persons followed for 4–6 years found no suicides or deaths from other causes.[9] A large Dutch single-centre study (N = 1,109), focusing on adverse events following hormonal treatment, compared the outcome after cross-sex hormone treatment with national Dutch standardized mortality and morbidity rates and found no increased mortality, with the exception of death from suicide and AIDS in male-to-females 25–39 years of age.[10] The same research group concluded in a recent report that treatment with cross-sex hormones seems acceptably safe, but with the reservation that solid clinical data are missing.[11] A limitation with respect to the Dutch cohort is that the proportion of patients treated with cross-sex hormones who also had surgical sex-reassignment is not accounted for.[10]

Data is inconsistent with respect to psychiatric morbidity post sex reassignment. Although many studies have reported psychiatric and psychological improvement after hormonal and/or surgical treatment,[7,12,13,14,15,16] other have reported on regrets,[17] psychiatric morbidity, and suicide attempts after SRS.[9,18] A recent systematic review and meta-analysis concluded that approximately 80% reported subjective improvement in terms of gender dysphoria, quality of life, and psychological symptoms, but also that there are studies reporting high psychiatric morbidity and suicide rates after sex reassignment.[19] The authors concluded though that the evidence base for sex reassignment "is of very low quality due to the serious methodological limitations of included studies."

The methodological shortcomings have many reasons. First, the nature of sex reassignment precludes double blind randomized controlled studies of the result. Second, transsexualism is rare [20] and many follow-ups are hampered by small numbers of subjects.[5,8,21,22,23,24,25,26,27,28] Third, many sex reassigned persons decline to participate in follow-up studies, or relocate after surgery, resulting in high drop-out rates and consequent selection bias.[6,9,12,21,24,28,29,30] Forth, several follow-up studies are hampered by limited follow-up periods.[7,9,21,22,26,30] Taken together, these limitations preclude solid and generalisable conclusions. A long-term population-based controlled study is one way to address these methodological shortcomings.

Here, we assessed mortality, psychiatric morbidity, and psychosocial integration expressed in criminal behaviour after sex reassignment in transsexual persons, in a total population cohort study with long-term follow-up information obtained from Swedish registers. The cohort was compared with randomly selected population controls matched for age and gender. We adjusted for premorbid differences regarding psychiatric morbidity and immigrant status. This study design sheds new light on transsexual persons' health after sex reassignment. It does not, however, address whether sex reassignment is an effective treatment or not.

Methods

National registers

The study population was identified by the linkage of several Swedish national registers, which contained a total of 13.8 million unique individuals. The Hospital Discharge Register (HDR, held by the National Board of Health and Welfare) contains discharge diagnoses, up to seven contributory diagnoses, external causes of morbidity or mortality, surgical procedure codes, and discharge date. Discharge diagnoses are coded according to the 8th (1969-1986), 9th (1987–1996), and 10th editions (1997-) of the International Classification of Diseases (ICD). The register covers virtually all psychiatric inpatient episodes in Sweden since 1973. Discharges that occurred up to 31 December 2003 were included. Surgical procedure codes could not be used for this study due to the lack of a specific code for sex reassignment surgery. The Total Population Register (TPR, held by Statistics Sweden) is comprised of data about the entire Swedish population. Through linkage with the Total Population Register it was possible to identify birth date and birth gender for all study subjects. The register is updated every year and gender information was available up to 2004/2005. The Medical Birth Register (MBR) was established in 1973 and contains birth data, including gender of the child at birth. National censuses based on mandatory self-report questionnaires completed by all adult citizens in 1960, 1970, 1980, and 1990 provided information on individuals, households, and dwellings, including gender, living area, and highest educational level. Complete migration data, including country of birth for immigrants for 1969–2003, were obtained from the TPR. In addition to educational information from the censuses, we also obtained highest educational level data for 1990 and 2000 from the Register of Education. The Cause of Death Register (CDR, Statistics Sweden) records all deaths in Sweden since 1952 and provided information on date of death and causes of death. Death events occurring up to 31 December 2003 are included in the study. The Crime Register (held by the National Council of Crime Prevention) provided information regarding crime type and date on all criminal convictions in Sweden during the period 1973–2004. Attempted and aggravated forms of all offences were also included. All crimes in Sweden are registered regardless of insanity at the time of perpetration; for example, for individuals who suffered from psychosis at the time of the offence. Moreover, conviction data include individuals who received custodial or non-custodial sentences and cases where the prosecutor decided to caution or fine without court proceedings. Finally, Sweden does not differ considerably from other members of the European Union regarding rates of violent crime and their resolution.[31]

Study population, identification of sex-reassigned persons (exposure assessment)

The study was designed as a population-based matched cohort study. We used the individual national registration number, assigned to all Swedish residents, including immigrants on arrival, as the primary key through all linkages. The registration number consists of 10 digits; the first six provide information of the birth date, whereas the ninth digit indicates the gender. In Sweden, a person presenting with gender dysphoria is referred to one of six specialised gender teams that evaluate and treat patients principally according to international consensus guidelines: Standards of Care.[3] With a medical certificate, the person applies to the National Board of Health and Welfare to receive permission for sex reassignment surgery and a change of legal sex status. A new national registration number signifying the new gender is assigned after sex reassignment surgery. The National

Board of Health and Welfare maintains a link between old and new national registration numbers, making it possible to follow individuals undergoing sex reassignment across registers and over time. Hence, sex reassignment surgery in Sweden requires (i) a transsexualism diagnosis and (ii) permission from the National Board of Health and Welfare.

A person was defined as exposed to sex reassignment surgery if two criteria were met: (i) at least one inpatient diagnosis of gender identity disorder diagnosis without concomitant psychiatric diagnoses in the Hospital Discharge Register, and (ii) at least one discrepancy between gender variables in the Medical Birth Register (from 1973 and onwards) or the National Censuses from 1960, 1970, 1980, or 1990 and the latest gender designation in the Total Population Register. The first criterion was employed to capture the hospitalization for sex reassignment surgery that serves to secure the diagnosis and provide a time point for sex reassignment surgery; the plastic surgeons namely record the reason for sex reassignment surgery, i.e., transsexualism, but not any co-occurring psychiatric morbidity. The second criterion was used to ensure that the person went through all steps in sex-reassignment and also changed sex legally.

The date of sex reassignment (start of follow-up) was defined as the first occurrence of a gender identity disorder diagnosis, without any other concomitant psychiatric disorder, in the Hospital Discharge Register after the patient changed sex status (any discordance in sex designation across the Censuses, Medical Birth, and Total Population registers). If this information was missing, we used instead the closest date in the Hospital Discharge Register on which the patient was diagnosed with gender identity disorder without concomitant psychiatric disorder prior to change in sex status. The reason for prioritizing the use of a gender identity disorder diagnosis after changed sex status over before was to avoid overestimating person-years at risk of sex-reassigned person.

Using these criteria, a total of 804 patients with gender identity disorder were identified, whereof 324 displayed a shift in the gender variable during the period 1973–2003. The 480 persons that did not shift gender variable comprise persons who either did not apply, or were not approved, for sex reassignment surgery. Moreover, the ICD 9 code 302 is a non specific code for sexual disorders. Hence, this group might also comprise persons that were hospitalized for sexual disorders other than transsexualism. Therefore, they were omitted from further analyses. Of the remaining 324 persons, 288 were identified with the gender identity diagnosis after and 36 before change of sex status. Out of the 288 persons identified after changed sex status, 185 could also be identified before change in sex status. The median time lag between the hospitalization before and after sex change for these 185 persons was 0.96 years (mean 2.2 years, SD 3.3).

Gender identity disorder was coded according to ICD-8: 302.3 (transsexualism) and 302.9 (sexual deviation NOS); ICD-9: 302 (overall code for sexual deviations and disorders, more specific codes were not available in ICD-9); and ICD-10: F64.0 (transsexualism), F64.1 (dual-role transvestism), F64.8 (other gender identity disorder), and F64.9 (gender identity disorder NOS). Other psychiatric disorders were coded as ICD-8: 290-301 and 303-315; ICD-9: 290-301 and 303-319; and ICD-10: F00-F63 as well as F65-F99.

Identification of population-based controls (unexposed group)

For each exposed person (N = 324), we randomly selected 10 unexposed controls. A person was defined as unexposed if there were no discrepancies in sex designation across the Censuses, Medical Birth, and Total Population registers and no gender identity disorder diagnosis according to the Hospital Discharge Register. Control persons were matched by sex and birth year and had to be alive and residing in Sweden at the estimated sex reassignment date of the case person. To study possible gender-specific effects on outcomes of interest, we used two different control groups: one with the same sex as the case individual at birth (birth sex matching) and the other with the sex that the case individual had been reassigned to (final sex matching).

Outcome measures

We studied mortality, psychiatric morbidity, accidents, and crime following sex reassignment. More specifically, we investigated: (1) all-cause mortality, (2) death by definite/uncertain suicide, (3) death by cardiovascular disease, and (4) death by tumour. Morbidity included (5) any psychiatric disorder (gender identity disorders excluded), (6) alcohol/drug misuse and dependence, (7) definite/uncertain suicide attempt, and (8) accidents. Finally, we addressed court convictions for (9) any criminal offence and (10) any violent offence. Each individual could contribute with several outcomes, but only one event per outcome. Causes of death (Cause of Death Registry from 1952 and onwards) were defined according to ICD as suicide (ICD-8 and ICD-9 codes E950-E959 and E980-E989, ICD-10 codes X60-X84 and Y10-Y34); cardiovascular disease (ICD-8 codes 390-458, ICD-9 codes 390-459, ICD-10 codes I00-I99); neoplasms (ICD-8 and ICD-9 codes 140-239, ICD-10 codes C00-D48), any psychiatric disorder (gender identity disorders excluded); (ICD-8 codes 290-301 and 303-315, ICD-9 codes 290-301 and 303-319, ICD-10 codes F00-F63 and F65-F99); alcohol/drug abuse and dependence (ICD-8 codes 303-304, ICD-9 codes 303-305 (tobacco use disorder excluded), ICD-10 codes F10-F16 and F18-F19 (x5 excluded); and accidents (ICD-8 and ICD-9 codes E800-E929, ICD-10 codes V01-X59).

Any criminal conviction during follow-up was counted; specifically, violent crime was defined as homicide and attempted homicide, aggravated assault and assault, robbery, threatening behaviour, harassment, arson, or any sexual offense.[32]

Covariates

Severe psychiatric morbidity was defined as inpatient care according to ICD-8 codes 291, 295-301, 303-304, and 307; ICD-9 codes 291-292, 295-298, 300-301, 303-305 (tobacco use disorder excluded), 307.1, 307.5, 308-309, and 311; ICD-10 codes F10-F16, F18-F25, F28-F45, F48, F50, and F60-F62. Immigrant status, defined as individuals born abroad, was obtained from the Total Population Register. All outcome/covariate variables were dichotomized (i.e., affected or unaffected) and without missing values.

Statistical analyses

Each individual contributed person-time from study entry (for exposed: date of sex reassignment; for unexposed: date of sex reassignment of matched case) until date of outcome event, death, emigration, or end of study period (31 December 2003), whichever came first. The association between exposure (sex reassignment) and outcome (mortality, morbidity, crime) was measured by hazard ratios (HR) with 95% CIs, taking follow-up time into account. HRs were estimated from Cox proportional hazard regression models, stratified on matched sets (1:10) to account for the matching by sex, age, and calendar time (birth year). We present crude HRs (though adjusted for sex and age through matching) and confounder-adjusted HRs [aHRs] for all outcomes. The two potential confounders, immigrant status (yes/no) and history of severe psychiatric morbidity (yes/no) prior to sex

reassignment, were chosen based on previous research[18,33] and different prevalence across cases and controls (Table 1).

Gender-separated analyses were performed and a Kaplan-Meier survival plot graphically illustrates the survival of the sex reassigned cohort and matched controls (all-cause mortality) over time. The significance level was set at 0.05 (all tests were two-sided). All outcome/covariate variables were without missing values, since they are generated from register data, which are either present (affected) or missing (unaffected). The data were analysed using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

Ethics

The data linking of national registers required for this study was approved by the IRB at Karolinska Institutet, Stockholm. All data were analyzed anonymously; therefore, informed consent for each individual was neither necessary nor possible.

Results

We identified 324 transsexual persons (exposed cohort) who underwent sex reassignment surgery and were assigned a new legal sex between 1973 and 2003. These constituted the sex-reassigned (exposed) group. Fifty-nine percent (N = 191) of sex-reassigned persons were male-to-females and 41% (N = 133) female-to-males, yielding a sex ratio of 1.4:1 (Table 1).

The average follow-up time for all-cause mortality was 11.4 (median 9.1) years. The average follow-up time for the risk of being hospitalized for any psychiatric disorder was 10.4 (median 8.1).

Characteristics prior to sex reassignment

Table 1 displays demographic characteristics of sex-reassigned and control persons prior to study entry (sex reassignment). There were no substantial differences between female-to-males and male-to-females regarding measured baseline characteristics. Immigrant status was twice as common among transsexual individuals compared to controls, living in an urban area somewhat more common, and higher education about equally prevalent. Transsexual individuals had been hospitalized for psychiatric morbidity other than gender identity disorder prior to sex reassignment about four times more often than controls. To adjust for these baseline discrepancies, hazard ratios adjusted for immigrant status and psychiatric morbidity prior to baseline are presented for all outcomes [aHRs].

Mortality

Table 2 describes the risks for selected outcomes during follow-up among sex-reassigned persons, compared to same-age controls of the same birth sex. Sex-reassigned transsexual persons of both genders had approximately a three times higher risk of all-cause mortality than controls, also after adjustment for covariates. Table 2

Table 1. Baseline characteristics among sex-reassigned subjects in Sweden (N = 324) and population controls matched for birth year and sex.

Characteristic at baseline	Sex-reassigned subjects (N = 324)	Birth-sex matched controls (N = 3,240)	Final-sex matched controls (N = 3,240)
Gender			
Female at birth, male after sex change	133 (41%)	1,330 (41%)	1,330 (41%)
Male at birth, female after sex change	191 (59%)	1,910 (59%)	1,910 (59%)
Average age at study entry [years] (SD, min-max)			
Female at birth, male after sex change	33.3 (8.7, 20–62)	33.3 (8.7, 20–62)	33.3 (8.7, 20–62)
Male at birth, female after sex change	36.3 (10.1, 21–69)	36.3 (10.1, 21–69)	36.3 (10.1, 21–69)
Both genders	35.1 (9.7, 20–69)	35.1 (9.7, 20–69)	35.1 (9.7, 20–69)
Immigrant status			
Female at birth, male after sex change	28 (21%)	118 (9%)	100 (8%)
Male at birth, female after sex change	42 (22%)	176 (9%)	164 (9%)
Both genders	70 (22%)	294 (9%)	264 (8%)
Less than 10 years of schooling prior to entry vs. 10 years or more			
Females at birth, males after sex change	49 (44%); 62 (56%)	414 (37%); 714 (63%)	407 (36%); 713 (64%)
Males at birth, females after sex change	61 (41%); 89 (59%)	665 (40%); 1,011 (60%)	595 (35%); 1,091 (65%)
All individuals with data	110 (42%); 151 (58%)	1,079 (38%); 1,725 (62%)	1,002 (36%); 1,804 (64%)
Psychiatric morbidity* prior to study entry			
Female at birth, male after sex change	22 (17%)	47 (4%)	42 (3%)
Male at birth, female after sex change	36 (19%)	76 (4%)	72 (4%)
Both genders	58 (18%)	123 (4%)	114 (4%)
Rural [vs. urban] living area prior to entry			
Female at birth, male after sex change	13 (10%)	180 (14%)	195 (15%)
Male at birth, female after sex change	20 (10%)	319 (17%)	272 (14%)
Both genders	33 (10%)	499 (15%)	467 (14%)

Note:
*Hospitalizations for gender identity disorder were not included.
doi:10.1371/journal.pone.0016885.t001

Table 2. Risk of various outcomes among sex-reassigned subjects in Sweden (N = 324) compared to population controls matched for birth year and birth sex.

	Number of events cases/ controls 1973–2003	Outcome incidence rate per 1000 person-years 1973–2003 (95% CI)		Crude hazard ratio (95% CI) 1973–2003	Adjusted* hazard ratio (95% CI) 1973–2003	Adjusted* hazard ratio (95% CI) 1973–1988	Adjusted* hazard ratio (95% CI) 1989–2003
		Cases	Controls				
Any death	27/99	7.3 (5.0–10.6)	2.5 (2.0–3.0)	2.9 (1.9–4.5)	2.8 (1.8–4.3)	3.1 (1.9–5.0)	1.9 (0.7–5.0)
Death by suicide	10/5	2.7 (1.5–5.0)	0.1 (0.1–0.3)	19.1 (6.5–55.9)	19.1 (5.8–62.9)	N/A	N/A
Death by cardiovascular disease	9/42	2.4 (1.3–4.7)	1.1 (0.8–1.4)	2.6 (1.2–5.4)	2.5 (1.2–5.3)	N/A	N/A
Death by neoplasm	8/38	2.2 (1.1–4.3)	1.0 (0.7–1.3)	2.1 (1.0–4.6)	2.1 (1.0–4.6)	N/A	N/A
Any psychiatric hospitalisation ‡	64/173	19.0 (14.8–24.2)	4.2 (3.6–4.9)	4.2 (3.1–5.6)	2.8 (2.0–3.9)	3.0 (1.9–4.6)	2.5 (1.4–4.2)
Substance misuse	22/78	5.9 (3.9–8.9)	1.8 (1.5–2.3)	3.0 (1.9–4.9)	1.7 (1.0–3.1)	N/A	N/A
Suicide attempt	29/44	7.9 (5.5–11.4)	1.0 (0.8–1.4)	7.6 (4.7–12.4)	4.9 (2.9–8.5)	7.9 (4.1–15.3)	2.0 (0.7–5.3)
Any accident	32/233	9.0 (6.3–12.7)	5.7 (5.0–6.5)	1.6 (1.1–2.3)	1.4 (1.0–2.1)	1.6 (1.0–2.5)	1.1 (0.5–2.2)
Any crime	60/350	18.5 (14.3–23.8)	9.0 (8.1–10.0)	1.9 (1.4–2.5)	1.3 (1.0–1.8)	1.6 (1.1–2.4)	0.9 (0.6–1.5)
Violent crime	14/61	3.6 (2.1–6.1)	1.4 (1.1–1.8)	2.7 (1.5–4.9)	1.5 (0.8–3.0)	N/A	N/A

Notes:
*Adjusted for psychiatric morbidity prior to baseline and immigrant status.
‡Hospitalisations for gender identity disorder were excluded.
N/A Not applicable due to sparse data.
doi:10.1371/journal.pone.0016885.t002

separately lists the outcomes depending on when sex reassignment was performed: during the period 1973-1988 or 1989–2003. Even though the overall mortality was increased across both time periods, it did not reach statistical significance for the period 1989–2003. The Kaplan-Meier curve (Figure 1) suggests that survival of transsexual persons started to diverge from that of matched controls after about 10 years of follow-up. The cause-specific mortality from suicide was much higher in sex-reassigned persons, compared to matched controls. Mortality due to cardiovascular disease was moderately increased among the sex-reassigned, whereas the numerically increased risk for malignancies was borderline statistically significant. The malignancies were lung cancer (N = 3), tongue cancer (N = 1), pharyngeal cancer (N = 1), pancreas cancer (N = 1), liver cancer (N = 1), and unknown origin (N = 1).

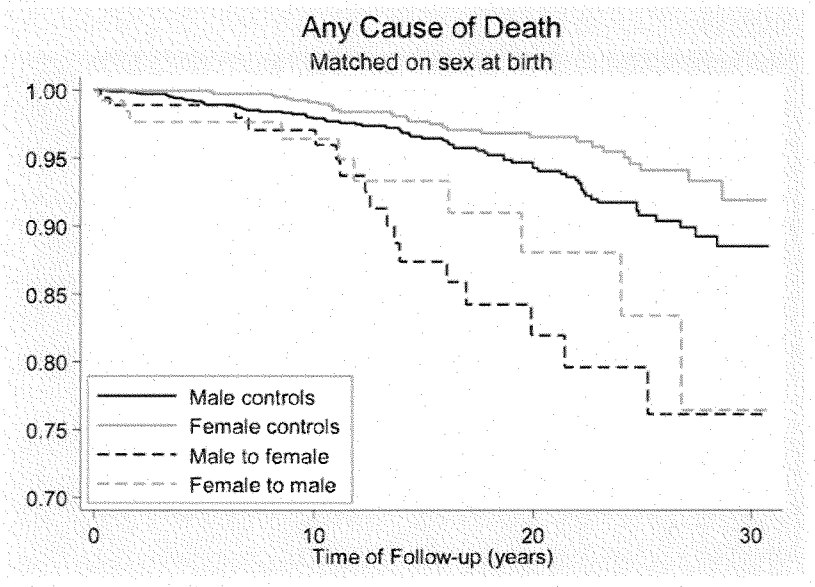

Figure 1. Death from any cause as a function of time after sex reassignment among 324 transsexual persons in Sweden (male-to-female: N = 191, female-to-male: N = 133), and population controls matched on birth year.
doi:10.1371/journal.pone.0016885.g001

Psychiatric morbidity, substance misuse, and accidents

Sex-reassigned persons had a higher risk of inpatient care for a psychiatric disorder other than gender identity disorder than controls matched on birth year and birth sex (Table 2). This held after adjustment for prior psychiatric morbidity, and was true regardless of whether sex reassignment occurred before or after 1989. In line with the increased mortality from suicide, sex-reassigned individuals were also at a higher risk for suicide attempts, though this was not statistically significant for the time period 1989–2003. The risks of being hospitalised for substance misuse or accidents were not significantly increased after adjusting for covariates (Table 2).

Crime rate

Transsexual individuals were at increased risk of being convicted for any crime or violent crime after sex reassignment (Table 2); this was, however, only significant in the group who underwent sex reassignment before 1989.

Gender differences

Comparisons of female-to-males and male-to-females, although hampered by low statistical power and associated wide confidence intervals, suggested mostly similar risks for adverse outcomes (Tables S1 and S2). However, violence against self (suicidal behaviour) and others ([violent] crime) constituted important exceptions. First, male-to-females had significantly increased risks for suicide attempts compared to both female (aHR 9.3; 95% CI 4.4–19.9) and male (aHR 10.4; 95% CI 4.9–22.1) controls. By contrast, female-to-males had significantly increased risk of suicide attempts only compared to male controls (aHR 6.8; 95% CI 2.1–21.6) but not compared to female controls (aHR 1.9; 95% CI 0.7–4.8). This suggests that male-to-females are at higher risk for suicide attempts after sex reassignment, whereas female-to-males maintain a female pattern of suicide attempts after sex reassignment (Tables S1 and S2).

Second, regarding any crime, male-to-females had a significantly increased risk for crime compared to female controls (aHR 6.6; 95% CI 4.1–10.8) but not compared to males (aHR 0.8; 95% CI 0.5–1.2). This indicates that they retained a male pattern regarding criminality. The same was true regarding violent crime. By contrast, female-to-males had higher crime rates than female controls (aHR 4.1; 95% CI 2.5–6.9) but did not differ from male controls. This indicates a shift to a male pattern regarding criminality and that sex reassignment is coupled to increased crime rate in female-to-males. The same was true regarding violent crime.

Discussion

Principal findings and comparison with previous research

We report on the first nationwide population-based, long-term follow-up of sex-reassigned transsexual persons. We compared our cohort with randomly selected population controls matched for age and gender. The most striking result was the high mortality rate in both male-to-females and female-to males, compared to the general population. This contrasts with previous reports (with one exception[8]) that did not find an increased mortality rate after sex reassignment, or only noted an increased risk in certain subgroups.[7,9,10,11] Previous clinical studies might have been biased since people who regard their sex reassignment as a failure are more likely to be lost to follow-up. Likewise, it is cumbersome to track deceased persons in clinical follow-up studies. Hence, population-based register studies like the present are needed to improve representativity.[19,34]

The poorer outcome in the present study might also be explained by longer follow-up period (median . 10 years) compared to previous studies. In support of this notion, the survival curve (Figure 1) suggests increased mortality from ten years after sex reassignment and onwards. In accordance, the overall mortality rate was only significantly increased for the group operated before 1989. However, the latter might also be explained by improved health care for transsexual persons during 1990s, along with altered societal attitudes towards persons with different gender expressions.[35]

Mortality due to cardiovascular disease was significantly increased among sex reassigned individuals, albeit these results should be interpreted with caution due to the low number of events. This contrasts, however, a Dutch follow-up study that reported no increased risk for cardiovascular events.[10,11] A recent meta-analysis concluded, however, that data on cardiovascular outcome after cross-sex steroid use are sparse, inconclusive, and of very low quality.[34]

With respect to neoplasms, prolonged hormonal treatment might increase the risk for malignancies,[36] but no previous study has tested this possibility. Our data suggested that the cause-specific risk of death from neoplasms was increased about twice (borderline statistical significance). These malignancies (see Results), however, are unlikely to be related to cross-hormonal treatment.

There might be other explanations to increased cardiovascular death and malignancies. Smoking was in one study reported in almost 50% by the male-to females and almost 20% by female-to-males.[9] It is also possible that transsexual persons avoid the health care system due to a presumed risk of being discriminated.

Mortality from suicide was strikingly high among sex-reassigned persons, also after adjustment for prior psychiatric morbidity. In line with this, sex-reassigned persons were at increased risk for suicide attempts. Previous reports [6,8,10,11] suggest that transsexualism is a strong risk factor for suicide, also after sex reassignment, and our long-term findings support the need for continued psychiatric follow-up for persons at risk to prevent this.

Inpatient care for psychiatric disorders was significantly more common among sex-reassigned persons than among matched controls, both before and after sex reassignment. It is generally accepted that transsexuals have more psychiatric ill-health than the general population prior to the sex reassignment.[18,21,22,33] It should therefore come as no surprise that studies have found high rates of depression,[9] and low quality of life[16,25] also after sex reassignment. Notably, however, in this study the increased risk for psychiatric hospitalisation persisted even after adjusting for psychiatric hospitalisation prior to sex reassignment. This suggests that even though sex reassignment alleviates gender dysphoria, there is a need to identify and treat co-occurring psychiatric morbidity in transsexual persons not only before but also after sex reassignment.

Criminal activity, particularly violent crime, is much more common among men than women in the general population. A previous study of all applications for sex reassignment in Sweden up to 1992 found that 9.7% of male-to-female and 6.1% of female-to-male applicants had been prosecuted for a crime.[33] Crime after sex reassignment, however, has not previously been studied. In this study, male-to-female individuals had a higher risk for criminal convictions compared to female controls but not compared to male controls. This suggests that the sex reassignment procedure neither increased nor decreased the risk for criminal offending in male-to-females. By contrast, female-to-males were at a higher risk for criminal convictions compared to female controls and did not differ from male controls, which suggests increased crime proneness in female-to-males after sex reassignment.

Strengths and limitations of the study

Strengths of this study include nationwide representativity over more than 30 years, extensive follow-up time, and minimal loss to follow-up. Many previous studies suffer from low outcome ascertainment,[6,9,21,29] whereas this study has captured almost the entire population of sex-reassigned transsexual individuals in Sweden from 1973–2003. Moreover, previous outcome studies have mixed pre-operative and post-operative transsexual persons,[22,37] while we included only post-operative transsexual persons that also legally changed sex. Finally, whereas previous studies either lack a control group or use standardised mortality rates or standardised incidence rates as comparisons,[9,10,11] we selected random population controls matched by birth year, and either birth or final sex.

Given the nature of sex reassignment, a double blind randomized controlled study of the result after sex reassignment is not feasible. We therefore have to rely on other study designs. For the purpose of evaluating whether sex reassignment is an effective treatment for gender dysphoria, it is reasonable to compare reported gender dysphoria pre and post treatment. Such studies have been conducted either prospectively[7,12] or retrospectively,[5,6,9,22,25,26,29,38] and suggest that sex reassignment of transsexual persons improves quality of life and gender dysphoria. The limitation is of course that the treatment has not been assigned randomly and has not been carried out blindly.

For the purpose of evaluating the safety of sex reassignment in terms of morbidity and mortality, however, it is reasonable to compare sex reassigned persons with matched population controls. The caveat with this design is that transsexual persons before sex reassignment might differ from healthy controls (although this bias can be statistically corrected for by adjusting for baseline differences). It is therefore important to note that the current study is only informative with respect to transsexuals persons health after sex reassignment; no inferences can be drawn as to the effectiveness of sex reassignment as a treatment for transsexualism. In other words, the results should not be interpreted such as sex reassignment *per se* increases morbidity and mortality. Things might have been even worse without sex reassignment. As an analogy, similar studies have found increased somatic morbidity, suicide rate, and overall mortality for patients treated for bipolar disorder and schizophrenia.[39,40] This is important information, but it does not follow that mood stabilizing treatment or antipsychotic treatment is the culprit.

Other facets to consider are first that this study reflects the outcome of psychiatric and somatic treatment for transsexualism provided in Sweden during the 1970s and 1980s. Since then, treatment has evolved with improved sex reassignment surgery, refined hormonal treatment,[11,41] and more attention to psychosocial care that might have improved the outcome. Second, transsexualism is a rare condition and Sweden is a small country (9.2 million inhabitants in 2008). Hence, despite being based on a comparatively large national cohort and long-term follow-up, the statistical power was limited. Third, regarding psychiatric morbidity after sex reassignment, we assessed inpatient psychiatric care. Since most psychiatric care is provided in outpatient settings (for which no reliable data were available), underestimation of the absolute prevalences was inevitable. However, there is no reason to believe that this would change the relative risks for psychiatric morbidity unless sex-reassigned transsexual individuals were more likely than matched controls to be admitted to hospital for any given psychiatric condition.

Finally, to estimate start of follow-up, we prioritized using the date of a gender identity disorder diagnosis after changed sex status over before changed sex status, in order to avoid overestimating person-years at risk after sex-reassignment. This means that adverse outcomes might have been underestimated. However, given that the median time lag between the hospitalization before and after change of sex status was less than a year (see Methods), this maneuver is unlikely to have influenced the results significantly. Moreover, all deaths will be recorded regardless of this exercise and mortality hence correctly estimated.

Conclusion

This study found substantially higher rates of overall mortality, death from cardiovascular disease and suicide, suicide attempts, and psychiatric hospitalisations in sex-reassigned transsexual individuals compared to a healthy control population. This highlights that post surgical transsexuals are a risk group that need long-term psychiatric and somatic follow-up. Even though surgery and hormonal therapy alleviates gender dysphoria, it is apparently not sufficient to remedy the high rates of morbidity and mortality found among transsexual persons. Improved care for the transsexual group after the sex reassignment should therefore be considered.

Supporting Information

Table S1 Risk of various outcomes in sex-reassigned persons in Sweden compared to population controls matched for birth year and birth sex.
(DOCX)

Table S2 Risk of various outcomes in sex-reassigned persons in Sweden compared to controls matched for birth year and final sex.
(DOCX)

Author Contributions

Conceived and designed the experiments: CD PL AJ NL ML. Performed the experiments: MB AJ. Analyzed the data: CD PL MB AJ NL ML. Contributed reagents/materials/analysis tools: PL NL AJ. Wrote the paper: CD PL MB AJ NL ML.

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Sex Reassignment Surgery for the Treatment of Gender Dysphoria

Summary

What We Found

There are some newly published studies on this technology. However, the review of abstracts indicates the results of these studies will not change the conclusions and/or ratings in the existing Hayes report.

Search Strategy

A cumulative literature search was performed on PubMed using *(vaginoplasty OR mammoplasty OR mastectomy OR phalloplasty OR metoidioplasty OR gender dysphoria) AND sex reassignment surgery*, 2014-2017.

Search Results

Six abstracts were retrieved, including 1 prospective case series, 2 retrospective studies, 2 systematic reviews, and 1 cost-effectiveness analysis.

Significance of Studies for

Efficacy: Evaluation of the literature indicates new evidence regarding efficacy is available since the 2014 publication of the Directory Report.

Patient Selection Criteria: Evaluation of the literature indicates patient selection criteria are unchanged since the 2014 publication of the Directory Report.

Safety: Evaluation of the literature indicates new evidence regarding safety is available since the 2014 publication of the Directory Report.

Long-Term Follow-Up: Evaluation of the literature indicates long-term data available up to 15.9 years since the 2014 publication of the Directory Report.

New Applications of Technology

Evaluation of the literature indicates no new application of technology available since the

2014 publication of the Directory Report.

Regulatory Status

Food and Drug Administration (FDA)

Sex reassignment surgeries are procedures, and therefore, not subject to FDA regulation.

Coverage Policies

CMS National Coverage Policy

National Coverage Determination (NCD) for Gender Dysphoria and Gender Reassignment Surgery (140.9), version 1, was effective August 30, 2016: click here.

Commercial Payer Coverage Policy:

Aetna: Policy titled *Gender Reassignment Surgery*, No. 0615, was updated January 12, 2017: click here.

Policy titled *Gonadotropin-Releasing Hormone Analogs and Antagonists*, No. 0501, was updated April 13, 2017: click here.

Cigna: The previously titled policy, *Gender Reassignment Surgery*, No. 0266, is now titled *Treatment of Gender Dysphoria* and was effective March 15, 2017: click here.

Humana: Policy titled *Gender Reassignment Surgery*, No. HGO-0518-010, was effective January 1, 2017: click here.

Regence Group: Policy titled *Transgender Services*, No. 153, was effective March 9, 2017: click here.

UnitedHealthcare (UHC): Policy titled *Gender Dysphoria Treatment*, No. 2017T0580A, was effective January 1, 2017: click here.

Professional Organizations

Professional Organization Guideline Update

American Academy of Child and Adolescent Psychiatry (AACAP): No update identified to the 2012 Committee on Quality Issues (CQI). *Practice parameter on gay, lesbian, or bisexual sexual orientation, gender nonconformity, and gender discordance in children and adolescents*: click here.

American College of Obstetricians and Gynecologists (ACOG): No update identified to

the 2011 *The American College of Obstetricians and Gynecologists. Committee Opinion. Committee on Health Care for Underserved Women. Health Care for Transgender Individuals*: click here.

American Psychiatric Association: No update identified to the 2012 *American Psychiatric Association Task Force on Treatment of Gender Identity Disorder. Report of the American Psychiatric Association Task Force on Treatment of Gender Identity Disorder*: click here.

The 2008 *American Medical Association House of Delegates. Resolution 122, Removing Financial Barriers to Care for Transgender Patients* was updated in 2016 and is now titled *Removing Financial Barriers to Care for Transgender Patients H-185.950*: click here.

American Psychological Association (APA): No update identified to the 2009 APA *Report of the APA Task Force on Gender Identity and Gender Variance*: click here.

The Endocrine Society: The 2009 *Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline* was published online April 30, 2011: click here.

World Professional Association for Transgender Health (WPATH): No update identified to the 2012 WPATH *Standards of care for the health of transsexual, transgender, and gender nonconforming people, version 7*: click here.

Society for Adolescent Health and Medicine (SAHM): No update identified to the 2013 *Recommendations for promoting the health and well-being of lesbian, gay, bisexual, and transgender adolescents: a position paper of the Society for Adolescent Health and Medicine*: click here.

Abstracts

Search Strategy

A cumulative literature search was performed on PubMed using *(vaginoplasty OR mammoplasty OR mastectomy OR phalloplasty OR metoidioplasty OR gender dysphoria) AND sex reassignment surgery*, 2014-2017.

Search Results

Six abstracts were retrieved, including 1 prospective case series, 2 retrospective studies, 2 systematic reviews, and 1 cost-effectiveness analysis.

1. Plast Reconstr Surg. 2017 Mar;139(3):649e-656e. doi: 10.1097/PRS.0000000000003108.
Penile Inversion Vaginoplasty with or without Additional Full-Thickness Skin Graft: To Graft or Not to Graft?

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BACKGROUND: Penile inversion vaginoplasty is considered to be the gold standard for gender reassignment surgery in transgender women. The use of additional full-thickness skin graft as neovaginal lining is controversial. Some believe that having extra penile skin for the vulva gives better aesthetic results. Others believe that it gives inferior functional results because of insensitivity and skin graft contraction.
METHODS: Transgender women undergoing penile inversion vaginoplasty were studied prospectively. The option to add full-thickness skin graft is offered in patients where the penile skin length lies between 7 and 12 cm. Neovaginal depth was measured at surgery and during follow-up (3, 13, 26, and 52 weeks postoperatively). Satisfaction with the aesthetic result, neovaginal depth, and dilation regimen during follow-up were recorded. Satisfaction, sexual function, and genital self-image were assessed using questionnaires.
RESULTS: A total of 100 patients were included (32 with and 68 without additional full-thickness skin graft). Patient-reported aesthetic outcome, overall satisfaction with the neovagina, sexual function, and genital self-image were not significantly associated with surgical technique. The mean intraoperative neovaginal depth was 13.8 ± 1.4 cm. After 1 year, this was 11.5 ± 2.5 cm. The largest decline (-15 percent) in depth is observed in the first 3 postoperative weeks ($p < 0.01$).
CONCLUSIONS: The authors can confirm neither of the suggested arguments, for or against full-thickness skin graft use, in penile inversion vaginoplasty. The additional use of full-thickness skin graft does not influence neovaginal shrinkage, nor does it affect the patient- and physician-reported aesthetic or functional outcome.
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

DOI: 10.1097/PRS.0000000000003108
PMID: 28234830

2. Aesthetic Plast Surg. 2017 Feb 15. doi: 10.1007/s00266-017-0812-4. [Epub ahead of print]
A Systematic Review of Patient-Reported Outcome Measures Following Transsexual Surgery.

Barone M(1), Cogliandro A(2), Di Stefano N(3), Tambone V(3), Persichetti P(1).

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BACKGROUND: The aims of our study were to identify studies that evaluated patient satisfaction after transsexual surgery, analyze existing questionnaires, and summarize their development, psychometric properties, and content.
METHODS: A systematic review of the English-language literature was performed. Patient-reported outcome measures designed to assess patient satisfaction and quality of life following transsexual surgery were identified. Qualifying instruments were assessed for content and adherence to international guidelines for development and validation.
RESULTS: From 796 articles, 19 studies had sufficient data and met the inclusion criteria. Included were a total of 2299 patients and 17 patient-reported outcome measures: 10 generic instruments that assessed quality of life, 4 specific for female genital or sexual satisfaction, 2 specific for transsexual body image or gender dysphoria, and 1 specific for plastic surgery. The questionnaires were analyzed by reviewers to assess the adherence to the rules of the US FDA and the Scientific Advisory Committee of the Medical Outcomes Trust. We identified 17 individual questionnaires that were included. All measures were limited by either their development, their validation, or their content.
CONCLUSIONS: There is a need for a new self-assessment tool, which should include functional, psychorelational, and cosmetic components, to measure satisfaction and quality of life of patients who have undergone transsexual surgery.
LEVEL OF EVIDENCE III: This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266 .

DOI: 10.1007/s00266-017-0812-4
PMID: 28204933

3. Plast Reconstr Surg Glob Open. 2016 Dec 23;4(12):e1131. doi: 10.1097/GOX.0000000000001131. eCollection 2016.

A Systematic Review of Metoidioplasty and Radial Forearm Flap Phalloplasty in Female-to-male Transgender Genital Reconstruction: Is the "Ideal" Neophallus an Achievable Goal?

Frey JD(1), Poudrier G(1), Chiodo MV(1), Hazen A(1).

Author information:
(1)Hansjörg Wyss Department of Plastic Surgery, NYU Langone Medical Center, New York, N.Y.

INTRODUCTION: The complex anatomy and function of the native penis is difficult to surgically replicate. Metoidioplasty and radial forearm flap phalloplasty (RFFP) are the 2 most commonly utilized procedures for transgender neophallus construction.
METHODS: A MEDLINE search for metoidioplasty and RFFP in female-to-male genital reconstruction was performed. Primary outcome measures were subsequently compared. A systematic review was planned in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyse guidelines. Grading of Recommendations Assessment, Development and Evaluation (GRADE) was utilized to evaluate the quality of evidence.
RESULTS: Using Population, Intervention, Comparison and Outcomes tool criteria, a total of 188 articles were identified; 7 articles related to metoidioplasty and 11 articles related to RFFP met inclusion criteria. The GRADE quality of evidence was low to very low for all included studies. In studies examining metoidioplasty, the average study size and length of follow-up were 54 patients and 4.6 years, respectively (1 study did not report [NR]). Eighty-eight percent underwent a single-stage reconstruction (0 NR), 87% reported an aesthetic neophallus (3 NR), and 100% reported erogenous sensation (2 NR). Fifty-one percent of patients reported successful intercourse (3 NR), and 89% of patients achieved standing micturition (3 NR). In studies examining RFFP, the average study size and follow-up were 60.4 patients and 6.23 years, respectively (6 NR). No patients underwent single-stage reconstructions (8 NR). Seventy percent of patients reported a satisfactorily aesthetic neophallus (4 NR), and 69% reported erogenous sensation (6 NR). Forty-three percent reported successful penetration of partner during intercourse (6 NR), and 89% achieved standing micturition (6 NR). Compared with RFFP, metoidioplasty was significantly more likely to be completed in a single stage ($P < 0.0001$), have an aesthetic result ($P = 0.0002$), maintain erogenous sensation ($P < 0.0001$), achieve standing micturition ($P = 0.001$), and have a lower overall complication rate ($P = 0.02$).
CONCLUSIONS: Although the current literature suggests that metoidioplasty is more likely to yield an "ideal" neophallus compared with RFFP, any conclusion is severely limited by the low quality of available evidence.

DOI: 10.1097/GOX.0000000000001131
PMCID: PMC5222645
PMID: 28293500

4. Plast Reconstr Surg. 2016 Nov;138(5):999-1007.
Surgical Outcome after Penile Inversion Vaginoplasty: A Retrospective Study of 475 Transgender Women.

Buncamper ME(1), van der Sluis WB, van der Pas RS, Özer M, Smit JM, Witte BI, Bouman MB, Mullender MG.

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Hand Surgery, the Center of Expertise on Gender Dysphoria, the EMGO+ Institute for Health and Care Research, and the Department of Epidemiology and Biostatistics, VU University Medical Center; and Gender Surgery Amsterdam.

BACKGROUND: For many transgender women, vaginoplasty is the final stage in the gender-confirming process. Penile inversion vaginoplasty is considered the gold standard for vaginal construction in transgender women. In this study, the authors assessed intraoperative and postoperative complications after penile inversion vaginoplasty.
METHODS: All patients who underwent penile inversion vaginoplasty between January of 2000 and January of 2014 were identified retrospectively from the authors' hospital registry. A retrospective chart review was conducted. Outcome measures were intraoperative and postoperative complications, reoperations, secondary surgical procedures, and possible risk factors.
RESULTS: Between January of 2000 and January of 2014, 475 patients underwent penile inversion vaginoplasty, 405 of whom did not have and 70 of whom did have additional full-thickness skin grafts. The median patient age at surgery was 38.6 years (range, 18.1 to 70.8 years). Median follow-up was 7.8 years (range, 1.0 to 15.9 years). The most frequently observed intraoperative complication was rectal injury [n = 11 (2.3 percent)]. Short-term postoperative bleeding that required transfusion [n = 23 (4.8 percent)], reoperation [n = 7 (1.5 percent)] or both [n = 2 (0.4 percent)] occurred in some cases. Major complications comprised three (0.6 percent) rectoneovaginal fistulas, which were successfully treated. Revision vaginoplasty was performed in 14 patients (2.9 percent). Comorbid diabetes was associated with a higher risk of local infection (OR, 9.8; p = 0.003; 95 percent CI, 2.8 to 34.4), and use of psychotropic medication predisposed to postoperative urinary retention (OR, 2.1; p = 0.006; 95 percent CI, 1.2 to 3.5).
CONCLUSIONS: Successful vaginal construction without the need for secondary functional reoperations was achieved in the majority of patients. Intraoperative complications are scarce. Postoperative complications occur frequently but are generally minor and easily treated.
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

DOI: 10.1097/PRS.0000000000002684
PMID: 27782992

5. Obstet Gynecol. 2016 Jun;127(6):1118-26. doi: 10.1097/AOG.0000000000001421.
Clinical Characteristics and Management of Neovaginal Fistulas After Vaginoplasty in Transgender Women.

van der Sluis WB(1), Bouman MB, Buncamper ME, Pigot GL, Mullender MG, Meijerink WJ.

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Health and Care Research, and the Centre of Expertise on Gender Dysphoria, VU University Medical Centre, Amsterdam, the Netherlands.

OBJECTIVE: To describe our experience and results obtained in the management of neovaginal fistulas after vaginoplasty as gender reassignment surgery in transgender women.
METHODS: A retrospective study was performed of 1,082 transgender women who underwent 1,037 primary and 80 revision vaginoplasty procedures between 1990 and 2015. Thirty-five women underwent both primary and later revision vaginoplasty at our institution. Patient, clinical, surgical, and outcome characteristics were reviewed.
RESULTS: We treated 25 (2.3%) patients for 13 rectoneovaginal, 11 urethroneovaginal, and one pouch-neovaginal fistulas. Patients undergoing revision vaginoplasty were at higher risk of rectoneovaginal fistula development (0.8% compared with 6.3%, P<.01, odds ratio 8.6, 95% confidence interval 2.7-26.9). Of 23 intraoperatively identified and oversewn rectal perforations, four (17.4%) patients developed a rectoneovaginal fistula. In four patients, fecal diversion was achieved through temporary colostomy or ileostomy with direct (n=1) or delayed (n=3) fistula closure. In six patients, urethroneovaginal fistula arose after a complication such as meatal stenosis. Two patients underwent temporary suprapubic cystostomy for urinary diversion. In most patients, fistulectomy and primary closure or a local advancement flap was sufficient to treat the fistula.
CONCLUSION: Neovaginal fistulas are uncommon after vaginoplasty. Symptoms of neovaginal fistulas are comparable with those of vaginal fistulas. In most patients, the diagnosis can be made based on symptoms and physical examination alone. It seems that a complicated course (eg, intraoperative rectal perforation or meatal stenosis) predisposes for fistula formation. Surgical repair of neovaginal fistulas is associated with few intraoperative and postoperative complications and does not seem to impair neovaginal function.

DOI: 10.1097/AOG.0000000000001421
PMID: 27159746

6. J Gen Intern Med. 2016 Apr;31(4):394-401. doi: 10.1007/s11606-015-3529-6. Epub 2015 Oct 19.
Societal Implications of Health Insurance Coverage for Medically Necessary Services in the U.S. Transgender Population: A Cost-Effectiveness Analysis.

Padula WV(1), Heru S(2), Campbell JD(3).
Author information: (1)Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, 624 N. Broadway, Baltimore, MD, 21205, USA. wpadula@jhu.edu. (2)Commonwealth of Massachusetts Group Insurance Commission (GIC), Boston, MA, USA. (3)Center for Pharmaceutical Outcomes Research (CePOR), Department of Clinical Pharmacy, University of Colorado, Aurora, CO, USA.

BACKGROUND: Recently, the Massachusetts Group Insurance Commission (GIC) prioritized research on the implications of a clause expressly prohibiting the denial of health insurance coverage for transgender-related services. These medically necessary services include primary and preventive care as well as transitional therapy.
OBJECTIVE: To analyze the cost-effectiveness of insurance coverage for medically necessary transgender-related services.
DESIGN: Markov model with 5- and 10-year time horizons from a U.S. societal perspective, discounted at 3% (USD 2013). Data on outcomes were abstracted from the 2011 National Transgender Discrimination Survey (NTDS).
PATIENTS: U.S. transgender population starting before transitional therapy.
INTERVENTIONS: No health benefits compared to health insurance coverage for medically necessary services. This coverage can lead to hormone replacement therapy, sex reassignment surgery, or both.
MAIN MEASURES: Cost per quality-adjusted life year (QALY) for successful transition or negative outcomes (e.g. HIV, depression, suicidality, drug abuse, mortality) dependent on insurance coverage or no health benefit at a willingness-to-pay threshold of $100,000/QALY. Budget impact interpreted as the U.S. per-member-per-month cost.
KEY RESULTS: Compared to no health benefits for transgender patients ($23,619; 6.49 QALYs), insurance coverage for medically necessary services came at a greater cost and effectiveness ($31,816; 7.37 QALYs), with an incremental cost-effectiveness ratio (ICER) of $9314/QALY. The budget impact of this coverage is approximately $0.016 per member per month. Although the cost for transitions is $10,000-22,000 and the cost of provider coverage is $2175/year, these additional expenses hold good value for reducing the risk of negative endpoints--HIV, depression, suicidality, and drug abuse. Results were robust to uncertainty. The probabilistic sensitivity analysis showed that provider coverage was cost-effective in 85% of simulations.
CONCLUSIONS: Health insurance coverage for the U.S. transgender population is affordable and cost-effective, and has a low budget impact on U.S. society. Organizations such as the GIC should consider these results when examining policies regarding coverage exclusions.
Conflict of interest statement: The Authors have no conflicts of interest to declare. Authorship of this manuscript follows ICMJE guidelines; each author is associated with conceptualization, writing, final approval, and accountability for the work.
DOI: 10.1007/s11606-015-3529-6
PMCID: PMC4803686
PMID: 26481647 [Indexed for MEDLINE]

Hayes annual review

April 12, 2016

Sex Reassignment Surgery for the Treatment of Gender Dysphoria

Summary

What We Found

There are no newly published studies on this technology; therefore, there will be no changes to the existing Hayes report.

Search Strategy

A cumulative literature search was performed on PubMed using *(vaginoplasty OR mammoplasty OR mastectomy OR phalloplasty OR metoidioplasty OR gender dysphoria) AND sex reassignment surgery*, 2014-2016.

Search Results

No abstracts were retrieved.

Significance of Studies for

Efficacy: Evaluation of the literature indicates efficacy is unchanged since the 2014 publication of the Directory Report.

Patient Selection Criteria: Evaluation of the literature indicates patient selection criteria are unchanged since the 2014 publication of the Directory Report.

Safety: Evaluation of the literature indicates safety is unchanged since the 2014 publication of the Directory Report.

Long-Term Follow-Up: Evaluation of the literature indicates no long-term data are available since the 2014 publication of the Directory Report.

New Applications of Technology

Evaluation of the literature indicates no new application of technology is available since the 2014 publication of the Directory Report.

Regulatory Status

Food and Drug Administration (FDA)

Sex reassignment surgeries are procedures and therefore not subject to FDA regulation.

Coverage Policies

CMS National Coverage Policy

According to CMS Transmittal 189, dated June 27, 2014, for claims with dates of service on and after May 30, 2014, Medicare coverage for transsexual surgery will be determined by the local Medicare Administrative Contractors.

Commercial Payer Coverage Policy:

Aetna: Policy titled *Gender Reassignment Surgery*, No. 0615, was updated October 23, 2015.

Cigna: Policy titled *Gender Reassignment Surgery*, No. 0266, was effective March 15, 2016.

Humana: Policy titled *Gender Reassignment Surgery*, No. HGO-0518-007, was effective January 1, 2016.

Regence Group: Policy titled *Transgender Services*, No. 153, was effective January 1, 2016.

UnitedHealthcare (UHC): Policy titled *Gender Dysphoria (Gender Identity Disorder) Treatment*, No. CDG.011.05, was effective October 1, 2015.

Professional Organizations

Professional Organization Guideline Update

American Academy of Child and Adolescent Psychiatry (AACAP): No update identified to the 2012 Committee on Quality Issues (CQI) *Practice parameter on gay, lesbian, or bisexual sexual orientation, gender nonconformity, and gender discordance in children and adolescents.*

American College of Obstetricians and Gynecologists (ACOG): No update identified to the 2011 *The American College of Obstetricians and Gynecologists. Committee Opinion. Committee on Health Care for Underserved Women. Health Care for Transgender Individuals.*

American Psychiatric Association: No update identified to the 2012 American Psychiatric Association *Task Force on Treatment of Gender Identity Disorder. Report of the American*

Psychiatric Association Task Force on Treatment of Gender Identity Disorder.

No update identified to the 2008 American Medical Association *House of Delegates. Resolution 122, Removing Financial Barriers to Care for Transgender Patients.*

American Psychological Association (APA): No update identified to the 2009 *APA Report of the APA Task Force on Gender Identity and Gender Variance.*

The Endocrine Society: The 2009 *Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline* was published online April 30, 2011.

World Professional Association for Transgender Health (WPATH): No update identified to the 2012 WPATH *Standards of care for the health of transsexual, transgender, and gender nonconforming people, version 7.*

Society for Adolescent Health and Medicine (SAHM): No update identified to the 2013 *Recommendations for promoting the health and well-being of lesbian, gay, bisexual, and transgender adolescents: a position paper of the Society for Adolescent Health and Medicine.*

Abstracts

Search Strategy

A cumulative literature search was performed on PubMed using *(vaginoplasty OR mammoplasty OR mastectomy OR phalloplasty OR metoidioplasty OR gender dysphoria) AND sex reassignment surgery*, 2014-2016.

Search Results

No abstracts were retrieved.

May 11, 2015

Sex Reassignment Surgery for the Treatment of Gender Dysphoria

Summary

What We Found

There are no newly published studies that meet the defined inclusion criteria described in the Hayes 2014 publication on this technology; therefore, there will be no changes to the conclusions and/or ratings in the existing Hayes report.

Search Strategy

A cumulative literature search was performed on PubMed using *(vaginoplasty OR mammoplasty OR mastectomy OR phalloplasty OR metoidioplasty OR gender dysphoria) AND sex reassignment surgery*, 2014-2015.

Search Results

No abstracts were retrieved.

Significance of Studies for

Efficacy: Evaluation of the literature indicates efficacy is unchanged since the 2014 publication of the Directory Report.

Patient Selection criteria: Evaluation of the literature indicates patient selection criteria are unchanged since the 2014 publication of the Directory Report.

Safety: Evaluation of the literature indicates safety is unchanged since the 2014 publication of the Directory Report.

Long-term follow-up: Evaluation of the literature indicates no long-term data is available since the 2014 publication of the Directory Report.

New Applications of Technology

Evaluation of the literature indicates no new application of technology is available since the 2014 publication of the Directory Report.

Regulatory Status

Food and Drug Administration (FDA)

Sex reassignment surgeries are procedures, and therefore, not subject to FDA regulation.

Coverage Policies

CMS National Coverage Policy

According to CMS Transmittal 189, dated June 27, 2014, for claims with dates of service on and after May 30, 2014, Medicare coverage for transsexual surgery will be determined by the local Medicare Administrative Contractors.

https://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/Downloads/R189BP.pdf

Commercial Payer Coverage Policy:

Aetna: Policy titled, Gender Reassignment Surgery, No. 0615, was revised September 19, 2014.

Cigna: Policy titled, Gender Reassignment Surgery, No. 0266, was effective January 15, 2015.

Humana: Policy titled, Gender Reassignment Surgery, No. CLPD-0518-005, was effective January 1, 2015.

Regence Group: Policy titled, Transgender Services, No. 153, was effective January 1, 2015.

Professional Organizations

Professional Organization Guideline Update

American College of Obstetricians and Gynecologists (ACOG): No update identified to the 2011 "The American College of Obstetricians and Gynecologists. Committee Opinion. Committee on Health Care for Underserved Women. Health Care for Transgender Individuals".

American Psychiatric Association (APA): No update identified to the 2012 "American Psychiatric Association Task Force on Treatment of Gender Identity Disorder. Report of the American Psychiatric Association Task Force on Treatment of Gender Identity Disorder".

No update identified to the 2008 "American Medical Association House of Delegates. Resolution 122, Removing Financial Barriers to Care for Transgender Patients".

American Psychological Association: No update identified to the 2009 APA "Report of the APA Task Force on Gender Identity and Gender Variance".

The Endocrine Society: The 2009 "Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline" was published online July 2, 2013.

World Professional Association for Transgender Health (WPATH): No update identified to the 2012 WPATH "Standards of care for the health of transsexual, transgender, and gendernonconforming people, version 7".

Society for Adolescent Health and Medicine (SAHM): No update identified to the 2013 "Recommendations for promoting the health and well-being of lesbian, gay, bisexual, and transgender adolescents: a position paper of the Society for Adolescent Health and Medicine".

Abstracts

Search Strategy

A cumulative literature search was performed on PubMed using *(vaginoplasty OR mammoplasty OR mastectomy OR phalloplasty OR metoidioplasty OR gender dysphoria) AND sex reassignment surgery*, 2014-2015.

Search Results

No abstracts were retrieved.

DEFENSE HEALTH AGENCY
7700 ARLINGTON BOULEVARD, SUITE 5101
FALLS CHURCH, VIRGINIA 22042-5101

NOV 13 2017

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE NAVY (MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE AIR FORCE (MANPOWER AND RESERVE AFFAIRS)

SUBJECT: Information Memorandum: Interim Defense Health Agency Procedures for Reviewing Requests for Waivers to Allow Supplemental Health Care Program Coverage of Sex Reassignment Surgical Procedures

The purpose of this memorandum is to share with you the procedures the Defense Health Agency (DHA) will follow to consider requests for a Supplemental Health Care Program (SHCP) waiver to allow coverage of sex reassignment surgical procedures.

Background

The 2016 Department of Defense (DoD) transgender service policy change included medical guidance that unless and until adequate surgical capabilities are established in military medical treatment facilities, requests for transgender surgery would be considered for DoD payment to non-DoD facilities under the SHCP and would require a waiver from the DHA Director.[1] That guidance noted that there are applicable statutory limitations. The statutory limitations include that DoD may not pay for surgery in non-DoD facilities for "sex gender changes," but this is subject to "such exceptions as the Secretary of Defense considers necessary," as long as they do not involve "elective private treatment."[2]

The Presidential Memorandum of August 25, 2017, "Military Service by Transgender Individuals," included direction that, effective March 23, 2018, the Military Health System halt all use of appropriations to fund sex-reassignment surgical procedures for military personnel, except to the extent necessary to protect the health of an individual who has already begun a course of treatment to reassign his or her sex. The Secretary of Defense Memorandum of September 14, 2017, "Military Service by Transgender Individuals – Interim Guidance," included direction that Service members who receive a gender dysphoria diagnosis from a military medical provider will be provided treatment for the diagnosed medical condition. The effect of this is to continue the July 2016 medical guidance until the Secretary promulgates final policy implementing the direction from the Commander In Chief of the Armed Forces.

[1] Assistant Secretary of Defense (Health Affairs) Memorandum, "Guidance for Treatment of Gender Dysphoria for Active and Reserve Component Service Members," July 29, 2016.
[2] 10 U.S.C. 1074(c)(2)(A), 1079(a)(11), 1074(c)(1).

This memorandum addresses procedures for considering requests for waivers under the SHCP for sex reassignment surgical procedures.[3] This memorandum does not apply to non-surgical care, nor to surgical care provided in military medical treatment facilities; those matters remain under the procedures of the Military Department concerned, consistent with the July 2016 guidance from the Assistant Secretary of Defense for Health Affairs, which remains in effect.

In evaluating potential coverage of otherwise non-covered services, the TRICARE regulation calls for review under the established hierarchy of reliable evidence,[4] which considers peer-reviewed publications of well controlled studies of clinically meaningful endpoints and published formal technology assessments as stronger than professional opinions, policy positions, and reports. (Although the TRICARE regulation is not binding on the SHCP, it provides a useful frame of reference). The effectiveness of gender transition surgery as a treatment for gender dysphoria is not well documented under this hierarchy of reliable evidence.[5]

Criteria for Considering SHCP Waiver Requests

Use of the Secretary's discretionary authority to waive the prohibition on paying for sex-reassignment surgery[6] under the SHCP will consider all relevant information in a case-by-case

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[3] 32 CFR 199.16(f) provides that generally applicable exclusions may be waived by the DHA based on a determination that such waiver is necessary to assure adequate availability of health care services to active duty members.

[4] 32 C.F.R. 199.2.

[5] Consistent with this hierarchy of reliable evidence, DoD often relies on health technology assessments conducted by Hayes, Inc. Hayes, Inc. uses a five-tier rating system. Under the most recent Hayes, Inc. assessment (Haynes Directory and Annual Review, May 15, 2014 and April 18, 2017 (updated)), for sex reassignment surgery (SRS) to treat gender dysphoria (GD) in adults for whom a qualified mental health professional has made a formal diagnosis of GD, have undergone hormone therapy and psychotherapy, and have undergone a Real-Life Experience, the rating reflects the reporting of some positive evidence but with serious limitations in the evidence of both effectiveness and safety. The evidence is rated a "C", which is a middle tier in the rating system, indicating there is potential but unproven benefit. Some published evidence suggests that safety and impact on health outcomes are at least comparable to standard treatment/testing. However, the "C" rating indicates that substantial uncertainty remains about safety and/or impact on health outcomes because of poor-quality studies, sparse data, conflicting study results, and/or other concerns.

[6] For purposes of this memorandum, sex reassignment surgery is defined as all surgical procedures related to transition from the birth sex to the preferred gender. These procedures include but are not limited to mastectomy, hysterectomy, gonadectomy, genital reassignment, breast augmentation, and cosmetic procedures to enhance the characteristics of the preferred gender. See Attachment for a more inclusive list.

review of the patient's record and circumstances, including the expected clinical benefit if the surgery is provided, the expected adverse effect on the patient's health if the surgery is not provided, and the potential impact of the requested health care service on the Service member's fitness for duty and military readiness. Updating guidance applicable to the SHCP, DHA's clinical review will adhere to the surgical care provisions of the 2017 Endocrine Society's Standards of Care, "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline,"[7] to provide consistent, evidence-based care. The standards applicable to surgical care are summarized in the Attachment. Use of SHCP funding for any proposed sex-reassignment surgical procedures requires case-by-case authorization from the DHA Director.

Requests for waivers require appropriate clinical documentation and a recommendation for approval by the Surgeon General concerned. Absent emergency circumstances, SHCP surgery should not be scheduled until a waiver has been approved by the Director, DHA.

My point of contact for this matter is Dr. John Kugler, Chief, Clinical Support Division, Operations Directorate (J-3). Dr. Kugler can be reached via email at john.p.kugler.civ@mail.mil.

R. C. BONO
VADM, MC, USN
Director

Attachments:
As stated

cc:
Assistant Secretary of Defense for Health Affairs
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force
Joint Staff Surgeon
Medical Officer of the Marine Corps
Director, Health, Safety, and Work Life, U.S. Coast Guard

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[7] The 2017 Endocrine Society guideline uses the terms "gender-reassignment surgery," "gender-confirming surgery" and "gender-affirming surgery." For purposes of this memorandum, the term "sex reassignment surgery" is interchangeable with the 2017 Endocrine Society guideline terms.

ATTACHMENT

SURGICAL PROCEDURES FOR GENDER DYSPHORIA

1. SRS GUIDELINES. Medically necessary sex reassignment surgery (SRS) may be considered when all of the following criteria are met:

a. Cross-sex hormones have been used continuously and responsibly for the required/recommended time according to the type of surgery;

b. Regular participation in psychotherapy throughout the transition period at a frequency determined jointly by the patient and the mental health provider has been completed if required;

c. Knowledge of all practical aspects of surgery (e.g., cost, required length of hospitalization, likely complications, post-surgical rehabilitation, SHCP policy including limitations, etc.) has been demonstrated;

d. Progress in consolidating one's gender identity has been demonstrated;

e. Progress in dealing with work, family, and interpersonal issues resulting in a significantly better state of mental health has been demonstrated; and

f. The endocrinologist or the physician responsible for endocrine treatment and the mental health provider must certify that the individual satisfies the eligibility and readiness criteria for SRS.

2. MEDICALLY NECESSARY PROCEDURES. Subject to receiving the relevant diagnosis/validation from an appropriate military medical provider, the following procedures may be recognized as "medically necessary" by DoD and may be funded through SHCP:

a. Female-to-Male

PROCEDURE	CPT Codes	CRITERIA
Hysterectomy and salpingo-oophorectomy (removal of uterus and ovaries)	58262/58291	1. Meet SRS Guidelines in Attachment 1, section 1, **required** 2. 12 months of hormonal therapy **required** (unless medically contraindicated) 3. 12 months of full time RLE **required**
Mastectomy (removal of breast)	19301/19303/19304	1. Meet SRS Guidelines in Attachment 1, section 1, **required** 2. 12 months of hormonal

		therapy **recommended** (unless medically contraindicated) 3. 12 months of full time RLE **recommended**
Metoidioplasty (enlargement/ lengthening of clitoris)	55899	1. Meet SRS Guidelines in Attachment 1, section 1, **required** 2. 12 months of hormonal therapy **required** (unless medically contraindicated) 3. 12 months of continuous full time RLE **required**
Phalloplasty (construction of "new" phallus from skin or muscle grafts)	55899	
Placement of testicular prostheses	54660	
Scrotoplasty (re-arrangement of labia to create scrotum)	55175	
Urethroplasty (creation of longer urethra from skin to enable standing voiding)	53430	
Vaginectomy (removal of vagina)	57106	

b. Male-to-Female

PROCEDURE	CPT Codes	CRITERIA
Orchiectomy (removal of testicles)	54520/54690	1. Meet SRS Guidelines in Attachment 1, section 1, **required** 2. 12 months of hormonal therapy **required** (unless medically contraindicated) 3. 12 months of full time RLE **required**
Penectomy (removal of penis)	54125	
Vaginoplasty (construction of "new" vagina from skin or intestinal tube)	57335	
Clitoroplasty (rearrangement of penile tissues to create "new" clitoris)	56805	
Labiaplasty (rearrangement of scrotum to create "new" labia)	58999	

3. COSMETIC PROCEDURES. The following procedures are considered "cosmetic procedures" by DoD and are not funded through SHCP (although some may be provided in an MTF subject to MTF capability and current Cosmetic Surgery Policy payment rules; this list is not all-inclusive):

a. Abdominoplasty (unless standard medical necessity criteria met)

b. Breast Augmentation[8]

c. Blepharoplasty (eyelid lift) (unless standard medical necessity criteria met)

d. Hair removal/Electrolysis9

e. Face-lift

f. Facial bone reduction

g. Hair transplantation

h. Liposuction

i. Reduction thyroid chondroplasty (Adam's Apple surgery)

j. Rhinoplasty

k. Voice modification surgery

4. OTHER SURGICAL CONSIDERATIONS

a. Cryopreservation of oocytes and/or sperm is not funded by DoD

b. Reversal of SRS is not funded by DoD

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[8] A waiver for breast augmentation (CPT code 19324/19325) may be authorized when the ADSM has undergone 24 months of feminizing hormone therapy (unless medically contraindicated) with insufficient breast development.

[9] A waiver for hair removal by laser or electrolysis (CPT codes 17380) may be authorized when the ADSM meets one of the following criteria for planned SRS:

A. The defined area of hair removal is to treat tissue donor site(s) for a planned phalloplasty.

B. The defined area of hair removal is to treat tissue donor site(s) for planned vaginoplasty.

Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People

Center of Excellence for Transgender Health

Department of Family & Community Medicine

University of California, San Francisco

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Editor - Madeline B. Deutsch, MD, MPH

UCSF

center OF excellence FOR TRANSGENDER health

Introduction to the guidelines

The Center of Excellence for Transgender Health (CoE) at the University of California – San Francisco is proud to present these Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People. Transgender people have a gender identity that differs from the sex which they were assigned at birth, and are estimated to represent 0.5% of the U.S. population.[1] Numerous needs assessments have demonstrated that transgender people encounter a range of barriers to accessing primary health care. A 2006 survey of more than 600 transgender people in California found that 30% postponed seeking medical care due to prior disrespect or discrimination, and that 10% were primary care outright.[2] The 2011 National Transgender Discrimination Survey of more than 6000 transgender people in all 50 U.S. states found several noteworthy disparities, including 28% who delayed care due to past discrimination and 19% who were denied care outright. Most alarmingly, 50% of respondents reported having to teach their providers about their own healthcare.[3]

These guidelines aim to address these disparities by equipping primary care providers and health systems with the tools and knowledge to meet the health care needs of their transgender and gender nonconforming patients. These guidelines expand on the original UCSF Primary Care Protocol for Transgender Care, which since its launch in 2011 has served thousands of providers and policymakers across the U.S. and around the world; the page on hormone administration alone received more than 5000 visitors in the month of November, 2015. These Guidelines complement the existing World Professional Association for Transgender Health Standards of Care and the Endocrine Society Guidelines in that they are specifically designed for implementation in every day evidence-based primary care, including settings with limited resources.[4,5]

The overall structure and list of topics for inclusion were developed in consultation with the CoE's Medical Advisory Board (MAB), a diverse group of expert clinicians from a variety of academic and community based settings. Also contributing to the overall design and structure was a review of the range of consultation requests received by the CoE since the 2011 launch of the original Protocol. The guidelines were then written using an authorship – peer review approach. Primary authors from both within and outside the MAB were invited for individual topics, after which a peer review and modified consensus process was used to arrive at the final guidelines presented here. The diverse authorship allows the development of a broadly applicable document, rather than one that solely reflects the practice at a single academic medical center, such as UCSF.

These guidelines would not be possible without the contributions of our Medical Advisory Board and other authors and reviewers, as well as the support of my CoE colleagues JoAnne Keatley, MSW and E. Michael Reyes, MD, MPH, as well as Lissa Moran who assisted immensely with literature reviews, bibliography management, version control, copy editing, formatting, and compiling peer reviewer comments. Ben Zovod also assisted with literature reviews, bibliography management, and compiling peer reviewer comments. Their dedication and hours of hard work has resulted in a final product that is relevant, broadly applicable, evidence based, and scientifically sound. I hope you find these guidelines useful and welcome any feedback or questions, which are

helpful in framing future revisions. Thank you for caring about the health of transgender and gender nonconforming people.

Madeline B. Deutsch, MD, MPH

Editor
Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People

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Table of Contents

1. Grading of evidence

Selected recommendations in these Guidelines have been graded using adaptation of some components of the GRADE scoring system,[1] with the addition of two additional domains to describe details of the research which underlies the recommendation, as well as the population(s) in which such research was conducted. Each graded recommendation will include mention of the population(s) in which research was conducted (transgender (T), non-transgender (NT), or both (T/NT); an indication of, among all sources informing that particular recommendation, the strongest form of underlying evidence (meta-analyses, randomized trials, observational studies, expert opinion). Lastly, an overall grading of the strength of recommendation is made (strong, moderate, weak) which is based on the above critera as well as strength of the consensus recommendation as determined by expert opinion interpretation of available data.

Key recommendations are listed in **bold**. Some recommendations are not graded as they are based on existing recommendations from other professional organizations.

Table 1-1. Grading of Evidence

Grading indicator	Description	Code
Populations in which data exists to inform a particular recommendation		
	At least some data in transgender population	**T**
	No data in transgender population, but data from other populations	**NT**
	No data (expert opinion only)	**X**
Strongest available data to inform a particular recommendation		
	Meta-analysis	**M**
	Randomized controlled studies	**R**
	Observational studies	**O**
	Consensus expert opinion	**C**
Overall strength of recommendation, taking into consideration the above as well as expert interpretation of available data in context		
	Strong	**S**
	Medium	**M**
	Weak	**W**

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2. Terminology and definitions

A detailed discussion of terminology in the context of the great diversity of transgender and gender nonconforming people encountered across cultures and languages is beyond the scope of these Guidelines. Below are definitions for some commonly encountered terms, which will be used throughout these Guidelines as indicated.

Gender / Gender identity: A person's internal sense of self and how they fit into the world, from the perspective of gender.

Sex: Historically has referred to the sex assigned at birth, based on assessment of external genitalia, as well as chromosomes and gonads. In everyday language is often used interchangeably with gender, however there are differences, which become important in the context of transgender people.

Gender expression: The outward manner in which an individual expresses or displays their gender. This may include choices in clothing and hairstyle, or speech and mannerisms. Gender identity and gender expression may differ; for example a woman (transgender or non-transgender) may have an androgynous appearance, or a man (transgender or non-transgender) may have a feminine form of self-expression.

Transgender: A person whose gender identity differs from the sex that was assigned at birth. May be abbreviated to **trans**. A **transgender man** is someone with a male gender identity and a female birth assigned sex; a **transgender woman** is someone with a female gender identity and a male birth assigned sex. A **non-transgender** person may be referred to as **cisgender** (cis=same side in Latin).

Gender nonconforming: A person whose gender identity differs from that which was assigned at birth, but may be more complex, fluid, multifaceted, or otherwise less clearly defined than a transgender person. **Genderqueer** is another term used by some with this range of identities.

Nonbinary: transgender or gender nonconforming person who identifies as neither male nor female.

Trans-masculine/trans-feminine: Terms to describe gender non-conforming or nonbinary persons, based on the directionality of their gender identity. A trans-masculine person has a masculine spectrum gender identity, with the sex of female listed on their original birth certificate. A trans-feminine person has a feminine spectrum gender identity, the sex of the male listed on their original birth certificate. In portions of these Guidelines, in the interest of brevity and clarity, transgender men/women are inclusive of gender non-conforming or nonbinary persons on the respective spectrae.

They/Them/Their: Neutral pronouns used by some who have a nonbinary or nonconforming gender identity.

Transsexual: A more clinical term which had historically been used to describe those transgender people who sought medical intervention (hormones, surgery) for gender affirmation. Term is less

commonly used in present day, however some individuals and communities maintain a strong and affirmative connection to this term.

Cross dresser / drag queen / drag king: These terms generally refer to those who may wear the clothing of a gender that differs from the sex which they were assigned at birth for entertainment, self-expression, or sexual pleasure. Some cross dressers and people who dress in drag may exhibit an overlap with components of a transgender identity. The term **transvestite** is no longer used in the English language and is considered pejorative.

Sexual orientation: Describes sexual attraction only, and is not directly related to gender identity. The sexual orientation of transgender people should be defined by the individual. It is often described based on the lived gender; a transgender woman attracted to other women would be a lesbian, and a transgender man attracted to other men would be a gay man.

For the purposes of clarity and simplicity, the term *transgender* will be used throughout these guidelines to refer to transgender, gender nonconforming, and genderqueer people as a set, unless otherwise indicated. *Non-transgender* people will be referred to as such.

3. Creating a safe and welcoming clinic environment

Primary author: Madeline B. Deutsch, MD, MPH

Introduction

Transgender people may avoid seeking care due to prior discrimination or disrespect in a clinic setting.[1,2] Providing a safe, welcoming and culturally appropriate clinic environment is essential to insure that transgender people not only seek care, but return for follow-up. There are several key components to creating an appropriate setting for transgender care.

Cultural humility is a concept through which individuals recognize that their own experiences or identities may not project onto the experiences or identities of others. Each patient should be approached as an individual with no preconceptions. Individual preferences of terminology, complex or novel gender identities, and differing desires for gender-affirming treatments will be encountered daily in the clinic. Meeting patients "where they are" without judgment or editorializing (including in some cases, even positive remarks about appearance) will enhance the patient-provider relationship and avoids the perception of stigma or pathologization. While some patients may be empowered by serving as a source of information for medical providers,[3] others may be uncomfortable doing so. It should not be routinely expected that patients explicitly "teach" their providers, and providers should limit historical questions to those that are relevant to the current visit or problem.

Staff training: In addition to healthcare providers, front desk staff, nursing staff, lab and x-ray staff, etc. are often on the front lines of patient care. Training on transgender health issues should be provided to all clinic staff and providers, and should be integrated into the standard hiring and on-boarding process for all employees.

Waiting areas should include transgender-themed posters, artwork, pamphlets, magazines, etc. to indicate a commitment to serving the transgender community.

Bathroom policies should either define all bathrooms as gender-neutral, or specifically state that patients may choose either the women's or men's rooms based on their own preference. In this latter case, making at least one gender-neutral bathroom available will provide a safe space for nonbinary people as well as for those in transition and who feel uncomfortable in any gendered space.

Fluency of terminology: Providers should be aware of basic terminology used by the trans community. In addition to the terminology described in these guidelines (which are based on North American English language use), other local or individual terms may exist and also may change over time. Terminology in other countries or languages may vary. Providers should familiarize themselves with local terminology, and approach individuals with cultural humility when determining which specific terms to use.

Gender identity data includes chosen name, chosen pronouns, current gender identity, and sex listed on original birth certificate. Failure to collect and use gender identity data has several important repercussions, including invisibility of gender and sexual minority populations to policy makers and researchers,[4] difficulties in tracking the organ inventories and preventive health needs of transgender people,[5] and reduced patient satisfaction due to a failure to use chosen names and pronouns.[6] Gender identity data have been added to the requirements for the U.S. Department of Health and Human Services Office of the National Coordinator for Health Information Technology Meaningful Use Stage 3 guidelines.[7]

The UCSF Center of Excellence for Transgender Health, Fenway Health in Boston, University of California, Davis, the Mayo Clinic, the U.S. Centers for Disease Control and Prevention (CDC), and many other organizations and experts advocate for the use of the "two-step" method for the collection of gender identity data. This method queries both gender identity as well as the sex listed on one's original birth certificate; transgender people can be identified as those whose gender identity differs from their birth sex. This method has been found to be superior to a single question querying gender/sex with choices of "male," "female," and "transgender," since some transgender people may choose "male" or "female," resulting in effective invisibility of their transgender status.[8]

Unfortunately many EMR vendors have lagged in developing functionality for gender identity data, resulting in a patchwork of practices and locations in which these data are stored within the record.[9] In addition to gender identity and birth sex, transgender people may also have a chosen name which differs from their legal name, and may use pronouns which differ from those associated with the legal sex listed on their identity documents. As such it is also recommended that EMRs contain functionality for the recording of chosen name and pronoun. An ideal EMR will then allow chosen name and pronoun to be displayed for all users in all views. Furthermore, EMRs there should include functionality to remove indicators of transgender status from the view of casual users once legal documents have been changed to reflect gender identity and chosen name, allowing transgender people to maintain privacy. Specific details regarding one's transgender status and transition history, including an inventory of organs and information on hormone use can be stored in the medical and surgical history sections of the chart.[6]

Recommended terminology for the collection of gender identity data is listed below.[10] Clinics can integrate these questions into their intake forms or processes by including a brief description or disclaimer to avoid confusing those patients to whom these questions do not apply.

Gender identity (two-step):

1. **What is your gender identity?**
   - ☐ Male
   - ☐ Female
   - ☐ Transgender man / Transman
   - ☐ Transgender woman / Transwoman
   - ☐ Genderqueer / Gender nonconforming
   - ☐ Additional identity (fill in) _____
   - ☐ Decline to state

2. **What sex were you assigned at birth?**
   - ☐ Male
   - ☐ Female
   - ☐ Decline to state

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4. Transgender patients and the physical examination

Primary author: Linda Wesp, MSN, NP-C

Introduction

Physical examination should be relevant to the anatomy that is present, regardless of gender presentation, and without assumptions as to anatomy or identity. Sensitive history taking is required to understand the myriad and individualized changes and characteristics in the context of hormone administration and surgical intervention. Consideration should be given throughout the visit to potential prior negative experiences within the health care setting, including discrimination as well as physical or emotional abuse.[1]

When conducting a physical exam, providers should use a gender-affirming approach. Gender affirmation is when an individual is affirmed in their gender identity through social interactions.[2] This includes being referred to by the correct name and pronouns during the entire visit. This may also include using general terminology for body parts, or asking patients if they have a preferred term to be used.[3] An examination should only be performed of those body parts that pertain to the reason for a specific visit. For example, examination of the genitalia is not appropriate in the context of an acute visit for an upper respiratory infection.

Secondary sex characteristics may present on a spectrum of development in patients undergoing hormone therapy, to some degree dependent on duration of hormone use and age of initiation. Transgender men may have facial and body hair growth, clitoromegaly, increased muscle mass, masculine fat redistribution, androgenic alopecia, and acne. Transender women may have breast development (often underdeveloped), feminine fat redistribution, reduced muscle mass, thinned or absent body hair, thinned or absent facial hair, softened, thinner skin, and testicles that have decreased in size or completely retract.[4] Patients who have undergone gender-affirming surgeries may have varying physical exam findings depending on the procedures performed, approaches used, and occurance of complications. Providers should maintain an organ inventory to guide screening and management of certain specific complaints.

Special considerations for a vaginal exam in transgender women

(See also guidelines for sexually transmitted infections, and for vaginoplasty)

The anatomy of a neovagina created in a transgender woman differs from a natal vagina in that it is a blind cuff, lacks a cervix or surrounding fornices, and may have a more posterior orientation. As such using an anoscope may be a more anatomically appropriate approach for a visual examination. The anoscope can be inserted, the trocar removed, and the vaginal walls visualized collapsing around the end of the anoscope as it is withdrawn.

Special considerations for conducting a pelvic examination with transgender men

(See also guidelines for *sexually transmitted infections*, and for *cervical cancer screening*)

The pelvic exam may be a traumatic and anxiety inducing procedure for transgender men and other trans-masculine persons. Transgender men are less likely to be up to date on cervical cancer screenings [5] and have a higher rate of inadequate cytologic sampling.[6] It is essential to make clear to the laboratory that the sample being provided is indeed a cervical pap smear (especially if the listed gender marker is "male") to avoid the sample being run incorrectly as an anal pap or discarded. The use of testosterone or presence of amenorrhea should be indicated on the requisition.

Should the individual express distress or concern about the examination, it may be deferred until a later date once a trusting relationship has been developed. A website with further details on pelvic examinations and screening can be found at checkitoutguys.ca.[7] Various techniques can be used to make a pelvic examination (including bimanual and/or speculum exam) less uncomfortable:

- Discuss procedures with the patient beforehand, including the order in which steps will occur. Allow time for the patient to express any concerns prior to beginning the exam.
- Allow the patient to have a support person in the room, listen to music on headphones, or utilize any other strategies they may have to provide distraction during the exam.
- Explain each step in a clear a direct way throughout, such as saying: "I will touch with my hand now," "you will experience some pressure next," "you will hear the clicking noise of the speculum now," and reminding the patient that the exam can be stopped at any time at their request.
- Avoid using medical terms for body parts, unless discussed beforehand that these are preferred terms the patient would like you to use. Some patients may prefer to refer to their vagina as their "front" or "front-hole."
- Offer the use of a mirror to allow the patient to directly observe the exam.
- Administration of an oral benzodiazepine 20-60 minutes prior to the exam may be helpful for those with severe anxiety.
- Administration of vaginal estrogens commonly used in menopausal management for 1-2 weeks prior to the exam may decrease the vaginal atrophy often seen with testosterone therapy.
- Allowing for self-collection of some tests may preclude the need for a speculum exam in certain scenarios, such as a swab for wet prep to analyze abnormal vaginal discharge. Specimen self-collection for HPV testing is currently under investigation.
- In the case of refusal of a speculum exam, consider offering an external and/or bimanual exam as an initial step toward establishing comfort and trust. A positive experience may lead to the patient considering further examinations in the future.

Other special considerations

Binding of the chest to create a masculine appearance may lead to skin breakdown or other complications of the skin. Patients may be hesitant to remove the binder for a physical exam.[3]

Appropriate and sensitive history taking and education about safe binding is recommended for all trans male patients.[8]

Tucking of the testicles and penis may lead to hernias or other complications at the external inguinal ring or skin breakdown at the perineum. Thorough and sensitive history and education is recommended for all trans women.[8]

When appropriate and indicated, findings suggestive of intersex conditions should be further evaluated.[4]

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5. Overview of gender-affirming treatments and procedures

Primary author: Madeline B. Deutsch, MD, MPH

Supporting evidence for providing gender-affirming treatments and procedures

Transgender people may seek any one of a number of gender-affirming interventions, including hormone therapy, surgery, facial hair removal, interventions for the modification of speech and communication, and behavioral adaptations such as genital tucking or packing, or chest binding. All of these procedures have been defined as medically necessary by the World Professional Association for Transgender Health.[1] Lower quality research has found improvements in a range of psychosocial measures after gender-affirming treatments such as hormones or surgery.[2–5] Sevelius' Model of Gender Affirmation describes the ways in which denial of access to gender affirmation is associated with high risk behaviors and increased rates of HIV infection.[6] Conversely, not all transgender people seek all interventions, and some may seek none. In contrast to past practices in which a set pathway involved a requirement of psychological assessment → hormones → genital surgery, the current standard of care is to allow each transgender person to seek only those interventions which they desire to affirm their own gender identity.[7]

Medical interventions: Gender-affirming hormone therapy is the primary medical intervention sought by transgender people. Such treatment allows the acquisition of secondary sex characteristics more aligned with an individual's gender identity.

Surgical interventions: A wide range of gender-affirming surgeries are available to transgender people. These include surgeries specific to gender affirmation, as well as procedures commonly performed in non-transgender populations.

Surgeries specific to transgender populations:

- Feminizing vaginoplasty
- Masculinizing phalloplasty / scrotoplasty
- Metaoidioplasty (clitoral release/enlargement, may include urethral lengthening)
- Masculinizing chest surgery ("top surgery")
- Facial feminization procedures
- Reduction thyrochondroplasty (tracheal cartilege shave)
- Voice surgery

Surgeries not specific to transgender populations:

- Augmentation mammoplasty
- Hysterectomy / oopherectomy
- Orchiectomy
- Vaginectomy

Other interventions: include facial hair removal, voice modification, genital tucking and packing, and chest binding.

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6. Initiating hormone therapy

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Assessing readiness and appropriateness

While historically a "referral letter" from a mental health professional was required prior to initiation of hormone therapy, many large volume and experienced providers of transgender care have for years used an "informed consent" pathway to hormone initiation. WPATH Standards of Care, 7th Version recognizes both of these pathways to the initiation of gender-affirming hormone therapy as valid. Medical providers who feel comfortable making an assessment and diagnosis of gender dysphoria, as well as assessing for capacity to provide informed consent (able to understand risks, benefits, alternatives, unknowns, limitations, risks of no treatment) are able to initiate gender-affirming hormones without a prior assessment or referral from a mental health provider.[1] A study of the practices of 12 such clinics in a diversity of settings found minimal risk of regret and no known cases of malpractice suits.[2] More detail on assessing readiness and appropriateness for various gender-affirming treatments can be found in the topic on mental health.

Qualifications of the prescribing provider

Prescribing gender-affirming hormones is well within the scope of a range of medical providers, including primary care physicians, obstetricians-gynecologists, and endocrinologists, advanced practice nurses, and physician assistants.[1] Depending on the practice setting and juris diction, other providers with prescriptive rights (naturopathic providers, nurse midwives) may also be appropriate to prescribe and manage this care. Most medications used in gender-affirming hormone therapy are commonly used substances with which most prescribers are already familiar due to their use in the management of menopause, contraception, hirsutism, male pattern baldness, prostatism, or abnormal uterine bleeding.

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7. Overview of feminizing hormone therapy

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Introduction

The goal of feminizing hormone therapy is the development of female secondary sex characteristics, and suppression/minimization of male secondary sex characteristics. General effects include breast development (usually to Tanner stage 2 or 3), a redistribution of facial and body subcutaneous fat, reduction of muscle mass, reduction of body hair (and to a lesser extent, facial hair), change in sweat and odor patterns, and arrest and possible reversal of scalp hair loss. Sexual and gonadal effects include reduction in erectile function, changes in libido, reduced or absent sperm count and ejaculatory fluid, and reduced testicular size. Feminizing hormone therapy also brings about changes in emotional and social functioning. The general approach of therapy is to combine an estrogen with an androgen blocker, and in some cases a progestagen.

Estrogens

The primary class of estrogen used for feminizing therapy is 17-beta estradiol, which is a "bioidentical" hormone in that it is chemically identical to that from a human ovary. The general approach is similar to estrogen replacement in agonadal (i.e Turner syndrome) or menopausal states, with some dosing modifications. 17-beta estradiol (or simply estradiol) is most commonly delivered to transgender women via a transdermal patch, oral or sublingual tablet, or injection of a conjugated ester (estradiol valerate or estradiol cypionate). No outcome studies have been conducted on injectable estradiol valerate or cypionate, presumably due to their uncommon modern use outside of transgender care settings; due to this limited use manufacturers have little incentive to produce this medicine, and shortages have been reported. Other delivery routes for estradiol such as transdermal gel or spray are formulated for the treatment of menopausal vasomotor symptoms and while convenient and effective in some transgender women, in others these routes may not be able to achieve blood levels in the physiologic female range. Compounded topical creams and gels also exist from specialty pharmacies; if these are to be used it is recommended that the prescriber consult with the compounding pharmacist to understand the specific details and dosing of the individual preparation. Compounded estradiol valerate or cypionate for injection also exists, and may be an alternative in times of shortage or more cost effective for those who must pay cash for their prescriptions.

Conjugated equine estrogens (Premarin®) have been used in the past but are not recommended for a number of reasons, including inability to accurately measure blood levels and some suggestion of increased thrombogenicity and cardiovascular risk.[1,2] Equine estrogens are obtained from the urine of pregnant, catheterized horses; no evidence exists to suggest that these estrogens are superior to bioidentical human estradiol. Ethical concerns have been raised regarding the methods of production of equine estrogens. (http://www.aspca.org/fight-animal-cruelty/equine-cruelty/premarin.aspx)

Ethinyl estradiol is a synthetic estrogen used in contraceptive preparations and is associated with an increased thrombotic risk.[3,4] In the context of contraception, ethinyl estradiol has more consistent and reliable cycle control and as such is better tolerated, balancing out the potentially increased risk of VTE.[5] **In the setting of gender affirmation there is no need for cycle or bleeding regulation, and thus the use of ethinyl estradiol and its inherent risks are not warranted (Grading: T O S).**

Side effects of estrogens may include migraines, mood swings, hot flashes, and weight gain.

Antiandrogens – common approaches

Suppression of testosterone production and blocking of its effects contributes to the suppression / minimization of male secondary sexual characteristics. Unfortunately many of these characteristics are permanent upon completion of natal puberty and are irreversible. Androgen blockers allow the use of lower estradiol dosing, in contrast to the supraphysiologic estrogen levels (and associated risks) previously used to affect pituitary gonadotropin suppression.[6]

Spironolactone is the most commonly used androgen blocker in the U.S. Spironolactone is a potassium sparing diuretic, which in higher doses also has direct anti-androgen receptor activity as well as a suppressive effect on testosterone synthesis.[6] Doses of 200mg daily in non-transgender women being treated for hair loss have been described as safe, though doses of up to 400mg/day have been reported without negative effect.[7] Hyperkalemia is the most serious risk but is very uncommon when precaution is taken to avoid use in individuals with renal insufficiency, and use with caution and frequent monitoring in those on ACE inhibitor or ARB type medications. Due to its diuretic effect, patients may experience self-limited polyuria, polydipsia, or orthostasis.

5-alpha reductase inhibitors include finasteride and dutasteride. Finasteride blocks 5-alpha reductase type 2 and 3 mediated conversion of testosterone to the potent androgen dihydrotestosterone.[8] Finasteride 1mg daily is FDA-approved for male pattern baldness, while the 5mg dose is approved for management of prostatic hypertrophy.[9] Dutasteride 0.5mg more effectively blocks the type 1 isozyme, which is present in the pilosebaceous unit and therefore may have more dramatic feminizing effects. Since these medications block neither the production nor action of testosterone, their antiandrogen effect is less than that encountered with full blockade. 5-alpha reductase inhibitors may be a good choice for those unable to tolerate, or with contraindications to the use of spironolactone. 5-alpha reductase inhibitors may also be an option for use as a single agent in patients seeking partial feminization, or for those who continue to exhibit virilized features or hair loss after complete androgen blockade or orchiectomy.

Antiandrogens – other approaches

Antiandrogens can also be used alone to bring reduced masculinization and minimal breast development, or in those patients who wish to first explore reduced testosterone levels alone, or in those with contraindications to estrogen therapy. In the absence of estrogen replacement, some patients may have unpleasant symptoms of hot flashes and low mood or energy. Long term full androgen blockade without hormone replacement in men who have undergone treatment for prostate cancer results in bone loss, and this effect would also be expected to occur in transgender individuals.[10] **In addition to titrating dosing to both clinical effect and testosterone levels as**

guided by patient goals, monitoring hormone levels to insure suppressed gonadotropins (leutinizing hormone [LH] and follicle stimulating hormone [FSH]) levels may serve as a surrogate marker to indicate adequate sex hormone levels for maintaining bone density in such patients (Grading: T O W).[11]

In many countries, cyproterone acetate, a synthetic progestagen with strong anti-androgen activity is commonly used. Cyproterone has been associated with uncommon episodes of fulminant hepatitis.[12] Bicalutamide, a direct anti-androgen used for the treatment of prostate cancer, also has a small but not fully quantified risk of liver function abnormalities (including several cases of fulminant hepatitis); while such risks are acceptable when considering the benefits of bicalutamide in the management of prostate cancer, such risks are less justified in the context of gender-affirming treatment.[13] No evidence at present exists to inform such an analysis.

In some patients, complete androgen blockade may be difficult or even impossible using standard regimens. In cases of persistent elevations of testosterone in the setting of maximal antiandrogen dosing with good medication adherance, autonomous endogenous production (i.e. tumor) as well as undisclosed exogenous testosterone (i.e. to maintain erectile function) should be considered. An evaluation for testicular neoplasms should be performed with a scrotal exam as well as testing for elevated serum human chorianogonadotropin (hCG), lactate dehydrogenase (LDH), alpha-fetoprotein (AFP) levels, and possibly scrotal imaging.[14] Once these causes have been ruled out, additional options can include gonadotropin releasing hormone analogues (GnRH) or orchiectomy. GnRH analogs are used routinely in the care of peripubertal transgender youth who require pubertal delay,[15] and have been described in the care of transgender adults as well.[16] Drawbacks to the use of GnRH analogs is primarily related to cost and difficulties in obtaining insurance coverage, as well as the need for either repeated injections, multiple daily nasal sprays, or surgical implantation. Orchiectomy may represent an ideal option in transgender women who do not desire to retain their gonads; this brief, inexpensive, outpatient procedure requires only several days for recovery and does not preclude future vaginoplasty.

Progestagens: There have been no well-designed studies of the role of progestagens in feminizing hormone regimens. Many transgender women and providers alike report an anecdotal improved breast and/or areolar development, mood, or libido with the use of progestagens.[17,18] There is no evidence to suggest that using progestagens in the setting of transgender care are harmful. In reality some patients may respond favorably to progestagens while others may find negative effects on mood. While progestagens have some anti-androgen effect through central blockade of gonadotropins, there is also a theoretical risk of a direct androgenizing effect of progestagens. This class includes micronized bioidentical progesterone (Prometrium) as well as a number of synthetic progestins. The most commonly used synthetic progestin in the context of transgender care is the oral medroxyprogesterone acetate (Provera).

While concerns exist from the Women's Health Initiative (WHI) regarding risks of cardiovascular disease and breast cancer in the setting of medroxyprogesterone use, these concerns likely do not apply in the context of transgender care for several reasons. First, the transgender women may be at lower risk of breast cancer than non-transgender women. Second, this arm of the WHI involved the use of conjugated equine estrogens in combination with medroxyprogesterone in a sample of menopausal women, some of whom were as long as 10 years post-menopausal at the time of hormone initiation. Third, while statistically significant, the clinical significance of the findings in the

WHI was subtle at best. The study aimed to evaluate the role of menopausal hormone therapy in the prevention of chronic disease. The actual findings in the conjugated equine estrogen plus medroxyprogesterone group were an excess absolute risk per 10 000 person-years of 7 more cardiac events events, 8 more strokes, 8 more pulmonary emboli, and 8 more invasive breast cancers, with no change in overall mortality.[19] As such this arm of the WHI was stopped early, and it was concluded that combined menopausal hormone therapy is not indicated for prevention of chronic disease.

In the setting of gender-affirming care, there are numerous differences to the findings of the WHI: populations tend to be younger, equine estrogens are not used, and the emphasis is on gender-affirming interventions which have numerous benefits on mental health and quality of life, rather than prevention. **Considering these differences in demographics and goals of therapy, extremely modest increase in overall risk, and lack of difference in mortality, as well as more recent reassuring data with other forms of estrogen, the risks of using progestagens in transgender women are likely minimal or even absent (Grading: NT O M).** Injected depo-medroxyprogesterone acetate (Depo-Provera®) is less commonly used in transgender women. Other synthetic progestins may be used as necessitated by formulary limitations; some evidence suggests that norpregnane derived progestins (norethindrone, norgestrel) may have an increased risk of venous thromboembolism.[20]

Table 7-1. Hormone preparations and dosing (Grading: T O M)

Hormone	Initial–low[b]	Initial	Maximum[c]	Comments
Estrogen				
Estradiol oral/sublingual	1mg/day	2-4mg/day	8mg/day	if > 2mg recommend divided bid dosing
Estradiol transdermal	50mcg	100mcg	100-400 mcg	Max single patch dose available is 100mcg. Frequency of change is brand/product dependent. More than 2 patches at a time may be cumbersome for patients
Estradiol valerate IM[a]	<20mg IM q 2 wk	20mg IM q 2 wk	40mg IM q 2wk	May divide dose into weekly injections for cyclical symptoms
Estradiol cypionate IM	<2mg q 2wk	2mg IM q 2 wk	5mg IM q 2 wk	May divide dose into weekly injections for cyclical symptoms
Progestagen				
Medroxyprogesterone acetate (Provera)	2.5mg qhs		5-10mg qhs	
Micronized progesterone			100-200mg qhs	
Androgen blocker				

Hormone	Initial–low[b]	Initial	Maximum[c]	Comments
Spironolactone	25mg qd	50mg bid	200mg bid	
Finasteride	1mg qd		5mg qd	
Dutasteride			0.5mg qd	

a. Available as standard U.S. Pharmacopia (USP) as well as compounded products
b. Initial-low dosing for those who desire (or require due to medical history) a low dose or slow upward titration.
c. Maximal effect does not necessarily require maximal dosing; as such maximal doses do not necessarily represent a target or ideal dose. Dose increases should be based on patient response and monitored hormone levels.

Many patients are eager to begin maximal feminizing hormone therapy and are opposed to the idea of a slow upward titration. Weak evidence suggests that initiation of estrogen therapy at lower doses and titrating up over time may result in enhanced breast development in transgender women. **The estrogen receptor agonist activity of spironolactone may play a role in reduced breast development due to premature breast bud fusion. As such an escalating regimen beginning with low dose estrogen only, and titrating up over several months, and then adding spironolactone may be an alternative approach,[17] consistent with management practices in children with delayed pubertal onset (Grading: T O W).** Upward titration of spironolactone can also help minimize side effects such as orthostasis or polyuria. It is recommended that providers discuss these considerations with patients before initiation of hormones in order to make an informed decision.

Table 7-2. Laboratory monitoring for feminizing hormone therapy

Test	Comments	Baseline	3 months*	6 months*	12 months*	Yearly	PRN
BUN/Cr/K+	Only if spiro used	X	X	X	X	X	X
Lipids	No evidence to support monitoring at any time; use clinician discretion	Based on USPSTF guidelines					X
A1c or glucose	No evidence to support monitoring at any time; use clinician discretion	Based on USPSTF guidelines					
Estradiol			X	X			X
Total Testosterone			X	X	X		X

Test	Comments	Baseline	3 months*	6 months*	12 months*	Yearly	PRN
Sex Hormone Binding Globulin (SHBG)**			X	X	X		X
Albumin**			X	X	X		X
Prolactin	Only if symptoms of prolactinoma						X

* In first year of therapy only

** Used to calculate bioavailable testosterone; monitoring bioavailable testosterone is optional and may be helpful in complex cases (see text) (http://www.issam.ch/freetesto.htm)

Overview of titration and monitoring

The interpretation of hormone levels for transgender individuals is not yet evidence based; physiologic hormone levels in non-transgender people are used as reference ranges. However, estrogen levels in non-transgender women may not be associated with specific secondary sex characteristics (i.e. higher estrogen levels in non-transgender women are not necessarily associated with larger breasts), and specific phenotypical end points are likely multifactorial and particularly dependent on genetics and the age at which gender-affirming hormone therapy is begun. Titration upwards of dose should be driven by patient goals, in the context of clinical response, hormone level monitoring, and safety monitoring (e.g. presence of risk factors such as smoking, renal function and K+ in patients using spironolactone). A general approach for titration would include increasing of both estrogen and antiandrogen dosing until the estrogen dose is in the female physiologic range. Once this has been achieved, titration efforts can focus on increasing androgen blockade. There can be several approaches to titration of androgens. One approach is to continue increasing estrogen until it reaches the upper limit of the female physiologic range. The drawback for this approach is that patients may begin to experience estrogenic side effects as described below. Another approach is to maintain current physiologic estrogen dosing and titrate upward on antiandrogens and/or addition of a progestagen.

Some providers choose to omit the use of hormone level testing and only monitor for clinical progress or changes. The risk of this approach is that if hormone levels (particularly testosterone) have not reached the target range, but progress is judged as appropriate based on clinical exam, a suboptimal degree of feminization is possible, and the presence of supraphysiologic levels would also be obscured. Conversely, Endocrine Society guidelines recommend monitoring of hormone levels every 3 months.[21] In practice this is not realistic and not likely to add value once a stable dosing has been achieved. A prospective study of transgender women taking 4mg/day divided dose oral estradiol or 100mcg transdermal estradiol, plus 100-200mg/day divided dose spironolactone found that all women achieved physiologic estradiol levels, though only 2/3 of the women achieved female range testosterone levels.[22] Some gender-nonconforming/nonbinary patients may prefer to maintain estradiol or testosterone levels in an intermediate range. Regardless of initial dosing scheme chosen, dosing may be titrated upwards over 3-6 months. Check estradiol and

testosterone levels at 3 and 6 months and titrate dose accordingly. For those patients using spironolactone, check renal function and K+ at 3 months and 6 months, then q 6-12 months. While laboratory monitoring of hormone levels may seem complex, it is of similar difficulty to the monitoring of other similarly complex lab-monitored conditions managed by primary care providers, such as thyroid disorders, anticoagulation, or diabetes.

Once hormone levels have reached the target range for a specific patient, it is reasonable to monitor levels yearly, or only as needed as described below. As with other situations involving maintenance of hormone therapy (menopause, contraception), annual visits are sufficient for transgender women on a stable hormone regimen. Other reasons for measuring hormone levels in the maintenance phase include significant metabolic shifts such as the onset of diabetes or a thyroid disorder, substantial weight changes, subjective or objective evidence of virilization, or new symptoms potentially precipitated or exacerbated by hormone imbalances such as hot flashes or migraines. Such patients may also require more frequent office visits to manage coexisting conditions. Increased frequency of office visits may also be useful for patients with complex psychosocial situations to allow for the provision of ancillary or wraparound services.

Current Endocrine Society recommendations include the measurement of only total testosterone and estradiol. This is consistent with Endocrine Society recommendations that only total testosterone be monitored in non-transgender men being managed for testosterone deficiency, except in cases of borderline testosterone levels. However, since testosterone is of particular concern is insuring maximal feminization, the calculation of bioavailable testosterone in transgender women may still be of value. Specifically, exogenous estrogens (especially oral) may be associated with elevated levels of sex hormone binding globulin (SHBG); such elevations can vary from person to person and across regimens. As such in cases of patient concern or persistent virilized features in the presence of a female-range total testosterone, calculation of the bioavailable testosterone may help fine tune hormone regimens for optimal effect.

Interpretation of laboratory results requires special attention in the context of transgender care. Numerous sources publish target ranges for serum estradiol, total estrogens, free, total and bioidentical testosterone, and sex hormone binding globulin. However, these specific ranges may vary between different laboratories and techniques. Furthermore, the interpretation of reference ranges supplied with lab result reports may not be applicable if the patient is registered under a gender that differs from their intended hormonal sex. For example, a transgender woman who is still registered as male will result in lab reference ranges reported for a male; clearly these ranges are not applicable for a transgender woman using feminizing hormone therapy. Hormone levels for genderqueer or gender nonconforming/nonbinary patients may intentionally lie in the mid-range between male and female norms. Providers are encouraged to consult with their local lab(s) to obtain hormone level reference ranges for both "male" and "female" norms, and then apply the correct range when interpreting results based on the current hormonal sex, rather than the sex of registration.

Monitoring estradiol levels

Historically estrogen levels have been monitored using the total serum estradiol. The 2009 Endocrine Society Guidelines recommend monitoring serum estradiol and maintaining levels at the

mid-cycle range for non-transgender women.[21] This recommendation is based on expert opinion only and may be overly conservative, and hormone levels are often not easy to tightly control.[23] Providers are encouraged to review the specific estradiol reference ranges for their local lab estradiol assays, as these can vary. There is no evidence that higher estradiol levels in patients with adequate androgen suppression results in additional feminization or breast development. Maintaining estrogen levels in the physiologic range for menstruating non-transgender women minimizes risks and side effects, and makes sense clinically. Note that the use of conjugated estrogens (Premarin®) or ethinyl estradiol (found in most combined oral contraceptives) are not accurately measured by estradiol assays and will typically result in low measured levels.

In patients who have been using self-administered conjugated estrogens, or ethinyl estradiol, it is reasonable to check a total estrogens level, which may provide a more accurate estimate in these cases. This assay also measures minor estrogens such as estriol and estrone. There is some evidence that the use of oral estradiol results in higher serum levels of estrone due to first pass hepatic metabolism, as compared to parenteral forms.[24,25] This may explain dose independent reasons why some patients "feel different" on different forms of estrogen.

Monitoring testosterone levels

Testosterone levels can be difficult to measure in non-transgender men due to rapid fluctuations in levels, relating to pulsatile release of gonadotropins, with higher levels in the morning hours. Free testosterone represents the portion of testosterone unbound to serum proteins and depends on levels of sex hormone binding globulin (SHBG). While free testosterone can be measured, assays are unreliable.[26] Consensus is lacking on the role of free vs. total testosterone levels; total testosterone levels are reliable and readily available, however they do not describe the actual bioavailable testosterone level. Bioavailable testosterone is free testosterone plus testosterone weakly bound to albumin.[27] SHBG is elevated in the presence of estrogen, and in particular with exogenous estrogen supplementation, more so with oral estrogen than with parenteral routes due to first pass hepatic activity.[28] **For transgender care, The Endocrine Society recommends monitoring of the total testosterone level, with a target range of <55ng/dl** .[21] Calculation of the bioavailable testosterone may help guide dosing, and can be calculated from the total testosterone, albumin, and SHBG levels (http://www.issam.ch/freetesto.htm).[29] A general reference range for bioavailable testosterone is > 72ng/dl (2.5nmol/L).[30–32]

Monitoring gonadotropin levels

When indicated, measuring of gonadotropins (leutenizing hormone: LH and follicle stimulating hormone: FSH) can be done using the local lab ranges for eugonadal state as a reference.

Monitoring hormone levels in patients using injected estrogen

Pharmacokinetic studies of injected estrogen have been limited. Two earlier studies only examined single-dose pharmacokinetics and are therefore unable to be applied to steady-state dosing.[33] Studies of estradiol levels in the context of a monthly combined injectible contraceptive of 5mg estradiol cypionate and 25mg medroxyprogesterone acetate found peak levels 2-4 days after injection, maximum estradiol levels of approximately 250 pg/ml, and trough levels of approximately

50pg/ml.[34,35] These findings suggest that injected estradiol in the middle of the dosing ranges recommended here will result in physiologic estradiol levels, and that use of more frequent dosing will reduce peak-trough effect. When measuring hormone levels in patients using injected forms of estradiol, a mid-cycle level is often sufficient, however if the patient is experiencing cyclic symptoms such as migraines or mood swings, peak (1-2 days post injection) and trough levels of both estradiol and testosterone may reveal wide fluctuations in hormone levels over the dosing cycle; in these cases, consider changing to an oral or transdermal preparation, or reducing the injection interval (with concomitant reduction in dose, to maintain the same total dose administered over time). A single study suggests similar pharmacokinetics when estradiol is injected subcutaneously, rather than intramuscular.[34]

Interpreting sex-specific, non-hormone labs

Alkaline phosphatase, hemoglobin and hematocrit (H&H), and creatinine may vary depending on the patient's current sex hormone configuration. Several factors contribute to these differences, bone mass, muscle mass, number of myocytes, presence or lack of menstruation, and the erythropoetic effect of testosterone. While transgender women do not menstruate, those with female-range hormone levels will lack the erythropoetic effects of male-range testosterone, and it may be reasonable to use the female-range lower limit of normal when interpreting H&H. Conversely, the lack of menstruation, and potential for pulsatile undetected androgen activity in those with retained gonads make it reasonable to use the male-range upper limit of normal for H&H. Using the male-range upper limit of normal for alkaline phosphatase and creatinine may also be appropriate for transgender women due to retained bone and muscle mass or myocyte counts, respectively. This is of particular importance in transgender women using spironolactone who are registered as female, and may have a lab result flag showing an abnormal elevated creatinine. In these cases the provider should reference the male normal ranges for their lab.[19]

Table 7-3. Lower and upper limits of normal to use when interpreting selected lab tests in transgender women using feminizing hormone therapy

Lab measure	Lower Limit of normal	Upper Limit of normal
Creatinine	Not defined	Male value
Hemoglobin/Hematocrit	Female value	Male value
Alkaline Phosphatase	Not defined	Male value

Individualized dosing based on patient centered goals

Some patients may desire limited hormone effects or a mix of masculine and feminine sex characteristics. Examples include retention of erectile function with otherwise maximum feminization, or minimal feminizing effects with the exception of body or facial hair elimination or breast growth. While manipulation of dosing regimens and choice of medication can allow patients

to achieve this goal, it is important to have a clear discussion with patients regarding expectations and unknowns. Specifically, it is not possible to select in advance an exact hormone regimen that will predictably allow patients to arrive at a specified configuration of sex characteristics. Furthermore, individual genetic and physiologic variation can result in wide variations in both blood levels and response to therapy between different individuals using the same route and dose. The best approach in these cases is to start with low doses and advance slowly, titrating to effect. At the same time, response to hormone therapy is also individualized and measures such as breast growth are variable in both degree and time course. Likely predictive factors of speed and degree of feminization include genetics, age at initiation of therapy, and body habitus.[17] Patients should be counseled on typical timeframes for changes and advised to avoid making comparisons to the experiences of others. Anecdotal sources suggest that maximal feminization may occur within 2-5 years.[36]

Specific considerations and conditions

Tobacco use:

Tobacco use in combination with estrogen therapy is associated with an increased risk of venous thromboembolism. All transgender women who smoke should be counselled on tobacco risks and cessation options at every visit. Many transgender women may be unable or unwilling to quit smoking; this should not represent an absolute contraindication to estrogen therapy. After an in depth and careful informed consent discussion, it is reasonable to prescribe estrogen using a harm reduction approach, with a preferred route of transdermal estrogen. **Aspirin 81mg/day can be considered as an additional preventive measure in smokers, though no evidence exists to allow and informed assessment of the risk/benefit ratio between VTE prevention and gastrointestinal hemorrhage (Grading: X C W). Transdermal estrogens are preferred to minimize risk (Grading: T O S).**

Loss of erectile function:

Sildenafil (Viagra) and tadalafil (Cialis) can be used for preservation of erectile function at any stage or with any feminizing hormone regimen, in consideration of the typical contraindications and precautions when using this class of medication. Individual results may vary. It is reasonable check both total and bioavailable testosterone levels, and consider reduction of androgen blockade to allow an increase in testosterone, depending on patient goals.

Low libido:

A study of sexual desire in transgender women found that 83% never or rarely experience spontaneous sexual desire, 76% never or rarely experience responsive sexual desire, and 22% meet the criteria for Hypoactive Sexual Desire Disorder (HSDD) by experiencing both of these in a way which results in personal or relational distress. This study also found decreases in sexual desire after genital surgery.[37] Another study found a rate of HSDD in transgender women of 34%, compared to 23% in non-transgender women. This study found no correlation between sexual desire and testosterone levels in the transgender women, though a significant correlation was found between hormones and desire in non-transgender women.[38] An unpublished study found positive correlations between libido and testosterone levels in transgender women treated with

testosterone, but no effect when treated with dihidroepiandrosterone sulfate (DHEA-S).[39] As such it remains unclear if HSDD relates to androgen blockade or post-gonadectomy hormonal changes, or due to anatomical, functional and psychological changes associated with hormone therapy or genital surgery.

Post-gonadectomy:

Since estrogen dosing should be based on physiologic female levels, no reduction in estrogen dosing is required after gonadectomy. Some patients may choose to use a lower dose, which is appropriate as long as dosing is adequate to maintain bone density. **Adequacy of dosing in those on low estrogen replacement post gonadectomy may be assessed by following LH and FSH levels (Grading: T O W).[11]**

Older transgender women:

Older transgender women initiating therapy may have less rapid and a lesser degree of changes. Due to higher levels of co-occurring conditions in older individuals, there may also be higher risk of adverse effects. Nevertheless a large number of women have started hormones at advanced ages and safety and satisfaction have been reported as acceptable.[40] There is no evidence to support continuation or cessation of hormones for older transgender women.

Since the mean age of menopause in the U.S. is 49,[41] it is reasonable in transgender women who have undergone gonadectomy to consider stopping hormone therapy around age 50. Expected effects of this may be similar to non-transgender women experiencing menopause. Transgender women who retain their gonads but withdraw hormone therapy may experience return of virilization. A discussion of the pros and cons of this approach, with individualized and shared decision making is recommended.

Pituitary adenoma (prolactinoma) and galactorrhea:

Prolactin elevations and growth of pituitary prolactinomas are theoretical risks associated with estrogen therapy; several cases have been reported.[42] However, with the administration of physiologic doses of estrogen, there is no clear basis for an increased risk of prolactinomas in comparison to the population background rate in non-transgender women. Furthermore, **Endocrine Society guidelines for the management of incidental prolactinomas are expectant management only, in the absence of suggestive visual or other symptoms (significant galactorrhea, headaches).[43] Routine screening with serum prolactin levels in asymptomatic transgender women would not have an impact on management, and could result in costs or harm if further workup if pursued. As such it is recommended that prolactin be checked only in cases of visual disturbances, excessive galactorrhea, and be considered in cases of new onset headaches.** It is noted that some transgender women experience a minimal amount of galactorrhea early in their hormone therapy course. The presence of non-bloody minimal galactorrhea from more than one duct and/or bilateral is almost certainly physiologic and would not warrant further evaluation.

Venous thromboembolism:

Data from studies of menopausal women suggest no increased risk of venous thromboembolism with the use of transdermal estradiol.[44] There are some data suggestive of increased

thrombogenicity and cardiovascular risk when conjugated equine estrogens (Premarin) are used.[1,2] Data on the risk associated with oral 17-beta estradiol are mixed, with some suggesting no increased risk and others suggesting a 2.5 - 4 fold increased risk.[20,44] Even in the case of a 2.5 fold increase, the background rate for VTE in the general population is very low (1 in 1000 to 1 in 10,000), so the absolute risk increase is minimal.[3] There is weak evidence that sublingual administration of oral estradiol tablets might reduce thromboembolic risk due to a bypass of hepatic first pass, with one study showing 13 fold increase in peak estradiol blood levels but similar 24 hour area-under-the-curve.[45] A study of sublingual estradiol for the management of post-partum depression found that it was well tolerated, and the increased pulsatile nature of this route may more closely mimics natural ovarian estrogen secretion.[46] Sublingual administration requires insuring that the estradiol tablets are micronized; while most commonly available estradiol tablets are micronized, specifying as such on the written prescription (or consultating with the dispensing pharmacist) is recommended.

There is also some limited evidence to suggest that the risk of VTE in menopausal women may be driven more by the choice of progestagen, and that pregnane derived progestagens such as medroxyprogesterone in combination with oral estradiol does not confer an increased risk, while norpregnane derived progestagens such as norethindrone may increase risk by 80% when used with oral estradiol.[20] Prior studies reporting a 20 to 40 fold increased risk of VTE in transgender women involved the use of high doses (100-200mcg/day) of thrombogenic ethinyl estradiol in a mix of smokers and non-smokers.[47,48] A retrospective cohort of Dutch transgender women found no increased risk in VTE once ethinyl estradiol was replaced by bioidentical estradiol as the standard regimen.[49]

Insufficient evidence exists to definitively guide estrogen therapy in transgender women with risk factors or with a personal history of prior VTE, either on or off estrogen. A report of 11 transgender women with a history of activated protein C resistance (the mechanism of action implicated in the hypercoaguable state associated with the Factor-V Lieden mutation) using transdermal estradiol without anticoagulation found no clotting events after a mean of 64 months of therapy.[50]

Figures 1-5 describe the approach to various scenarios of VTE history or risk factors and estrogen use. The decision to initiate episodic (i.e. before long airplane flights) or long term anticoagulation or antiplatelet therapy should be considered in the context of risks associated with major gastrointestinal or intracranial hemorrhage. ***Routine* VTE prophylaxis with aspirin in unselected transgender populations is not recommended.** Routine screening for prothrombotic mutations is not recommended in the absence of risk factors.[50] Regardless of the circumstances, estrogen therapy should not be administered in patients with significant risk factors for or history of VTE who continue to smoke tobacco.

Figure 7-1. Approach to management of estrogen in patients with a personal history of VTE

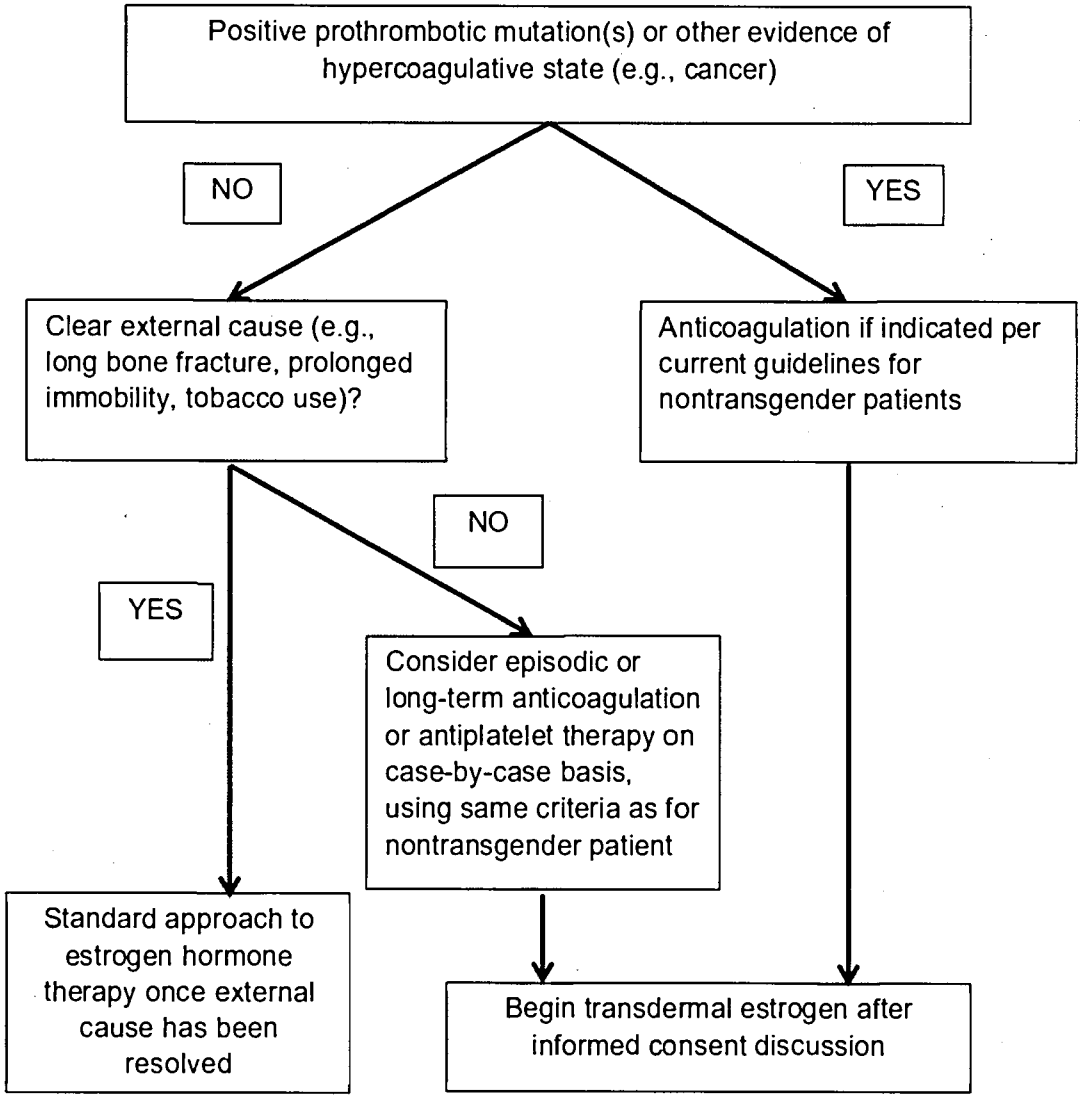


Figure 7-2. Approach to management of estrogen in patients with a family history of VTE but no personal history of VTE

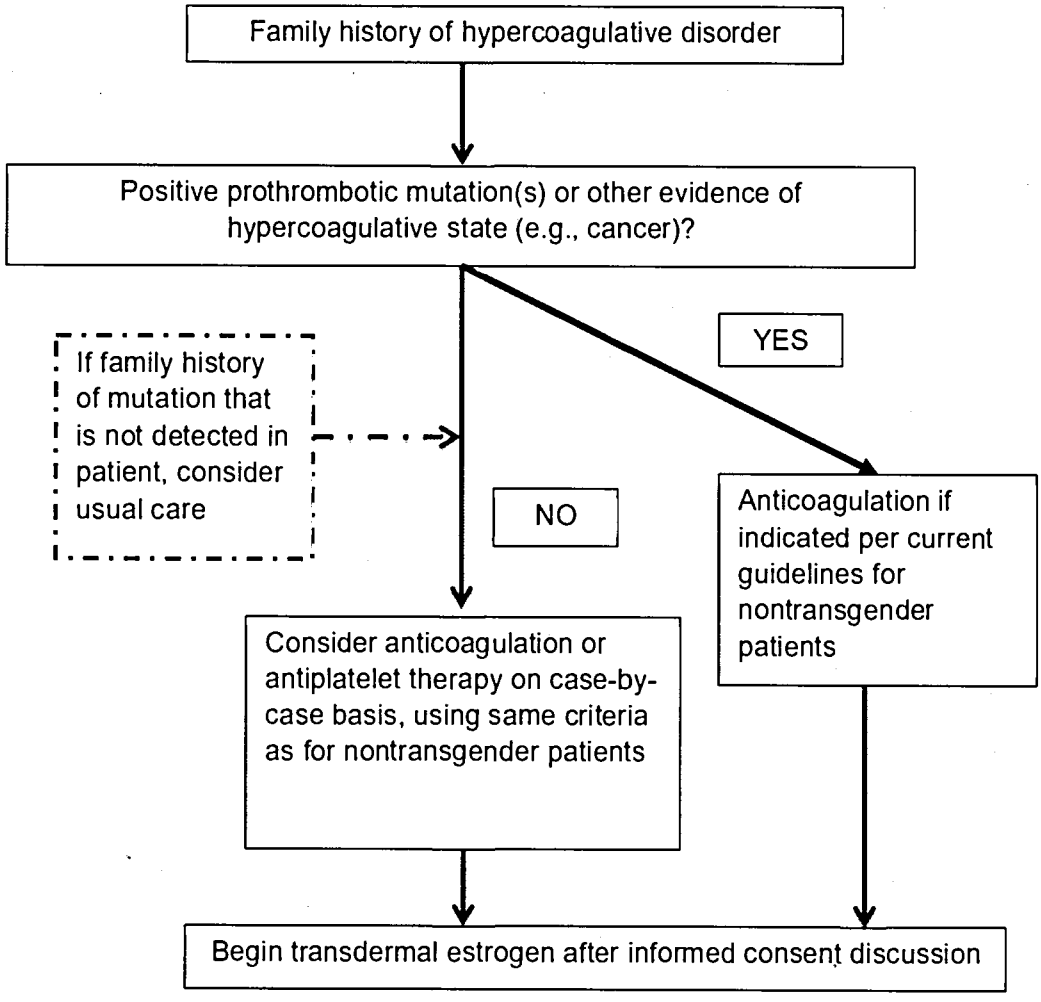


Figure 7-3. Approach to patient using oral or injected estrogen at time of first diagnosis of VTE

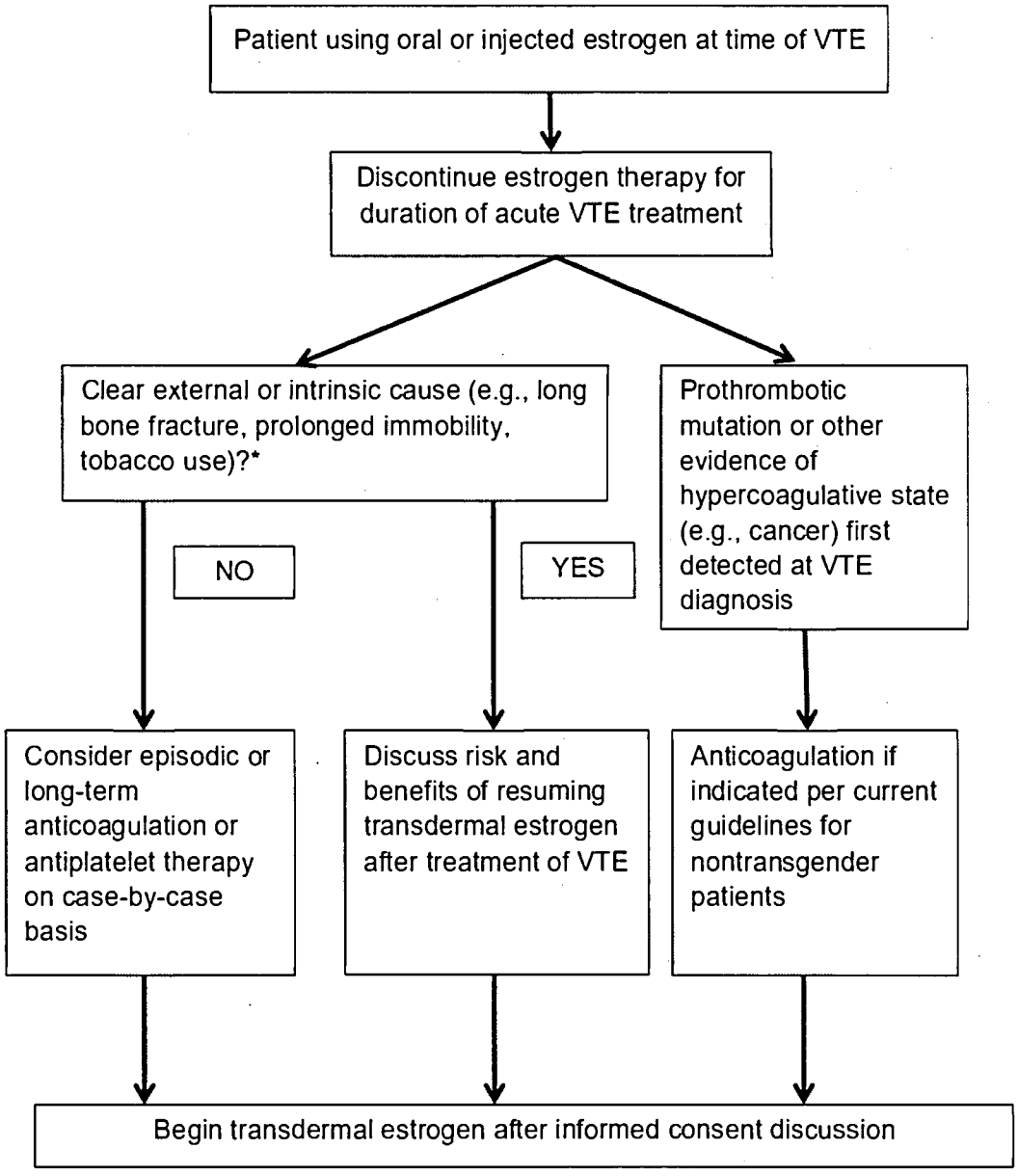


Figure 7-4. Approach to patient using transdermal estradiol at time of first diagnosis of VTE

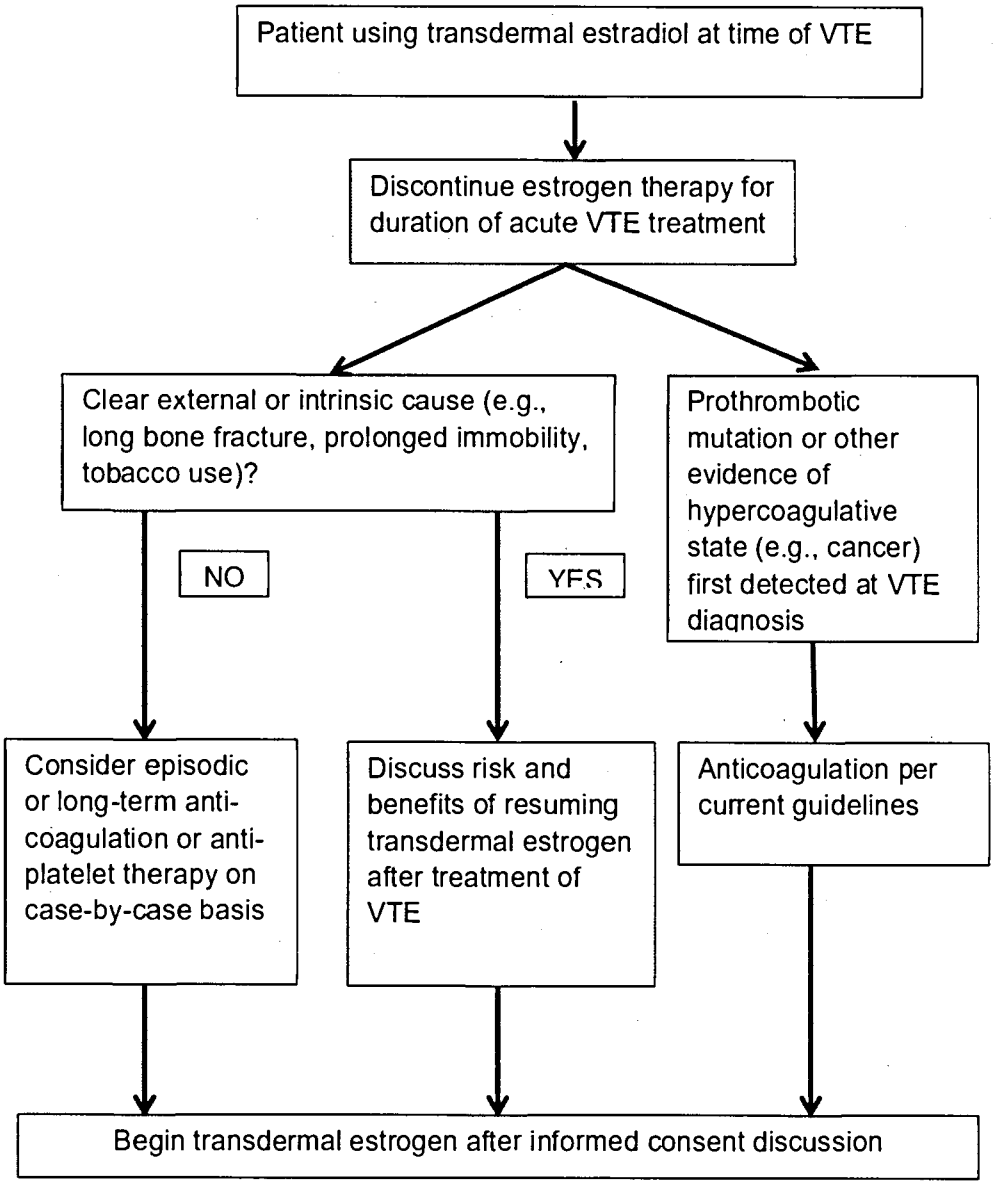
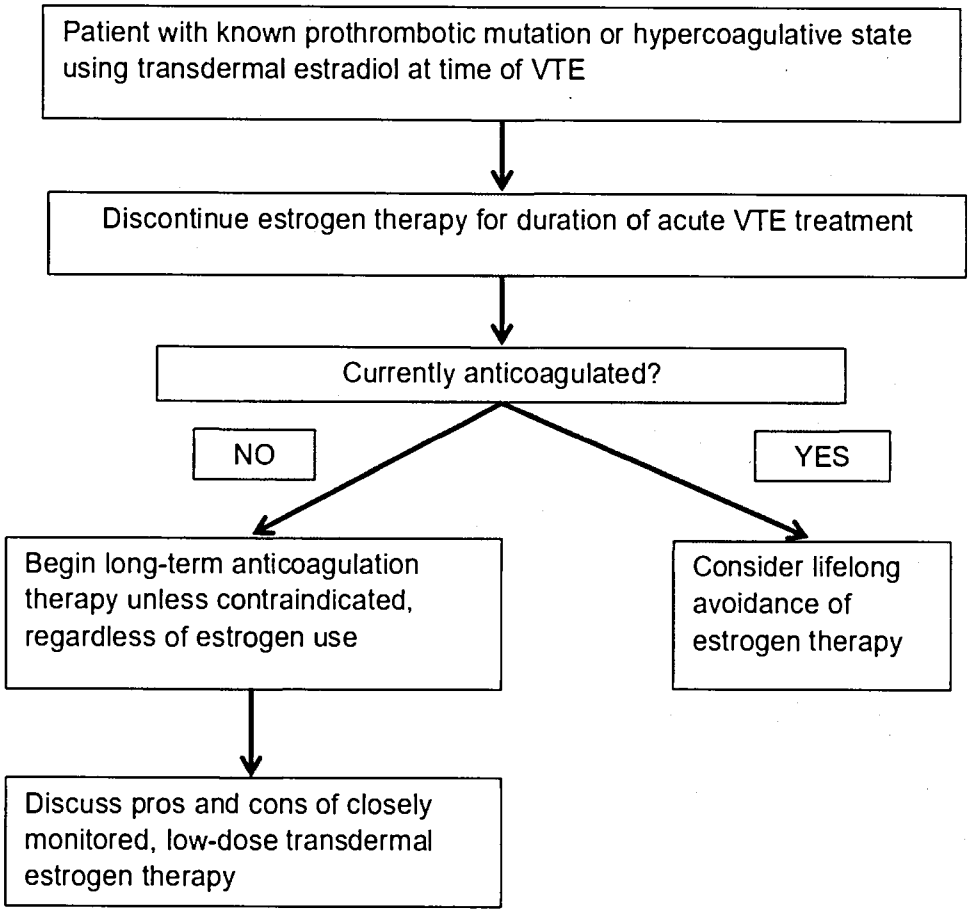


Figure 7-5. Approach to patients with known hypercoagulative state who use transdermal estradiol and present with acute VTE



Autoimmunity:

There is a certain but incompletely defined linkage between sex hormones and autoimmune conditions. Testosterone has been associated with overall immune suppression, and autoimmune conditions are more common in non-transgender women than men.[51] Testosterone deprivation results in an increased Th1:Th2 ratio.[52] However the relationship is more complex, as demonstrated by the paradoxical improvements seen in multiple sclerosis during pregnancy.[51] In transgender women who have undergone orchiectomy or have full androgen blockade, some evidence suggests that supplementation with dihydroepiandrosterone (DHEA) may counteract some of the shift toward autoimmunity.[53] Patients with autoimmune conditions should be informed that their condition could potentially worsen (or improve) once feminizing therapy has begun. Hormone dosing should begin low and advance slowly, monitoring for worsening symptoms, and in collaboration with any specialists who may be managing the autoimmune condition.

Migraine:

Migraines have a clear hormonal component and may be exacerbated by estrogen therapy. Patients with a history of migraines should consider starting with a low dose and titrating upward as tolerated. Oral or transdermal estrogen may be preferred to the potentially cyclic levels associated with injected estrogen.[54] While migraine with aura is associated with an increased risk of stroke in women using oral contraceptives,[55] it is not clear if this risk translates to the use of bioidentical estradiol.

Mental health conditions:

While hormones may contribute to mood disorders (such as in premenstrual dysphoric disorder or postpartum depression), there is no clear evidence that estrogen therapy is directly associated with the onset of or worsening of mental health conditions. In fact one study found that transgender women experience improvements in social functioning and reduced anxiety and depression once estrogen therapy is begun.[56] Mental health conditions in transgender women should be approached with a broad differential diagnosis as in any other patient. It may be advisable to avoid injected estrogen due to the potentially cyclic levels, which could bring about or worsen existing mood symptoms.

Estrogen therapy in patients with a prior history of cancer:

An active estrogen-sensitive cancer is a contraindication to estrogen therapy. For patients with a prior history of estrogen sensitive cancer (breast, pituitary), consultation with an oncologist is recommended. While androgen deprivation is a mainstay of treatment for advanced prostate cancer, it is unclear if estrogen therapy may confer an independent protection or increased risk of prostate cancer.[57] PSA should be considered unreliable in those using antiandrogen or estrogen therapy due to the high risk of false negative tests.

Perioperative use of feminizing hormones:

No direct study of the risk of perioperative venous thromboembolism in users of bioidentical estrogens has been conducted. Guidelines from two British professional organizations make a weak recommendation to discontinue menopausal hormone therapy in the perioperative period, however both acknowledge that this may not be needed in the setting of proper prophylaxis (i.e.

heparin or compression devices).[58] Studies of perioperative ethinyl estradiol in users of hormonal contraception have mixed findings and are wrought with confounding and methodological limitations.[59] Many surgeons insist that transgender women discontinue estrogen for several weeks before and after any gender-affirming procedure.[60,61] These recommendations may appear as benign to the surgeon; however to the transgender woman undergoing a life and body-altering procedure simultaneous with gonadectomy, sudden and prolonged complete withdrawal of estrogens can have a profound impact. Postoperative depression is a nontrivial concern and may have some basis in the drastic hormone shifts, including cessation of estrogens, experienced in the perioperative period. **There is no evidence to suggest that transgender women who lack specific risk factors (smoking, personal or family history, excessive doses or use of synthetic estrogens) must cease estrogen therapy before and after surgical procedures, in particular with appropriate use of prophylaxis and an informed consent discussion of the pros and cons of discontinuing hormone therapy during this time. Possible alternatives include using a lower dose of estrogen, and/or changing to a transdermal route if not already in use.**[62]

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8. Overview of masculinizing hormone therapy

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Introduction

The goal of masculinizing hormone therapy is the development of male secondary sex characteristics, and suppression/minimization of female secondary sex characteristics. General effects include the development of facial hair, virilizing changes in voice, a redistribution of facial and body subcutaneous fat, increased muscle mass, increased body hair, change in sweat and odor patterns, frontal and temporal hairline recession, and possibly male pattern baldness. Sexual and gonadal effects include an increase in libido, clitoral growth, vaginal dryness, and cessation of menses. An ovulatory state is common, though not absolute and long-term fertility may be affected, though some transgender men are able to discontinue testosterone and achieve successful pregnancy.[1] Masculinizing hormone therapy may bring about changes in emotional and social functioning, though these can vary from person to person and stereotypes should be avoided. The general approach involves the use of one of several forms of parenteral testosterone.

All testosterone preparations currently used in the U.S. are "bioidentical", meaning they are chemically equivalent to the testosterone secreted from the human testicle. Prior use of oral methyltestosterone and other synthetics commonly encountered in bodybuilding communities has resulted in unsubstantiated concerns about negative hepatic effects of testosterone use in transgender men. Testosterone is available in a number of injected and topical preparations, which have been designed for use in non-transgender men with low androgen levels (see table). Since the label dosing (not included in table) for these medications are based on the treatment of men with low, but not no, testosterone, higher dosing may be needed in transgender men (see table) than are commonly used in non-transgender men.

Table 8-1. Hormone preparations and dosing (Grading: T O M)

Androgen	Initial – low dose[b]	Initial - typical	Maximum - typical[c]	Comment
Testosterone Cypionate[a]	20 mg/week IM/SQ	50mg/week IM/SQ	100mg/week IM/SQ	For q 2 wk dosing, double each dose
Testosterone Enthanate[a]	20mg/week IM/SQ	50mg/week IM/SQ	100mg/week IM/SQ	"
Testosterone topical gel 1%	12.5-25 mg Q AM	50mg Q AM	100mg Q AM	May come in pump or packet form
Testosterone topical gel 1.62%[d]	20.25mg Q AM	40.5 – 60.75mg Q AM	103.25mg Q AM	"
Testosterone patch	1-2mg Q PM	4mg Q PM	8mg Q PM	Patches come in 2mg and 4mg size. For lower doses, may cut patch

Androgen	Initial – low dose[b]	Initial - typical	Maximum - typical[c]	Comment
Testosterone cream[e]	10mg	50mg	100mg	
Testosterone axillary gel 2%	30mg Q AM	60mg Q AM	90-120mg Q AM	Comes in pump only, one pump = 30mg
Testosterone Undecanoate[f]	N/A	750mg IM, repeat in 4 weeks, then q 10 weeks ongoing	N/A	Requires participation in manufacturer monitored program[f]

a. Available as standard U.S. Pharmacopia (USP) as well as compounded products.
b. Initial – low dose recommended for genderqueer and nonbinary dosing.
c. Maximum dosing does not mean maximal effect. Furthermore, these dosage ranges do not necessarily represent a target or ideal dose. Dose increases should be based on patient response and/or monitored hormone levels. Some patients may require less than this amount, and some may require more.
d. Doses of less than 20.25mg with 1.62% gel, or less than 30mg with 2% axillary gel may be difficult, since measuring one-half of a pump or packet can present a challenge. Patients requiring doses lower than 20.25mg and whose insurance does not cover 1% gel may require prior authorization or an appeal.
e. Testosterone creams are prepared by individual compounding pharmacies. Specific absorption and activity varies and consultation with the individual compounding pharmacist is recommended.
f. Testosterone undecanoate has been used extensively for transgender care outside of the U.S. for many years.[2,3] It has recently become available in the U.S. Testosterone undecanoate has been associated with rare cases of pulmonary oil microembolism and anaphylaxis. As such in the United States, the drug is available only through a restricted program called the AVEED Risk Evaluation and Mitigation Strategy (REMS) Program (https://www.aveedrems.com/AveedUI/rems/preHome.action). All injections must be administered in an office or hospital setting by a trained and registered health care provider and monitored for 30 minutes afterwards for adverse reactions.

Route of injection (intramuscular vs. subcutaneous): While testosterone for injection is labeled for the intramuscular route, many providers have administered testosterone using the subcutaneous route with good efficacy and patient satisfaction, and without complications. Benefits of subcutaneous administration include a smaller and less painful needle, and may avoid scarring or fibrosis from long term (possibly > 50 years) intramuscular therapy (Grading: T O M).[4,5]

Proper use of transdermal testosterone gel: These gels involve an evaporable vehicle which contains the testosterone medication. Manufacturer labeling recommends applying in the morning. After application, the testosterone moves into the dermis, where it slowly releases over the course of the day. Care should be taken to avoid any contact of the gel with others, especially women and

children. This includes gel, which remains on clothing or other fomites. Gel should be applied only to upper arms or shoulders, and not to other sites. Site of application should remain dry for at least 2 hours. It is also recommended that the application site be washed at a later time if close skin-skin contact with another person is expected.

Table 8-2. Titration and monitoring of masculinizing hormone therapy

Therapy	Comments	Baseline	3 months*	6 months*	12 months*	Yearly	PRN
Lipids	No evidence to support lipid monitoring at any time; use clinician discretion	Based on USPSTF guidelines					X
A1c or fasting glucose	No evidence to support lipid monitoring at any time; use clinician discretion	Based on USPSTF guidelines					X
Estradiol							X
Total Testosterone			X	X	X		X
Sex Hormone Binding Globulin (SHBG) **			X	X	X		X
Albumin **			X	X	X		X
Hemoglobin & Hematocrit		X	X	X	X	X	X

* In first year of therapy only;

** Used to calculate bioavailable testosterone; monitoring bioavailable testosterone is optional and may be helpful in complex cases (see text) (http://www.issam.ch/freetesto.htm)

Titration upwards of dose should be driven by patient goals, in the context of clinical response, hormone level monitoring, and safety monitoring (i.e. hemoglobin and hematocrit [H&H]). Clinical response can be measured objectively by the presence of amenorrhea by 6 months.[4] Once within the normal male physiologic range, there is no evidence that higher doses/levels of testosterone result in a greater degree of virilization. Lab reference ranges for total testosterone levels are generally very wide (roughly 350-1100ng/dl); if men have testosterone levels at the lower end of the normal male range and are either concerned about slow progress or are having symptoms of low

energy, libido, or mood, it is reasonable to slowly increase the dose while monitoring for side effects. Once total testosterone is greater than the midpoint value in the lab reported reference range, it is unclear if an increase in dose will have any positive effect on perceived slow progress, or on mood symptoms or other side effects.

While some providers choose to omit hormone level monitoring, and only monitor for clinical progress or changes, this approach runs the risk of a suboptimal degree of virilization if testosterone levels have not reached the target range. A prospective study of 31 transgender men newly started on either subcutaneous 50-60mg/week testosterone cypionate, 5g/day 1% testosterone gel, or 4mg/day testosterone patch found that after 6 months only 21 (68%) achieved male range testosterone levels and 5 (16%) had persistent menses, with only 9 (29%) achieving physiologic male-range estradiol levels.[5] Some genderqueer and gender-nonconforming/nonbinary patients may prefer to maintain testosterone levels in an intermediate range. Regardless of initial dosing scheme chosen, titrate upwards based on testosterone levels measured at 3 and 6 months. Once hormone levels have reached the target range for a specific patient, it is reasonable to monitor levels yearly. As with testosterone replacement in non-transgender men, annual visits and lab monitoring are sufficient for transgender men on a stable hormone regimen. Endocrine Society guidelines recommend monitoring of hormone levels every 3 months.[6] In practice this is not realistic and not likely to add value once a stable dosing has been achieved.[7] Other reasons for measuring hormone levels in the maintenance phase include significant metabolic shifts such as the onset of diabetes or a thyroid disorder, substantial weight changes, subjective or objective evidence of regression of virilization, or new symptoms potentially precipitated or exacerbated by hormone imbalances such as hot flashes, pelvic cramping or bleeding, or migraines. Such patients may also require more frequent office visits to manage coexisting conditions. Increased frequency of office visits may also be useful for patients with complex psychosocial situations to allow for the provision of ancillary or wraparound services.

General comments on hormone level interpretation

Interpretation of laboratory results requires special attention in the context of transgender care. Numerous sources publish target ranges for serum estradiol, total estrogens, free, total and bioidentical testosterone, and sex hormone binding globulin. However, these specific ranges may vary between different laboratories and techniques. Furthermore, the interpretation of reference ranges supplied with lab result reports may not be applicable if the patient is registered under a gender that differs from their intended hormonal sex. For example, a transgender man who is still registered as female will result in lab reference ranges reported for a female; clearly these ranges are not applicable for a transgender man using virilizing hormone therapy. Hormone levels for genderqueer or gender nonconforming/nonbinary patients may intentionally lie in the mid-range between male and female norms. Providers are encouraged to consult with their local lab to obtain hormone level reference ranges for both "male" and "female" norms, and then apply the correct range when interpreting results based on the current hormonal sex, rather than the sex of registration. Testosterone levels must also be interpreted in the context of knowing whether the specimen was drawn at the peak, trough or mid-cycle of the dosing interval, as values can vary widely (and if so may cause symptoms, see below and pelvic pain and bleeding guidelines)

Monitoring testosterone levels

Testosterone levels can be difficult to measure in non-transgender men due to rapid fluctuations in levels, relating to pulsatile release of gonadotropins. In transgender men who are receiving exogenous testosterone, levels may lack these rapid fluctuations (though they may vary over the dosing interval). Free testosterone represents the portion of testosterone unbound to serum proteins and depends on levels of sex hormone binding globulin (SHBG). Free testosterone can be measured, however assays are unreliable.[8] Consensus is lacking on the role of free vs. total testosterone levels; total testosterone levels are reliable and readily available, however they do not describe the actual bioavailable testosterone level. Bioavailable testosterone is free testosterone plus testosterone weakly bound to albumin.[9] SHBG is elevated in the presence of estrogen and thyroxine.[10] It is decreased in the presence of androgens, prolactin, and high levels of insulin and growth hormone. For transgender care, The Endocrine Society recommends monitoring of the total testosterone level.[11] Calculation of the bioavailable testosterone is also likely to help guide dosing in complicated cases, or in cases where results or side effects exist in the setting of a normal range total testosterone. Bioavailable testosterone can be calculated from the total testosterone, albumin, and SHBG levels (http://www.issam.ch/freetesto.htm). A general reference range for bioavailable testosterone is > 72ng/dl (2.5nmol/L).[12–15]

Monitoring hormone levels in patients using injected testosterone

When measuring hormone levels in patients using injected forms of testosterone, a mid-cycle level is often sufficient however if the patient is experiencing cyclic symptoms such as migraines, pelvic cramping, or mood swings. Peak (1-2 days post injection) and trough levels of testosterone may reveal wide fluctuations in hormone levels over the dosing cycle; in these cases, consider changing to a transdermal preparation, or reducing the injection interval (with concomitant reduction in dose, to maintain the same total dose administered over time).[16,17]

Monitoring estradiol levels

A six-month prospective study of 31 transgender men newly started on testosterone found that only 9 (29%) achieved physiologic male-range estradiol levels.[18] In reality, physiologic female estradiol ranges are wide and vary over the menstrual cycle; there can be significant overlap with the physiologic male range. Estradiol may play a role in pelvic pain or symptoms, persistent menses, or mood symptoms. It is unclear what role estrogen blockade with aromatase inhibitors (AI) or selective estrogen receptor modulators (SERM) might play in managing these symptoms, or in routine virilizing regimens. An in-depth discussion of pelvic pain and persistent menses is covered elsewhere in these guidelines.

Interpreting sex-specific, non-hormone labs

Alkaline phosphatase, hemoglobin and hematocrit, and creatinine may vary depending on the patient's current sex hormone configuration. Several factors contribute to these differences, bone mass, muscle mass, number of myocytes, presence or lack of menstruation, and erythropoetic effect of testosterone. Many transgender men do not menstruate, and those with male-range testosterone levels will experience an erythropoetic effect. As such an amenorrheic transgender

man taking testosterone, registered as female and with hemoglobin/hematocrit in the range between the male and female lower limits of normal, may be considered to have anemia, even though the lab report may not indicate so. Conversely, the lack of menstruation, and presence of exogenous testosterone make it reasonable to use the male-range upper limit of normal for hemoglobin/hematocrit. Using the male-range upper limit of normal for alkaline phosphatase and creatinine may also be appropriate for transgender men due to increased bone and muscle mass, respectively. In these cases the provider should reference the male normal ranges for their lab.[19]

Table 8-3. Lower and upper limits of normal to use when interpreting selected lab tests in transgender men using masculinizing hormone therapy

Lab measure	Lower Limit of normal	Upper Limit of normal
Creatinine	Not defined	Male value
Hemoglobin/Hematocrit	Male value if menorrheic*	Male value
Alkaline Phosphatase	Not defined	Male value

* If menstruating regularly, consider using female lower limit of normal.

Individualized dosing based on patient centered goals

Some patients may desire limited hormone effects or a mix of masculine and feminine sex characteristics. Examples include deepening of voice or growth of a beard (both irreversible), with retention of breasts or female body habitus. Some patients may choose to undergo testosterone therapy for a period of time to develop such irreversible changes, and then discontinue testosterone and revert to their endogenous estrogen hormonal milieu. While manipulation of dosing regimens and choice of medication can allow patients to achieve individual goals, it is important to have a clear discussion with patients regarding expectations and unknowns. Specifically, it is not possible to prospectively choose a regimen that will predictably allow patients to arrive at a specified configuration of sex characteristics. Furthermore, individual genetic and physiologic variation can result in wide variations in blood levels and response to therapy between different individuals using the same route and dose. The best approach in these cases is to start with low doses and advance slowly, titrating to effect. At the same time, response to hormone therapy is also individualized and measures such as beard growth or voice changes are variable in both degree and time course. Likely predictive factors of speed and degree of virilization include genetics and particulars of body habitus; younger age at start also likely contributes to faster progress and a greater degree of virilization once an endpoint is reached. Patients beginning hormone therapy later in life may experience more limited results. Patients should be counseled on setting reasonable expectations based on these factors, and avoid making comparisons to the experiences of others. Anecdotal sources suggest that maximal virilization may occur within 2-5 years.[20]

Specific considerations and conditions

Pelvic pain and **persistent menses** are covered elsewhere in these guidelines.

Post-gonadectomy: Since testosterone dosing should be based on physiologic male replacement levels, no reduction in testosterone dosing is required after gonadectomy. Some patients may choose to use a lower dose, which is appropriate as long as dosing is adequate to maintain bone density, however they should be informed of possible reduced muscle mass, energy and libido. Adequacy of dosing in those on low testosterone replacement post gonadectomy may be assessed by following LH and FSH levels and titration of dosing to maintain these in the premenopausal range.[21]

Erythrocytosis/polycythemia: Hemoglobin and hematocrit (H&H) values in transgender men should be interpreted in the context of the dose of testosterone used and menstruation status. Transgender men with physiologic male testosterone levels and who are amenorrheic would be expected to have H&H values in the male normal range. Note this may differ from the normal female range listed on the lab report if the patient is registered in the lab system as a female. Providers should reference their lab(s)' normal male range H&H, and disregard reported high flags if an amenorrheic transgender man on testosterone has an H&H above the female upper limit, but below the male upper limit. Similarly in this same patient, an H&H below the male lower limit but above the female lower limit may *not* be flagged as abnormal, but in reality may represent a true anemia. Patients with persistent menses or on lower doses of testosterone should have their H&H interpreted accordingly. Transgender men with true polycythemia should first have their testosterone levels checked, including a peak level, and have dose adjusted accordingly. Changing to a more frequent injection schedule (maintaining the same total amount of testosterone over time) or transdermal preparations may limit the risk of polycythemia.[16] Phlebotomy or blood donation may be an appropriate short term solution depending on the level of elevation; in all cases other pathologic causes of polycythemia should be excluded. In addition to neoplasms and cardiopulmonary disease, specific conditions of concern in transgender men include obesity-related obstructive sleep apnea, and tobacco use.

Older transgender men: No upper age limit exists for testosterone replacement in non-transgender men.[22] As such, there is no age recommendation for the termination of testosterone therapy in transgender men. It is reasonable to consider discontinuing hormome therapy at or around age 50, the age at which non-transgender women undergo menopause. Regardless of the presence of gonads at this age, withdrawl of testosterone will result in reduced muscle mass, body hair and libido.

Autoimmunity: There is a certain but incompletely defined linkage between sex hormones and autoimmune conditions. Testosterone has been associated with overall immune suppression, and autoimmune conditions are more common in non-transgender women than men.[23] Testosterone deprivation results in an increased Th1:Th2 ratio.[24] However the relationship is more complex, as demonstrated by the paradoxical improvements seen in multiple sclerosis during pregnancy.[23] Patients with autoimmune conditions should be informed that their condition could potentially worsen (or improve) once virilizing therapy has begun. Hormone dosing should begin low and advance slowly, monitoring for worsening symptoms, and in collaboration with any specialists who may be managing the autoimmune condition.

Migraine: Migraines have a clear hormonal component and relationship to estrogen. Given the persistence and possible fluctuation of estrogen levels in many transgender men taking testosterone, migraines may be precipitated or exacerbated in the context of testosterone therapy. Patients with a history of migraines should consider starting with a low dose and titrating upward as tolerated. Transdermal testosterone may be preferred to avoid any potential cyclic effect associated with injected testosterone.[25]

Mental health conditions: While hormones may contribute to mood disorders (such as in premenstrual dysphoric disorder or postpartum depression), these is no clear evidence that testosterone therapy is directly associated with the onset of or worsening of mental health conditions. In fact it has been found that transgender men experience improvements in social functioning and reduced anxiety and depression once testosterone therapy is begun.[26,27] Mental health conditions in transgender men should be approached with a broad differential diagnosis as in any other patient, taking caution to avoid relating all symptoms directly to gender dysphoria or testosterone therapy. Consider using a non-injected medication form to avoid the potentially cyclic levels, which could bring about or worsen existing mood symptoms.

Testosterone therapy in patients with a prior history of cancer: An active sex hormone-sensitive cancer is an absolute contraindication to testosterone therapy. For patients with a prior history of hormone sensitive cancer (i.e. breast), consultation with an oncologist is recommended.

Hair loss: Hair loss may begin soon after beginning hormone therapy, and is dependent on genetic factors. There are two patterns of hair loss seen in transgender men; Frontal and temporal recession, and male-pattern baldness (receding at the forehead and thinning at the crown). Both forms may cause alarm for patients, and in some cases result in a desire to discontinue therapy. Patients should be counseled prior to initiation of therapy on the risk, unpredictable nature, extent and time course of this condition. Management is similar to that in non-transgender men. Over the counter minoxidil, 5-alpha reductase inhibitors, and surgical approaches may be used. The 5-alpha reductase inhibitor finasteride blocks conversion of testosterone to the potent androgen dihydrotestosterone.[28] Finasteride 1mg daily (Propecia) is approved for male pattern baldness, while the 5mg daily dose (Proscar) is approved for management of prostatic hypertrophy.[29] Side effects may include reduced libido or sexual dysfunction, though impact on erectile function (manifesting as genital engorgement) may be less relevant for transgender men who have not undergone metaoidioplasty. In general, the 1mg daily dose has minimal sexual side effects. The negative impact on results of 5-alpha reductase inhibition on transgender men early in their course of testosterone therapy is unknown. As with non-transgender men, use of the 5mg daily dose of finasteride, or use of the more potent 5-alpha reductase inhibitor dutasteride, may result in excessive testosterone blockade, and resultant sexual side effects and regression of some virilization.

Metabolic syndrome and related conditions (obesity, hyperlipidemia, impaired glucose tolerance, polycystic ovarian syndrome/PCOS): Cardiovascular and diabetes considerations are covered elsewhere in these guidelines. Polycystic ovarian syndrome can manifest with any combination of impaired fasting glucose, dyslipidemias, hirsutism, obesity, and oligo- or amenorrhea with anovulation. Some of these features (hirsutism, oligo- or amenorrhea) may be welcomed by transgender men and present prior to testosterone administration. Testosterone administration is not contraindicated in the presence of PCOS, but patients should be monitored for

hyperlipidemia and diabetes. **Transgender men with amenorrhea in the presence of testosterone are not believed to be at elevated risk of endometrial hyperplasia, due to the atrophic effects of testosterone on the endometrium (Grading T O M).**[30,31] It may be prudent to pursue endometrial evaluation prior to initiation of testosterone in transgender men with a current history of amenorrhea/oligomenorrhea. Testosterone replacement in non-transgender men is associated with an increased risk of obstructive sleep apnea (OSA).[22] It is unknown whether OSA is increased in transgender men after the initiation of testosterone. However, the behavioral health improvements seen with testosterone therapy may result in positive lifestyle changes that reduce obesity, disorders of glucose metabolism, or hyperlipidemia. **In all but the most severe cases (diabetes out of control, active unstable coronary artery disease), transgender men should be informed of risks, and if testosterone therapy continues to be desired, it should be continued with concurrent conventional management of metabolic disorders and their sequelae (Grading: X C S).**

Acne: Acne of the face and body are common side effects of virilizing hormone therapy. Approach to symptom management is consistent with established practices in non-transgender people. Patients can be reassured that acne tends to peak in the first year of testosterone therapy, and then declines.[32] Maintaining physiologic testosterone levels, and avoiding excessive peaks associated with prolonged inection dosing intervals may help minimize acne.

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9. Pelvic pain and persistent menses in transgender men

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Introduction: Pelvic Pain

Pelvic pain in transgender men can be a clinical challenge and has a broad differential diagnosis. Pelvic pain less than 6 months of duration is considered acute. Chronic pelvic pain, which is continuous or episodic pain in the lower abdomen or pelvis lasting more than 6 months, has a large differential.[1] History is a critical component to assessment and diagnosis. Key to the history is a detailed description of pain including onset, precipitating and palliating features, quality, radiation, severity and timing. A pain diary can be helpful to elucidate pain pattern and features and there are many available online (See http://www.partnersagainstpain.com/printouts/Daily_Pain_Diary.pdf).

The general approach to the workup of pelvic pain in transgender men is similar to that for non-transgender women. An anatomic approach to history gathering that considers urological, gynecologic, gastrointestinal, musculoskeletal, and psychological components is critical. Specific etiologies may be multifactorial, such as post-surgical adhesions with or without gastrointestinal symptoms, or endometriosis and/or pelvic floor muscle dysfunction. It is also critical to assess quality of life impact and determine what the patient would consider a favorable outcome. Most evaluation and treatment guidelines stress that chronic pelvic pain can be a diagnostic and therapeutic challenge, and success will depend on comprehensive and customized evaluation and multidisciplinary care.[2,3]

Etiologies

Specific medical etiologies to consider in transgender men include: atrophic or infectious vaginitis, cervicitis, cystitis, STIs, adhesions, post-surgical sequelae, musculoskeletal disorders, and neurogenic. Specific behavioral etiologies to consider include: depression, history of emotional trauma (including sexual assault or abuse, adverse childhood events),[4] and post-traumatic stress disorder. The use of testosterone has a dose dependent effect on vaginal tissue by inducing a hypoestroenic state which promotes atrophy, increases vaginal pH and thus increases increases the risk of vaginitis and cervicitis. Additionally, transgender men may have decreased access to or utilization of screening and therefore treatment for cervicitis and sexually transmitted infections.[5–7] Prior surgery may cause adhesions, scar tissue, bladder dysfunction, or nerve injury, which may lead to a lack of visceral mobility and contribute to pain.[8] It is unclear to what extent post-surgical adhesions cause pain independently, or via secondary mechanisms such as constriction or incarceration of other organs. Transgender men who have pelvic pain after hysterectomy but have retained one or both ovaries/gonads should be screened for a gonadal pathology. The interaction between a genotypic female skeleton and increased muscle mass as a result of testosterone therapy may result in changes in postural carriage. Additionally, recent and/or history of sexual trauma may be exacerbated among those with gender minority status. Engaging with medical

professionals can be re-traumatizing in this setting; in all cases a trauma informed approach should be taken.[9]

Taking a pelvic pain history

The initial history should include a menstrual history including age of onset, frequency of menses or cyclical menstrual-like symptoms even if amenorrheic, duration of menses, last menstrual period, and if amenorrheic, for how long. Also assess for use of pain medication, and any association with testosterone dosing cycles. A comprehensive sexual history, including assessing for specific behaviors with other individuals such as (vaginal-vaginal), vaginal or anal or receptive penile sex, recognizing that many transgender men may engage in receptive vaginal sex.[10] Assess for potential risk of pregnancy and ectopic pregnancy; transgender men who have receptive vaginal sex with a partner with sperm are at risk for unintended pregnancy, including ovulation and conception without preceding menstrual bleeding. Also note any history of pelvic inflammatory disease. A surgical history should note for history of an open, laparoscopic or vaginal approach to inform suspicions of scar tissue and adhesions and subsequent symptomatology. Note any specific risks such as a ruptured appendix or history of pelvic inflammatory disease (PID). Other history should include screens for adverse childhood events, current domestic violence, and for substance use and overuse, including tobacco.

Physical exam

On exam assess for involvement of various abdominopelvic organs, including a check for costo-vertebral angle tenderness, palpation of the abdominal wall, noting any particular tenderness along prior surgical scars or point tenderness along scars or the abdominal wall in general. Palpate the bladder for localized sensitivity, and palpate the abdomen for visceral organ involvement. Consider a speculum exam only if clearly indicated, noting vaginal discharge or any evidence of vaginitis, and assess the general condition of vaginal tissues and the cervix. If a pelvic exam is necessary, consider starting with a pediatric speculum. If a bimanual exam is performed, note any cervical, adnexal or ovarian tenderness to palpation.[5] Also assess sensation in the vulvar area with cotton tipped nerve testing as well as sharp/dull differentiation, and examine of the pelvic floor via palpation of the obturator internus (two-digit exam with palpation of muscles at 4 to 5 o'clock and 7 to 8 o'clock; pain on flexion of the two fingers at these locations suggests pelvic floor dysfunction). Also if indicated consider a rectal exam, noting masses, tenderness, or hardened stool. Laboratory testing includes a urinalysis and culture, testing for Chlamydia and gonorrhea, vaginal pH, vaginal wet mount and KOH prep, and possibly a vaginal culture. A pregnancy test should be considered, however some patients who are not sexually active with someone capable of insemination may be offended by the suggestion of this test. It is best to explain to patients in advance that this test is part of a standard protocol, and if it is certain that pregnancy is not possible based on sexual behaviors, a pregnancy test may be omitted. Imaging should be performed using transabdominal or transvaginal ultrasound; in those men who have had a vaginectomy, a transrectal ultrasound may be an option. Some transgender men may decline vaginal ultrasound and/or bimanual exams due to potential exacerbation of gender dysphoria. These patients should not be forced to undergo a pelvic examination. In these cases proceed with an abdominal exam as well as laboratory and transabdominal ultrasound for the initial workup.

Specifically for transgender men, critical components of the assessment include timing of pain and associated symptoms in relation to initiation of testosterone therapy, moliminal timing (symptoms in relation to an expected menstrual cycle) even in the presence of amenorrhea, and a detailed history of prior surgeries and related organ inventory.

Testosterone-induced dyspareunia, vaginitis, and cervicitis

The use of testosterone often results in estrogen deficient, atrophic vaginal tissues akin to a post-menopausal state in cisgender women.[11–13] These atrophic vaginal tissues represent a decline in tissue resilience, skin barrier function, and increased susceptibility to altered microbial environment and resistance which may result in bacterial vaginosis, cystitis, or cervicitis.[14] Additionally, thin atrophic vaginal tissues are more susceptible to traumatic irritation from friction and sexual contact,[13] which may result in atrophic dyspareunia or vaginitis. Symptoms are often described as "rough" "sand-paper" and "burning" or "dry" vaginal irritation. Visual inspection consistent with atrophy will demonstrate thin pale tissues, a loss of rugae, loss of elasticity, friability, and dryness. It is also possible to find hyperemic, deep red vaginal tissue. Bacterial vaginosis is more common in the estrogen-deprived state. Wet mount, vaginal culture, vaginal pH and STI testing can aid in directing treatment. Interstitial cystitis should be considered when infectious causes have been rules out and symptoms localize to the urinary bladder. Vaginal estrogen to treat underlying atrophy may be warranted and a short course may be successful in restoring comfort. Patients may be reassured that vaginal estrogen is associated with mnimal systemic absorption and should not interfere with the desired effects of Testosterone. Other therapeutic approaches may include vaginal lubricants or vaginal moisturizers.[15]

Cyclic symptoms relating to testosterone dosing

Transgender men on testosterone may complain of pain that is associated with cyclical testosterone dosing, pelvic, and/or vaginal pain with penetration (with penis, fingers, dildo, etc), or orgasmic pain. The etiology of post-testosterone administration cramping is unclear. In one cross-sectional study 20% of respondents had a hysterectomy to decrease post-testosterone cramping and another 22% to stop "extreme bleeding and cramping."[16] Trauma informed care can be effective, as are other treatments used for chronic pelvic pain such as pelvic floor therapy, vaginal lubrication with unscented products, or the use of tricyclic antidepressants.

Co-occurring mental health conditions

As with any pain syndrome, patients with chronic pelvic pain should be evaluated for depression and post-traumatic stress disorder (PTSD). These conditions may be simultaneously present in up to 35% of non-transgender female patients with chronic pelvic pain.[1] Multiple studies link adverse childhood events with increased incidence of chronic pain and depression. Pre-existing depression may exacerbate pelvic pain. Conversely, pelvic pain and living with a chronic pain condition may result in depression. A high percentage of those who have undergone sexual assault develop PTSD, and many of those who have PTSD may develop pelvic floor muscle dysfunction and pain.[17,18] The presence of pelvic pain as well as the related workup and evaluation may trigger PTSD, especially if such trauma relates to a prior sexual assault or otherwise involves the lower abdomen and pelvis. These symptoms may be even greater in transgender men for whom examination of genital and reproductive organs may be particularly challenging and triggering of

gender dysphoria, and result in avoidance of pelvic exams.[19] Collaboration with a specialist in mental health can be an important adjunct to pathophysiological evaluation and treatment.

Pharmacologic management

The initial approach to management should include NSAIDS, with other pain management medications used as indicated and appropriate. Changing to a more even testosterone transdermal testosterone regimen, or adding a progestagen such as the levonorgesterel IUD may address underlying hormonal causes.

Role of hysterectomy

In addition to non-surgical approaches, in some cases hysterectomy may have a role in the management of pelvic pain. **Depending on the preferences and reproductive goals of an individual patient, gynecologists may revise their therapeutic approach to consider hysterectomy earlier than they might in non-transgender women (Grading: X C S).** At the same time hysterectomy should not be viewed as a cure-all, and in some cases is not effective in improving pain. For this reason, transgender men with pelvic pain must be evaluated on a case-by-case basis due to the lack of evidence-based guidance at this time. Decision to perform oophorectomy should be based on the etiology of pelvic pain, presence of comorbidities, future fertility desires, and any future plans to stop taking testosterone.

Management of specific symptoms and syndromes

If pain is vulvar and there are no identifiable lesions or infections, Consider the use of topical 2-5% topical lidocaine placed on soaked cotton-ball and left in the vestibule overnight for general pain relief, or for 30 minutes prior to sexual activity as desired.

If pain is vulvar and exam is consistent with vaginal atrophy in the setting of testosterone administration, consider a short course of vaginal estrogen in doses and administration similar to that used for post-menopausal non-transgender women. Patients who are uncomfortable with intravaginal use may be instructed to place treatment cream on their external genitalia. Choice between tablets, creams, and rings depends on patient preference and formulary considerations.[20]

If pain is triggered by pelvic floor muscle palpation, consider referral to pelvic floor physical therapy, pelvic floor relaxation exercises, and even guided instruction on massage using self or partner's fingers or a massage tool.

If pain is abdominal, present in the abdominal wall or associated with abdominal scar tissue, consider treatment with 1% lidocaine instilled at trigger points in repeated administration.

If transvaginal ultrasound is required, consider a low-dose benzodiazepine such as lorazepam 0.5mg orally, 30 minutes prior to the procedure, in coordination with administration of 2-5% lidocaine ointment applied to the vulva and vagina 10 minutes prior to the procedure. Some patients may feel safer and more comfortable placing the ultrasound probe intra-vaginally themselves. These approaches may also be used in advance of a pelvic examination.

Introduction: Persistent menses & unexpected vaginal bleeding

Many transgender men chose not to undergo hysterectomy, oopherectomy and/or gender-affirming genital procedures.[19,21,22] For transgender men of reproductive age undergoing transition without hormones, or those whom have used testosterone and later discontinued it due to unwanted side effects such as balding, menses would be expected to be within standard reference ranges from 21-35 days between cycles with no inter-menstrual bleeding and lasting on average 2-6 days and ceasing on average at age 49.[23] Variation from these ranges warrants further gynecological investigation.

For those transgender men using physiologic doses of testosterone, cessation of menses is expected, typically within 6 months. Cessation of menses is driven by a combination of testosterone induced ovulation suppression, which may be incomplete, and endometrial atrophy.[12] However, the time to cessation of menses may vary. Factors that affect time to cessation of menses likely include: dose of testosterone, route of administration, frequency of testosterone administration, presence and functioning of ovaries, body habitus, and the presence of other structural or non-structural medical conditions of the uterus or ovaries. Transgender men with a history of abnormal cycles prior to initiating testosterone (*e.g.* frequent cycles, heavy irregular bleeding) may have underlying pathology, which could result in a prolonged or complicated path to cessation of menses once on testosterone. Therefore in patients with risk factors for endometrial hyperplasia and a degree of clinical suspicion, evaluation for and elimination of known causes of irregular bleeding should be considered concurrent with testosterone administration; those with pre-existing amenorrhea or oligomenorrhea may require evaluation for endometrial abnormalities prior to initiating testosterone. This includes ruling out pregnancy in transmen who are sexually active with partners who produce sperm.

Etiologies

Abnormal uterine bleeding (AUB) may be considered present in those who have continued bleeding after 6-12 months of male-range testosterone levels and suppressed LH and FSH. AUB may be related to a variety of structural and non-structural causes. These causes can be summarized by the internationally recognized Federation of Gynecology and Obstetrics (FIGO) PALM-COEIN classification system.[24] Structural causes of AUB include: endometrial polyps, adenomyosis, leiomyomata, endometrial hyperplasia, or malignancy. As a group these are best evaluated with imaging and endometrial biopsy. Despite prior suggestions that endometrial cancer risk may be increased in transgender men on testosterone,[25] longer-term data do not support this risk.[26] Non-structural causes of AUB include: pregnancy, coagulopathy, ovulatory dysfunction, endometrial, or iatrogenic causes. While the gold standard for pelvic imaging is transvaginal ultrasound, other approaches such as a sono-hystogram, transabdominal ultrasound, CT Scan, or MRI may be warranted. Both structural and non-structural causes should be investigated in consultation with a gynecologist. The decision to pursue transvaginal ultrasonography or endometrial biopsy should not be taken lightly in transgender men who may find these procedures invasive. Noninvasive diagnostic approaches such as watchful waiting for induction of amenorrhea 6 months after initiation of testosterone, observing for a withdrawal bleed after a progestin challenge, or use of a transabdominal approach to ultrasonography should all be considered. Persistent menses despite testosterone may also be related to body habitus; those with higher

levels of body adipose tissue have higher endogenous estrogen levels and increased conversion of testosterone to estradiol through the peripheral aromatization process.

Therapeutic approaches based on etiology

Increasing the dosage and frequency of dosing (1 and 2 weeks) of intramuscular testosterone has been found to be positively correlated with rapidity of amenorrhea induction.[27] The time to cessation of menses has been reported as ranging from 1-13 months [27–31] and in addition to individual genetic and physiologic factors may very well depend on the formulation or route of testosterone administration.[28]

Physiologically, amenorrhea induction rates should correlate to increased testosterone levels (to physiologic male range) as well as possible decreased estrogen levels seen with androgen therapy, however many will achieve amenorrhea despite elevated estrogen levels and sub-physiologic male testosterone levels. For example, one study of transgender men presenting for initiation of cross-sex hormones found that 84% of those completing the study were amenorrheic at 6 months. This was despite many only 58% achieving physiologic male total testosterone levels and 68% achieving physiologic male free testosterone levels.[30] However in the setting of persistent menses, adjustment of hormone regimen and dosing may be appropriate. The addition of an oral, injected, implanted, or intrauterine (IUD) progestagen may serve as an adjunct to induction of amenorrhea. Endometrial ablation can be considered [31] for those transgender men who do not desire future fertility and who also either decline hysterectomy or have surgical complications. The levonorgestrel intrauterine system (IUS/IUD), which in non-transgender women can either significantly decrease menstrual flow or fully induce amenorrhea, has the added contraceptive benefit for those at risk since some may still ovulate despite male physiologic testosterone levels.[32]

Aromatase inhibitors (AIs) such as anastrazole or letrazole may be considered as short-term adjunctive therapy in achieving amenorrhea for those with persistent menses on testosterone. Aromatase is expressed throughout the body including the ovaries, endometrium, skin, bone, breast, brain and adipose tissue. AIs have been used for the treatment of estrogen receptor positive breast cancer, endometriosis, and ovulation induction. AIs have also been shown to reduce vaginal bleeding and pelvic pain in combination with other hormone therapies such as progestins or combined oral contraceptives.[33–35] In non-transgender women, treatment with AIs without add-back estrogen therapy has led to symptoms of medical menopause: hot-flashes, arthralgias, mood disturbances, fatigue, vaginal dryness, decreased bone mineral density, and fractures.[36] In transgender men concurrently using testosterone, these symptoms may be attenuated or even absent.

What remains unclear is the AI dose necessary in the setting of male-range testosterone levels in comparison with the roughly 10 fold lower physiological female estrogen levels released by the ovaries. Since AIs have been used for ovulation induction, contraception should be considered in transgender men who may be at risk for pregnancy. Weight loss plays a critical role in all cases for health promotion as well as resulting in amenorrhea through reduction of adipose containing aromatase.

Helpful resources

- International Pelvic Pain society: http://www.pelvicpain.org

- American Physical Therapy Association: http://moveforwardpt.com/Default.aspx

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10. Approach to genderqueer, gender non-conforming, and gender nonbinary people

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Introduction

Genderqueer, gender non-conforming, and gender nonbinary (GNB) people do not live within the binary gender narrative. A brief discussion of terminology and pronouns will be followed by an overview of the unique considerations for nonbinary hormonal and surgical transition.

Terminology

With a broad spectrum of gender identities and expressions, GNB people may identify as both male and female; neither male nor female; in between genders; on or outside the gender spectrum; or beyond the gender binary system, not having a gender at all—identifying as agender or genderless. Some may simply identify as "queer," which has been reclaimed as a respectful umbrella term encompassing a broad range of gender identities, expressions, and sexual orientations. GNB people are as authentic in their gender status as transgender people who present with more binary gender identities or expressions. Nonbinary gender terms evolve and change rapidly; spelling and hyphenation vary widely. Some additional examples of terms used by GNB people include [1]:

- gender fluid
- gender ambiguous
- pangender
- neutrois
- gender bender
- gender blender
- gender smoothie
- gender expansive
- masculine of center
- feminine of center
- androgyne

Pronouns: People who are gender nonbinary may choose to use gender neutral pronouns such as "they," "them," and "their," or other gender neutral pronouns such as "zie(ze)/hir," instead of she/her, he/his.

As with all transgender people, identifying and using the chosen name and pronoun are central to appropriate patient care. Providers are encouraged to familiarize themselves with the diversity of pronouns which may be used by GNB people. It is not essential to memorize the chart, and if there are any questions as to how to use and conjugate pronouns for a specific person, it is recommended that you ask for clarification. Conjugation of gender neutral pronouns are described below:

Table 10-1. Pronoun Reference Sheet

3rd Person Singular Subjective	3rd Person Singular Objective	3rd Person Singular Possessive	3rd Person Singular Reflexive
She	Her	Her	Herself
He	Him	His	Himself
They	Them	Their	Themselves
Ze	Zir	Zir/Zirs	Zirself
Xe	Xem	Xyr/Xyrself	Xemself
Ze	Hir	Hir/Hirs	Hirself
Per	Per	Per/Pers	Perself

Source: Adapted from the University of Alberta Student Union

Transition

As with people who have binary transgender identities, the process of gender affirmation and transition for those who are nonbinary is for some limited to an internal or purely social process; for others the process may involve a variety of gender-affirming medical and/or surgical interventions. The WPATH Standards of Care Version 7 are now more inclusive of GNB identities and recognize the need for and appropriateness of an individualized approach. [2]

Specific approaches to gender affirmation for GNB people

The approach to hormone therapy should be guided by the person's desired configuration of secondary sex characteristics. Strategies may include using hormones at a lower dose or for a limited period of time. Nonbinary people on the feminine spectrum may choose to only use an androgen blocker, and/or use estrogen at a very low dose, or for a short time.

For those on the masculine spectrum, low dose testosterone can be acceptable, especially if menses is not a source of dysphoria, as low dose may not stop menses. If gender dysphoria worsens with menses, testosterone may be increased. If a GNB person does not want the degree of masculinization resulting from the higher doses of testosterone that could induce menstrual cessation, other approaches can be explored. These could include intramuscular medroxyprogesterone, the levonorgestrel intrauterine system or an etonogestral implant, all of which also provide contraception. On occasion, masculine spectrum clients might choose continuous combined oral contraceptives for cessation of menses as well as for contraception. Surgical options for cessation of menses may include uterine ablation or hysterectomy.

It is important to remember to address reproductive and fertility considerations as part of informed consent for medical and surgical approaches, discussed in greater detail in other sections of this protocol.

Limitations on the ability to predict specific outcomes with any given regimen should be discussed with GNB patients. Some desired combinations of results (such as a deepened voice without facial or body hair growth) may not be possible.

GNB persons may also pursue a variety of gender-affirming surgeries and procedures, including chest reconstruction or breast augmentation and genital surgeries. A masculine spectrum nonbinary person may choose to keep their vagina when pursuing metoidioplasty; this is also an option for a more traditionally binary transgender man. A feminine spectrum nonbinary person may choose to have vaginoplasty but not desire breast development and not pursue hormonal transition; in these cases hormone replacement will be necessary after gonadectomy to maintain bone health, and surgery should only be pursued after an appropriate evaluation by an experienced and qualified mental health provider. Non-medical approaches such as packing, tucking, and binding may be central to a GNB person's expression. Some GNB people may express sharply contrasting masculine and feminine characteristics simultaneously; for example, breasts and facial hair as part of authentic expression.

Other considerations: Challenges for the gender nonbinary person include the lack of nonbinary gender markers for documentation in medical records and in legal identification, such as passports and drivers licenses. Advocacy groups are making efforts to challenge the binary system, introducing nonbinary gender concepts and terminology into legal, medical, mental health, and educational arenas.

A more substantial discussion of gender nonbinary experiences can be found in blogs and websites (e.g., Neutrois Nonsense) [3] and books such as *Trans Bodies, Trans Selves.*[4]

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11. Cardiovascular disease

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Introduction

Sex is an independent predictor of cardiovascular health outcomes. The role played by sex hormones in this difference between the sexes is unclear. A 2010 Cochrane analysis found no interaction between menopausal hormone therapy and all-cause mortality, cardiovascular-related mortality, non-fatal myocardial infarction or angina, or the need for bypass surgery or coronary angioplasty.[1] This same analysis found a slight increase in risk of stroke (RR 1.26, 95% CI 1.11-1.43, number needed to harm = 164); however a 2015 Cochrane update found no increased risk of stroke among the subgroup of women who began hormone therapy less than 10 years after menopause, which is more likely representative of transgender women.[2] Few studies have investigated cardiovascular disease risk and burden among transgender people on hormone therapy, adjusting for risk factors such as tobacco use. Larger studies have been retrospective and did not adjust for numerous coexisting risk factors. Prospective studies have been smaller and over shorter terms. Any analysis of the possible negative effects of hormone therapy on cardiovascular disease and stroke should take into consideration the significant benefits of hormone therapy on quality of life and psychosocial functioning.[3–5]

Evidence from several studies suggests that cardiovascular risk is unchanged among transgender men using testosterone compared with non-transgender women.[6–8] Evidence in transgender women is less clear. Some studies have found increased morbidity and mortality from myocardial infarction and stroke compared with non-transgender men, however these studies did not adjust for a number of risk factors including tobacco use, obesity, and diabetes.[6–8] The largest study published to date is a report on mortality in a retrospective cohort of more than 1000 Dutch transgender women and men which did not control for a number of risk factors, including tobacco use. All-cause as well as cardiovascular- and cerebrovascular-specific mortality among transgender men did not differ from the general Dutch population. Among transgender women, all-cause mortality was 51% higher (95% CI 47 to 55) than in the general Dutch population, with the overwhelming majority of the difference due to HIV, drug overdose and suicide; a 64% increased risk (95% CI 43 to 87) in cardiovascular mortality was seen, however no significant difference was seen for cerebrovascular mortality.[9]

Several factors may contribute to an elevation of cardiovascular disease in transgender women, such as higher rates of tobacco use, obesity, diabetes and lipid disorders, and reduced physical activity.[7] Older studies demonstrating increased morbidity and mortality among transgender women included users of high doses (>100mcg/day) of ethinyl estradiol, a known thrombogenic synthetic estrogen used in oral contraceptives at typical doses of only 20-30mcg/day.[10] A meta-analysis of lipids and blood pressure in transgender people using hormone therapy found a mean increase in triglycerides of 23mg/dl (95% CI 5 to 42) among

transgender women, and a mean increase in triglycerides of 31mg/dl (95% CI 7 to 55) and systolic blood pressure of 1.7mmHg (95% CI 0.2 to 3.3), and mean decrease in HDL of 6mg/dl (95% CI 0.7 to 11) among transgender men; all other lipid and blood pressure parameters showed no statistically significant change.[11] Such statistically significant changes have small effect sizes and are of questionable clinical significance, especially in the context of primary prevention.

Direct study of the effects of hormones on lipids and blood pressure in transgender people has been limited. A retrospective study of lipids in 169 Austrian transgender people found trends of poorer lipid profiles in both transgender women and men at 5 years however these changes were mild at most, and seemed to be mitigated to some degree by the use of transdermal estradiol.[12] A prospective 6 month study of a young and healthy cohort of 31 transgender women and 17 transgender men in the U.S. found modest overall improvement in lipids in transgender women and only a slight reduction in HDL in transgender men; while statically significant, the effect sizes were small and of questionable clinical significance.[12–14]

Calculating risk

Current American Heart Association – American College of Cardiology guidelines for prevention and lipid management involve the use of sex-specific calculators to determine risk and guide interventions.[14] Determination for the use of aspirin also uses these calculators when conducting a risk-benefit assessment for gastrointestinal bleeding. Currently there is no guidance on whether to use risk calculators based on natal sex or affirmed gender. It may be reasonable to use natal sex-based calculators in transgender people who have transitioned later in life, given their long-term exposure to the natal hormonal milieu. However with an increasing percentage of transgender people beginning hormone therapy in adolescence and young adulthood, affirmed gender-based calculators may be more appropriate in these cases. Ultimately a primary goal is to calculate a realistic risk-benefit ratio between the benefits of statin therapy or aspirin and the risks of these treatments. **Depending on the age at which hormones are begun and total length of exposure, providers may choose to use the risk calculator for the natal sex, affirmed gender, or an average of the two (Grading: X C M)**. Another goal of calculating risk is to provide adequate information during the informed consent process to allow transgender people of any age, and with or without existing cardiovascular or cerebrovascular disease, to make informed decisions about the long term implications of gender-affirming hormones.

Reducing risk

For transgender women with cardiovascular risk factors or established CVD, using the transdermal route of estrogen may be preferred due to lower rates of venous thromboembolism, and lack of associated changes in lipid profile or markers of coagulation (Grading: NT O M).[15,16] Additional modifiable interventions to reduce risk include smoking cessation, weight loss, management of diabetes, and encouraging physical activity. It is theoretically possible that the psychosocial benefits of hormone therapy may

have an independent and protective effect through reduction of stress, improved body image resulting in healthier lifestyle choices, reduced tobacco use, and increased physical activity.

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12. Diabetes mellitus

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Recommendations for diabetes screening in transgender patients (regardless of hormone status) do not differ from current national guidelines.

The effect of gender-affirming hormone therapy on diabetes risk or disease course is unclear. A Dutch case-control study noted an increased prevalence of type 2 diabetes mellitus among transgender men and women in comparison to both age matched non-transgender male and female groups, however the study did not adjust for other risk factors.[1] A study of the effects of gender-affirming hormones on insulin resistance in transgender women and men found that transgender women may experience some increase in markers of insulin resistance, while transgender men exhibited no change.[2] Some data from non-transgender men suggests that testosterone lowers insulin resistance.[3] Data are mixed on the presence of increased rates of polycystic ovarian syndrome (PCOS) in transgender men prior to hormone therapy. While non-transgender female patients with PCOS require close monitoring for development of diabetes due to marked insulin resistance,[4,5] it is unclear if this risk remains once the hormonal milieu has been modified with the addition of testosterone. While insulin resistance serves as a useful surrogate marker to inform risk, outcome studies using a diagnosis of diabetes as the end point have not been conducted.

Otherwise young and healthy transgender people will often seek medical care with the sole purpose of obtaining hormone therapy or surgery. When this care is provided within the context of comprehensive primary care, identification of risk factors such as obesity, PCOS, metabolic syndrome, impaired fasting glucose, or diabetes may occur earlier than would have happened if the person were not transgender. This can be viewed as an opportunity to improve health particularly in transgender women, who may be at increased cardiovascular risk. However, caution should be used to avoid making gender-affirming care contingent on tight control of these other conditions. Numerous anecdotes exist of poorly controlled diabetic transgender patients who had improvements in self-care and resultant decline in hemoglobin A1c after initiation of gender-affirming hormones.

Management of diabetes in transgender patients has not been specifically studied. Testosterone package inserts recommend monitoring as serum glucose may be lowered in patients with diabetes receiving testosterone. It is reasonable to maintain heightened monitoring of indicators such as fasting glucose and hemoglobin A1c when initiating or adjusting hormone therapy. While the WPATH Standards of Care recommend that conditions such as diabetes be "reasonably well controlled" prior to initiating hormone therapy, no absolute criteria have been proposed, and the potential adverse effects on blood sugar should be weighed in consideration of the benefits of hormone therapy.

Patients with diabetes seeking gender-affirming surgeries represent a special group for whom aggressive treatment to normalize glucose control is desirable. Genital surgeries and breast/chest surgeries involve microvascular techniques. Healing, avoidance of infection,

functionality and cosmesis are thought to be improved with better glycemic control. While the presence of diabetes in itself may not be a contraindication for any of these surgeries, careful coordination between the surgeon and the provider managing the diabetes is recommended.[6]

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13. Bone health and osteoporosis

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Introduction

Adaptation of recommendations for osteoporosis screening to transgender populations is complicated by existing recommendations that vary widely for non-transgender people, including lack of consensus about screening for non-transgender men, and no U.S. national level recommendations on the frequency of screening.

Osteoporosis screening is currently age- and sex- based, and also individualized on the basis of risk factors. There are a number of lifestyle, genetic, endocrinologic, hematologic, rheumatoid and autoimmune diseases, as well as medications that contribute to osteoporosis. Known risk factors for osteoporosis include Caucasian or Asian race, older age, alcohol > 10 drinks/week, low body mass index, smoking, chronic corticosteroid use, hypogonadism, rheumatoid arthritis, hyperparathyroidism, immobility, vitamin D deficiency and HIV infection.[1,2]

Osteoporosis risk in transgender women

In one study, researchers found that transgender women had factors which may contribute to an increased risk of osteoporosis, independent of and existing prior to hormone use, such as reduced levels of physical activity, lower muscle mass and grip strength, and lower levels of vitamin D.[3] Studies investigating BMD in transgender women receiving hormones have shown both lower, higher and no change in bone density after initiating hormones.[4–11] The differences in results may be due to the regimens used (some used unopposed androgen blockers for a period of time before initiating hormones) and length of follow-up. Known risk factors for osteoporosis include underutilization of hormones after gonadectomy or use of androgen blockers without or with insufficient estrogen. GnRH analogues also may result in short term decrease in bone mineral density (ie. GnRH analogues without concurrent estrogen, and when estrogen added, or blockers stopped bone density returns to normal).

Osteoporosis risk in transgender men

Most published studies to date have shown either no change, or an increase in bone mineral density in transgender men treated with testosterone. Risk factors for osteoporosis in this population include oophorectomy before age 45 without optimal hormone replacement.[4,6,9–13]

Current screening guidelines in non-transgender populations

There are no consistent guidelines on the optimal frequency of screening in non-transgender people. The WHO guidelines suggest every 10 years. A recent U.S. NIH funded study suggests intervals of approximately 15 years for normal bone density or mild osteopenia, 5

years for moderate osteopenia, and 1 year for advanced osteopenia. Screening intervals in transgender people can be based on these recommendations as well. All professional organizations recommend screening for all non-transgender women over age 65. Some recommend earlier screening in those with risk factors. Some older guidelines recommend screening in non-transgender men after age 70 or in those with risk factors, while others and more recent guidelines make no recommendations for men.

Recommended screening for transgender women and men

There is insufficient evidence to guide recommendations for bone density testing in transgender women or men. **Transgender people (regardless of birth-assigned sex) should begin bone density screening at age 65. Screening between ages 50 and 64 should be considered for those with established risk factors for osteoporosis. Transgender people (regardless of birth assigned sex) who have undergone gonadectomy and have a history of at least 5 years without hormone replacement should also be considered for bone density testing, regardless of age (Grading: X C W).**

Modality of screening

Dual-energy x-ray absorptiometry (DEXA) of the hip and lumbar spine.

Special considerations

There have been no studies to determine whether clinicians should use the natal sex or affirmed gender for assessment of osteoporosis, e.g., when using the FRAX® tool (http://www.shef.ac.uk/FRAX/). Although some researchers use the natal sex, with the assumption that bone mass has usually peaked for transgender people who initiate hormones in early adulthood, this should be assessed on a case by case basis until there is more data available. This assumption will be further complicated by the increasing prevalence of transgender people who undergo hormonal transition at a pubertal age, or soon after puberty. Sex for comparison within risk assessment tools may be based on the age at which hormones were initiated, and length of exposure to hormones. In some cases it may be reasonable to assess risk using both the male and female calculators and using an intermediate value.

Weak evidence suggests that agonadal states contribute to an increased risk of osteoporosis, however long term studies are lacking.[14] **Transgender people without gonads, and who are not using hormone replacement, should follow screening and prevention guidelines for agonadal or postmenopausal women, regardless of birth-assigned sex or gender identity (Grading: X C W).**

Advice should be given to modify risk factors for osteoporosis, including tobacco cessation, Correct low vitamin D levels, maintain calcium intake in line with current guidelines for non-transgender people, weight bearing activity, and moderation of alcohol consumption.

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14. Transgender health and HIV

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Introduction

General guidelines for HIV screening, prevention, and care do not differ for transgender people; however, **HIV services for transgender people should address the specific biological, psychological, and social needs of this population.**[1] HIV prevention and care programs adapted from practices developed for non-transgender men who have sex with men (MSM) or for non-transgender women fail to address the unique structural factors and inequities that increase HIV risk and produce barriers to care among transgender people. For example, many trans women (especially young adults, racial/ethnic minorities and undocumented individuals) experience intersecting discrimination and high rates of trauma, unstable housing, poverty, incarceration, and unemployment, which all negatively impact HIV risk, testing, and continuing care.

Antiretroviral treatment (ART) recommendations for transgender women using feminizing hormones are complicated by lack of data on forms of estrogen commonly used for gender-affirming hormone therapy; therefore there is a need to extrapolate data on drug-drug interactions from studies using combination oral contraceptives. Little data exist on HIV among transgender men, likely due to much lower HIV prevalence. However, evidence for HIV risk among transgender men who have sex with men is growing.[2–4]

In line with national guidelines from the U.S. Centers for Disease Control (CDC) and the U.S. Preventive Services Task Force (USPSTF) that recommend universal screening for HIV, all transgender persons should be screened at least once for HIV. After initial screening of all patients, repeat screening is based on HIV risk assessment. **Effective risk assessment requires the ability to obtain an accurate sexual history that includes anatomy-specific sexual behavior**. Transgender women who have a penis should be asked about insertive intercourse as well as receptive intercourse. Transgender women and men who have a vagina should be asked about vaginal as well as anal intercourse, although the risk of HIV acquisition via receptive vaginal sex in a transgender woman who has undergone vaginoplasty is unknown. Risks associated with male genital reconstructions such as phalloplasty or metaoidioplasty are unknown. Open-ended questions that do not assume the anatomy and sex or gender of partners are likely to provide the most information.

Prevention

Condoms continue to be a mainstay of HIV prevention. However, using condoms may be difficult for transgender women taking feminizing hormones due to reduced tumescence. Transgender women may also lack the agency to negotiate the use of condoms during sex, especially those who engage in sex work.[5] The role of condoms in transgender men who have undergone phalloplasty is unknown and likely depends on the specific anatomy and

surgical approach used. "Female" condoms may be an option for transgender men who engage in receptive vaginal sex.

Newer biomedical HIV prevention interventions increase the options available to reduce HIV risk. There are two categories of medications currently available that are designed to be taken by people who do NOT have HIV for the purposes of preventing HIV acquisition: 1) pre-exposure prophylaxis (PrEP) and 2) non-occupational post-exposure prophylaxis (nPEP).

Pre-exposure prophyalxis (PrEP)

Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in studies with MSM, non-transgender heterosexual adults, and people who inject drugs. CDC has published detailed clinical guidelines for the use of PrEP for individuals at high risk for HIV acquisition.[6]

A sub-analysis of data from a large multi-national randomized controlled trial of PrEP suggests that PrEP is effective in preventing HIV in transgender women when they take the medication as prescribed. However, no efficacy was found among transgender women on "intent-to-treat" analysis.[7] Importantly, all of the transgender women who seroconverted in the PrEP arm of the study had no detectable TDF in their blood, suggesting that they did not take the medication as prescribed. There are no known drug-drug interactions between TDF/FTC and gender-affirming hormones, nor are there any known contraindications to concomitant use of PrEP with gender-affirming hormone therapy. To effectively engage transgender women, PrEP programs should use trans-inclusive marketing strategies, address community concerns about drug interactions between TDF and gender-affirming hormones, and ensure services are delivered by a provider who is knowledgeable about trans health.[8]

Non-occupational post-exposure prophylaxis (nPEP)

The use of nPEP in transgender people should follow guidelines as in non-transgender people. As with PrEP, social marketing and awareness campaigns should be tailored to transgender populations.

Treatment of HIV concurrent with hormone therapy

HIV and its treatment are not contraindications to hormone therapy. In fact, providing hormone therapy in the context of HIV care may improve engagement and retention in care [9] as well as adherence and viral load.[10,11] The World Health Organization [12] as well as the U.S. Department of Health and Human Services [13] recommend antiretroviral therapy for everyone living with HIV, regardless of HIV viral load or CD4 count.[14]

Metabolism of estrogens occurs via the cytochrome P450 enzyme system; therefore there are potential drug-drug interactions with ART agents. Information about these interactions are based on studies in the context of contraception and typically include ethinyl estradiol rather than 17-beta estradiol recommended for feminization. Data are not available on drug interactions between hormones and ARTs in the setting of transgender care. However, **based on available data, most ART can be likely used safely used with estrogen with two**

exceptions: Amprenavir (Agenerase) and unboosted fosamprenavir (Lexiva) are not recommended for co-administration with estrogens due to a decrease in amprenavir serum concentrations.[13]

Limited data suggest that non-nucleoside reverse transcriptase inhibitors (NNRTIs), ritonavir (RTV)-boosted protease inhibitors (PIs), or cobicistat with integrase strand inhibitors (INSTIs) may have an effect on blood levels of some hormonal contraceptive agents. There are no known drug-drug interactions between ethinyl estradiol and nucleoside reverse transcriptase inhibitors (NRTIs), CCR5 antagonists, fusion inhibitors, or non-boosted INSTs. Interactions vary between an decrease or increase in blood levels of ethinyl estradiol, norethindrone, or norgestimate. Such interactions could potentially result in decreased hormonal efficacy or increase hormonal adverse effects.

Transgender women may prioritize hormone therapy over other care; such symptoms may result in decreased ART adherence if it is perceived that these symptoms are due to ART. Consider monitoring estradiol levels and/or making empiric dosing or regimen adjustments based on development of or changes in estrogenic symptoms when initiating or changing anti-retroviral therapy.

There are limited data on the interactions between ART and masculinizing hormones or other drugs used as anti-androgens for feminization. Currently, there are no documented interactions between ART and either androgens (e.g., testosterone) or anti-androgens (e.g., spironolactone).

Hormone therapy and management of HIV-related opportunistic infections and prophylaxis

Patients with immunosuppression due to HIV may require treatment or prophylaxis for opportunistic infections. Most commonly this involves Trimethoprim – Sulfamethoxazole (TMP-SMX) daily for prevention of PCP pneumonia. A significant interaction leading to hyperkalemia, hospitalizations and deaths has been described in non-transgender patients between spironolactone and TMP-SMX. It is advisable to maintain a high index of suspicion when these drugs are used in combination, with frequent monitoring of serum electrolytes and renal function. Avoiding this combination is especially recommended especially in older patients.[15,16]

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15. Transgender health and hepatitis C

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Introduction

While there is no evidence that being transgender is an independent risk factor for hepatitis C, some transgender sub-populations may be at increased risk. Rates of HIV and injection drug use are higher among transgender people, and transgender people may inject hormones or soft tissue fillers such as silicone.[1] Sharing or use of contaminated needles, syringes, or vials represents a possible risk factor for infection with blood borne pathogens, including hepatitis C, though the actual prevalence of needle sharing among transgender people is believed to be low.[2,3] Nevertheless, patient education for transgender people using injectable hormones should include advice to use sterile syringes only once without sharing. Providers should screen all transgender people for hepatitis C risk factors and perform an antibody screen in those determined to be at risk, as per current guidelines. All transgender people who inject soft tissue fillers should be screened for hepatitis C.

Chronic HCV and hormone therapy

Chronic Hepatitis C is not a contraindication to hormone therapy. Both estrogen and testosterone undergo hepatic metabolism, and routine monitoring of hepatic function has been recommended. However, neither hormone has been associated with hepatic injury or abnormal liver function tests. Monitoring of liver function in patients with chronic hepatitis C infection should proceed as routinely recommended by disease stage and risk factors for progression dictate. Non-oral forms of hormone therapy avoid first pass through liver metabolism and may be preferred for patients with liver disease, though there is no specific evidence to support this recommendation.[4]

Hepatic dysfunction and malignancies have been noted with oral methyltestosterone. However, methyltestosterone is no longer available in most countries and should no longer be used as part of a gender-affirming hormone regimen. Oral testosterone undeconoate gel caps available outside the United States were not associated with hepatic dysfunction in a 10-year safety study among non-transgender males.[5] No published data is available on clinical outcomes among transgender individuals with chronic viral hepatitis taking hormone therapy.

Chronic HCV treatment and hormone therapy

The American Association for the Study of Liver Diseases recommends treatment for all patients with chronic HCV infection, except those with short life expectancies owing to comorbid conditions.[6] Antiviral medications used for treatment of hepatitis C vary based on HCV genotype, stage of disease, and HCV treatment history; most are metabolized via the same cytochrome P450 pathway as oral estrogens.[7] The table below summarizes currently known drug interactions between estrogens and hepatitis C antivirals.

Table 15-1. Drug Interactions between Estrogens and HCV Antivirals

Contraceptives & Hormone Replacement	Boce-previr	Daclat-asvir	Ledipasvir/ Sofosbuvir	OBV/P TV/r	OBV/PTV/r + DSV	Sime-previr	Sofos-buvir	Tela-previr
Desogestrel	?	✓	✓	?	?	✓	✓	?
Dienogest	?	✓	✓	?	?	✓	✓	?
Drospirenone	X	✓	✓	✓	✓	?	✓	?
Estradiol	?	✓	✓	?	?	✓	✓	?
Ethinyl estradiol	?	✓	✓	X	X	✓	✓	?
Norethisterone (Norethindrone)	?	✓	✓	?	?	✓	✓	?

Legend
X = These drugs should not be coadministered
? = Potential interaction – may require close monitoring, alteration of drug dosage or timing of administration
✓ = No clinically significant interaction expected

Abbreviations
OBV/PTV/r = ombitasvir/paritaprevir/ritonavir;
OBV/PTV/r + DSV = ombitasvir/paritaprevir/ritonavir + dasabuvir.

Table drawn from HEP Drug Interactions Checker (http://www.hep-druginteractions.org/interactions.aspx)

Co-administration of estradiol with boceprevir, ombitasvirparitaprevir/ritonavir, dasabuvir, or telaprevir could potentially increase estradiol exposure; however, co-administration has not been studied. Co-administration of ethinyl estradiol with boceprevir or telaprevir was found to decrease estrogen levels.[8] Elevated liver enzymes were seen in cisgender women taking ethinyl estradiol with OBV/PTV/r and concomitant use (with or without DSV) is not recommended. In summary, ethinyl estradiol is contraindicated with ombitasvir/paritaprevir/ritonavir. There is no evidence on potential interactions between HCV anti-viral meds and 17-beta estradiol, and providers should consider avoiding OBV/PTV/r with or without DSV in patients using estradiol.[8] Transgender women on estrogen therapy should be closely monitored when starting or stopping HCV treatment.

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16. Transgender people and sexually transmitted infections (STIs)

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Introduction

National guidelines exist on how to take a sexual history and the recommended frequency for sexually transmitted infections (STIs) screening by gender and risk group.[1] The 2015 CDC guidelines 2015 STD Treatment Guidelines do include transgender men and women as special populations, and recommend risk assessment based on current anatomy and sexual behaviors, awareness of symptoms consistent with common STIs, and screening for asymptomatic STIs based on behavioral history and sexual practices.[2] However, these guidelines do not include specific screening or interval recommendations. Presented here are specific considerations when screening for STIs in transgender people. Recommendations for management of confirmed STIs does not differ from those for non-transgender people. Screening intervals should be based on risk, with screening every three months in individuals at high risk (multiple partners, condomless sex, transactional sex/sex work, sex while intoxicated).

In practice, transgender people may avoid screening procedures and physical examinations due to fear of discrimination,[3] encountering providers who are inadequately trained in transgender health,[4] or personal discomfort with the visit or exam.[5] It is important for clinicians to build a trusting and respectful rapport and to clearly explain reasons for asking sexually explicit questions and performing various components of the exam.

Sexual history and risk assessment

Clinicians should assess risk for sexually transmitted infections (STIs) based on the patient's sexual behaviors and current anatomy. Because transgender people differ in hormone use, history of gender-affirming surgical procedures, and patterns of sexual behavior, providers should avoid making any assumptions about presence or absence of specific anatomy; sexual orientation; or sexual practices. Anatomy and behavior may change over time; therefore, it will be important to assess for changes that may impact STI risk. To facilitate a respectful rapport, use the patient's preferred terminology to refer to anatomic parts.

The Fenway Guide provides suggested sexual risk assessment questions [6] including:

- Are you having sex? How many sex partners have you had in the past year?
- Who are you having sex with? (including anatomy and gender of partners)
- What types of sex are you having? What parts of your anatomy do you use for sex?
- How do you protect yourself from STIs? (How often do you use condoms/barriers? Any use of PrEP?)
- What STIs have you had in the past, if any? When were you last tested for STIs?

- Has your partner(s) ever been diagnosed with any STIs?
- Do you use alcohol or any drugs when you have sex?
- Do you exchange sex for money, drugs, or a place to stay?

These questions are components of a complete sexual history which would include relationship types, frequency of sexual activity, age of sexual debut, use of drugs or alcohol during sex, sex work history, history of sexual abuse, and sexual function.[7]

Physical exam and STI screening

Serologic screening recommendations for transgender people (HIV, Hepatitis B and C, Syphilis) do not differ in recommendations or technique from those for non-transgender people.

Many transgender people have experienced violence, including sexual violence.[3] Therefore, providers should take a chaperone trauma-informed approach to the exam, whenever possible.[8] This approach is grounded in providing a sense of control to the patient and includes: greeting patients while they are dressed; explaining what you plan to do and why; providing information, choices, and decision-making ability.[9] Some transgender patients may prefer to collect their own specimens to allow for greater control over the screening process. Self-collected vaginal and rectal swabs as well as urine specimens have equivalent sensitivity and specificity to provider-collected samples for nucleic acid amplification testing for gonorrhea, chlamydia, and trichomonas.[1] The physical exam should focus on organs that are present and have the potential for infection based on the sexual history.

Transgender women who have undergone vaginoplasty (either penile inversion or colo-vaginoplasty) do not have a cervix, therefore screening for cervical HPV is not appropriate. Some surgical approaches include the use of urethral tissue, which could result in mucosal infectious such as chlamydia or gonorrhea. The risk of infection of intact, inverted penile skin with these organisms is unknown, though lesions such as a syphilitic chancre, herpes or chancroid are possible. When clinically indicated due to symptoms, a physical examination and appropriate testing should be performed. The anatomy of a neovagina created in a transgender woman differs from a natal vagina in that it is a blind cuff, lacks a cervix or surrounding fornices, and may have a more posterior orientation. As such using an anoscope may be a more anatomically appropriate approach for a visual examination. The anoscope can be inserted, the trocar removed, and the vaginal walls visualized collapsing around the end of the anoscope as it is withdrawn. There is no evidence to guide a decision to perform routine pelvic exams on transgender women in order to screen for such conditions as [formerly penile skin] warts or lesions.

Transgender women who have undergone vaginoplasty retain prostate tissue, therefore infectious prostatitis should be included in the differential diagnoses for sexually active trans women with suggestive symptoms. There is no evidence to guide routine screening for Chlamydia in asymptomatic transgender women who have undergone vaginoplasty, though it is reasonable to consider urinary screening in women with risk factors. The role of vaginal gonorrhea and Chlamydia specimens, as opposed to urine testing only, is unknown in women

who have undergone penile inversion. Providers may consider vaginal testing however urine testing should be considered essential.

Pelvic inflammatory disease should be in the differential for transgender men with a uterus and fallopian tubes who have vaginal intercourse. Testosterone use is associated with vaginal atrophy; therefore, use of lubricant and a small speculum may be appropriate for pelvic and speculum exams among transgender men with vaginas. Some transgender men retain patent vaginas after metoidoplasty and may require vaginal screening based on sexual history. Screening for cervical cancer and HPV are covered elsewhere in these guidelines.

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17. Testicular and scrotal pain and related complaints

Primary author: Barry Zevin, MD

Introduction

The prevalence of scrotal contents complaints is unknown, though anecdotally are not rare.

A common cause of scrotal contents pain in transgender women is "tucking," which allows a female-appearing genital contour in tight fitting clothing. Tucking involves manually displacing the testes upward into the inguinal canal, and then positioning the penis and scrotal skin between the legs and rearward toward the anus. Tight underwear, tape or a special garment known as a gaff is then used to maintain this positioning. Many transgender women find this practice to be gender-affirming, and may maintain this positioning even at night when asleep. Resulting pain may be traumatic, mechanical or neuropathic. Prolonged tucking may also result in urinary reflux and symptoms of prostatism or even infection such as epididymo-orchitis, prostatitis, or cystitis. Prolonged positioning of a compressed urethral meatus in close approximation to the anus may also serve as a portal of infection. Pain related to the onset of hormone therapy is a common complaint however the etiology of this symptom is unknown.

Acute scrotal contents pain requires a workup to rule out conditions requiring emergency treatment. A physical exam to rule out tumors, hernia, hydrocele or other causes of pain is appropriate. Appropriate imaging should be performed when indicated.[1,2]

Treatment approaches

For acute scrotal contents pain investigation for torsion, infection (especially gonorrhea and chlamydia), inguinal hernia, and occult trauma should be performed when appropriate. If no condition requiring emergency treatment is found, treatment with NSAIDs can be effective.[2]

Counseling and education on safer ways of tucking may be the most effective approach to relieving pain believed to be related to this practice. This might include shorter periods of tucking or less tight tucking. Ready access to transgender surgeries when medically necessary, including orchiectomy and vaginoplasty for the treatment of gender dysphoria, may also minimize this condition.

Chronic orchialgia algorithms for non-transgender men often suggest an empirical course of antibiotics (after attempting diagnosing an etiology) and discourage orchiectomy as a last resort measure. This algorithm may not be appropriate for transgender women. Patients often have gender dysphoria and maybe relieved to be offered orchiectomy (as opposed to non-transgender men, who are typically resistant to even unilateral orchiectomy when indicated); orchiectomy may be raised much higher in the treatment algorithm in these cases. When orchiectomy is not indicated, medications used in the treatment of neuropathic pain may be

useful. Pain related to onset of hormone therapy is generally benign, improves spontaneously, and can be treated expectantly and with reassurance.[1,3]

All providers should be aware that physical examination of the genitals may be traumatizing for trans women and must be done with sensitivity and care if necessary. Providers should not discount testicular pain complaints in transgender individuals, and should avoid any perception that transgender women with this complaint are malingering in hope of obtaining an orchiectomy.

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18. Free silicone and other filler use

Primary authors: Barry Zevin, MD and Madeline B. Deutsch, MD, MPH

Introduction

Medical grade silicone has origins in aircraft lubricants developed after World War II; U.S. Army staff noticed that drums of Dow 200 silicone lubricant were disappearing from supply rooms, and traced these drums to providers who were injecting the material. By the 1960s, Dow Chemical had introduced a purified medical silicone (Dow 360), intended for use as a syringe lubricant and as a pharmaceutical vehicle. Subsequent off-label use of Dow 360 was associated with a number of poor outcomes, and by the 1970s some laws had been passed banning the use of such injections.[1] By the 1990s, a more viscous silicone material (Silikon-1000) had been approved by the FDA for vitreal injections, with soft tissue injections considered "acceptable off-label use".[1] Medically appropriate use of free silicone injections involves recurrent injections of <0.1cc by a trained practitioner, with the intention of causing a local fibroblasic reaction and collagen growth, ultimately resulting in changes in the subcutaneous contour.[2] Such an approach has been described in the management of HIV-related lipodystrophy.[2]

"Silicone injections" in the context of transgender health actually refer to any one of a number of soft tissue fillers, typically injected by an unlicensed or unscrupulous medical provider. The actual composition of the injected substances is often unknown and may not be of medical grade; contents may include aircraft lubricant, tire sealant, window caulk, mineral oil, methylacrylates, petroleum jelly, or other substances.[3] In cases of these unsupervised injections, the injected volume (1-3 liters or more) far exceeds what may be performed by a licensed medical provider. Additionally, attention sterility and techniques to avoid embolization may be lacking. Large events ("pumping parties") may take place at which many transgender women receive large volume injections.[4] Estimates of the frequency of injections range from 20% to more than 50% of some populations of transgender women.[5,6] Data from outside the U.S. includes an estimate of 40% of transgender women in Lima, Peru,[3] and 68% of transgender women in several large Thai cities.[7] While most data and anecdotes on soft tissue injections are in transgender women, use among transgender men is also theoretically possible.

Motivations for seeking soft tissue injections

Motivation for receiving the injections may include a strong desire for immediate body changes to relieve gender dysphoria, especially when other modalities of treatment are, unavailable, inaccessible, or perceived as ineffective or slow. The immediate results may encourage community members to recommend the procedures to their peers before any signs of adverse effects appear. A qualitative study of silicone use in transgender women found four contributing factors to this epidemic: poor self-image, misperceptions about silicone, discomfort in public settings (rapid and extensive feminization from silicone helps transgender

women blend or "pass"), and low access to health insurance.[8] Other contributing factors include lack of a general awareness of risks in the community, peer pressure, enhanced feminine features to support survival sex work, and the ability to achieve feminization without hormones in order to retain erectile function.[9]

Complications and adverse reactions

Complications may be categorized by time of onset (immediate, early, delayed/late) and by location of effect (local, remote, systemic).[10–12]

Immediate adverse effects of silicone and other substances include silicone embolization, bleeding, pain, and focal erosions and necrosis. Localized skin papules and hypersensitivity reactions are possible. Silicone embolization involving the lungs may result in adult respiratory distress syndrome (ARDS) and death. Some patients have survived multisystem failure due to this condition with severe disability as sequelae including loss of limbs.[11,13–18]

Early adverse effects in the days or weeks following injection include inflammatory nodules with infection due to traditional skin and soft tissue pathogens as well as atypical mycobacteria, and which may be fluctuant. Non-inflammatory nodules may also develop causing pain, itching, and abnormal pigmentation.[18,19] Angioedema is also possible.

Long term adverse effects occurring weeks to years after the injection include migration of silicone with associated pain or deformity. Local or remote inflammatory and non-inflammatory nodules may develop; some may evolve into sterile abscesses or fistulas. Silicone granulomas may develop, with findings of pain, swelling, ulcerations, lymphadenopathy, and possible systemic constitutional symptoms. Biopsy of such lesions shows foreign body granulomas with white vacuoles and surrounding inflammatory cells. Pathogenesis of these lesions may include T cell activation and the presence of biofilms. Other potential complications include secondary lymphedema, telangiectasias and persistent erythema.[18]

Major systemic complications include systemic inflammatory response syndrome (SIRS)/ARDS, sepsis, embolization, hypersensitivity pneumonitis, immune reconstitution inflammatory syndrome (IRIS), or hypercalcemia,[14,18,20] Organ failure is also possible due to direct mass-effects.

Diagnosis

A detailed history can help identify any prior soft tissue injections, or risk factors for use. Patients may be hesitant to disclose prior procedures. Ultrasound, CT or MRI may be helpful adjuncts. Mammography may be ineffective in breasts that have been previously injected. In those patients with a history of extensive injections, soft tissue ultrasound may be a useful tool to guide therapeutic injections for the management of syphilis, gonorrhea, HIV (enfuvirtide), or for vaccines.[21]

Prevention: No research has been conducted on the best practices in preventing the use of medically unsupervised soft tissue fillers. Strategies likely to reduce the prevalence of unlicensed silicone injection include: educating transgender women about risks and alternatives, as well as making available more conventional gender-affirming treatment such

as hormones and surgery. Community level interventions, utilizing peer health advocates or promotoras may be more effective than provider-originated interventions.

Treatment Approaches: Successful treatment of acute emergencies related to soft tissue injections requires rapid recognition and quick application of intensive care. Delays occur both because of patient hesitation to seek care or report that they received soft tissue injections, and a failure of health care providers to recognize the emergency and to have the knowledge of the necessary treatment.

Management of most complications is supportive and symptom-driven. Minocycline shows promise as a first line antibiotic in the setting of infections due to additional anti-inflammatory properties.[12] Use of surgical excision and reconstruction flaps/grafts may be necessary.[22] Complete mastectomy with breast reconstruction may be necessary for patients with free silicone spread throughout the breasts.[23,24] Other potential approaches include intralesional corticosteroid injections, topical imiquimod, or etanercept 25mg subcutaneously twice/weekly.[19] Liposuction has been described in the past but is not likely to be of benefit.[25]

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19. Fertility options for transgender persons

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Introduction

Transgender people have the same range of reproductive desires as do non-transgender people. Although data are limited, there is no evidence that children of transgender parents are harmed in any unique way.[1] **It is recommended that prior to transition all transgender persons be counseled on the effects of transition on their fertility as well as regarding options for fertility preservation and reproduction (Grading: T O S).**[2,3]

Exogenous hormones and gonadectomy (removal of testes or ovaries) have clear impacts on fertility. Reproduction in transgender persons who have initiated transition and retain their gonads generally involves discontinuation of exogenous hormones, though ovulation and spermatogenesis may continue in the presence of hormone therapy. If an individual has not undergone gonadectomy, and if an initial evaluation demonstrates an absence of ovulation or spermatogenesis, return of fertility may be possible after discontinuing hormone therapy for a period of time. Anecdotally the time to return of fertility can range from 3-6 months, though some may experience permanent loss of fertility, or require assisted technologies as described below.

Because infertility is not absolute or universal in transgender people undergoing hormone therapy, all transgender people who have gonads and engage in sexual activity that could result in pregnancy should be counseled on the need for contraception. Gender-affirming hormone therapy alone is not a reliable form of contraception, and testosterone is a teratogen that is contraindicated in pregnancy. It is unknown how long of a testosterone washout period is appropriate in transgender men prior to pregnancy (Grading: X C S).

Fertility preservation options may include sperm, oocyte, embryo, ovarian tissue or testicular tissue cryopreservation.[4] These are similar to options available to men and women undergoing gonadotoxic cancer therapies or elective fertility preservation for social reasons.

Assisted reproduction may include the full range of fertility services. Whether long-term hormone exposure confers any unique medical risks to the patient undergoing assisted reproduction procedures or any long-term impact on gametes and to future offspring is currently unknown. Transgender patients who undergo fertility preservation or assisted reproduction should be informed of the lack of data on outcomes.

Reproductive options for transgender women

In transgender women, research suggests that prolonged estrogen exposure of the testes has been associated with testicular damage.[2] Restoration of spermatogenesis following extended estrogen treatment, however, has not been well studied.[2] The most successful option for fertility preservation for transgender women is cryopreservation of sperm prior to

initiation of hormone therapy. Clomiphene citrate or hCG injections are sometimes used to stimulate spermatogenesis. Several recently reported cases of uterine transplantation into non-transgender women represent a potential future option, however this technology is still in infancy.

Reproductive options for transgender men

The effect of prolonged treatment with exogenous testosterone on ovarian function is unclear. Testosterone therapy usually leads to anovulatory state and amenorrhea. This is usually reversible upon discontinuation of testosterone therapy, and pregnancies have been reported in transmen following prolonged testosterone treatment.

Fertility preservation options for transgender men include oocyte cryopreservation, embryo cryopreservation, and ovarian tissue cryopreservation. The frozen-thawed oocytes or embryos can then be later used for establishing a pregnancy using the patient's uterus or by transfer into a female partner or gestational carrier. While solid data are lacking, transgender men who have initiated transition have been able to discontinue testosterone treatment and undergo insemination of sperm or IVF with embryo transfer to the patient's uterus, a female partner or gestational carrier.

A recently published report surveyed transgender men who experienced pregnancy after initiation of testosterone.[5] Eighty percent resumed menses within 6 months of stopping testosterone. Seven percent used fertility medications. Obstetrical outcomes were similar in the testosterone and non-testosterone users, however it is not clear if participants reporting testosterone use were receiving testosterone at the time of conception and during pregnancy. The men in the study also expressed a desire for more supportive resources and reported a lack of provider awareness and knowledge regarding fertility in transgender patients. One third of the pregnancies were unplanned, though it is not clear how many of these unplanned pregnancies occurred in the setting of current testosterone use. Nevertheless, such findings highlight the need for contraception in some patients.

Ovarian tissue cryopreservation is currently still considered experimental. There have been several live births reported worldwide resulting after autotransplantation of cryopreserved ovarian tissue.[6,7] However, there have yet to be any live births resulting from in-vitro maturation of oocytes derived from frozen-thawed ovarian tissue fragments. Research to create gametes through stem cell techniques is also ongoing.

All patients should also be informed that these assisted reproductive options are expensive and often not covered by insurance. Mental health counseling and support should be made available for those transgender people pursuing reproductive options who request or require such services.

Fertility preservation for children & adolescents

It is recommended that transgender children and adolescents, and their guardians, also be informed and counseled regarding options for fertility preservation prior to the initiation of pubertal suppression and treatment with gender-affirming hormones. In children who have

initiated natal puberty, fertility preservation options include sperm, oocyte, and embryo cryopreservation. Currently it is not possible for children who have not undergone natal puberty (and who may have used gender-affirming hormones) to preserve gametes.

Prolonged pubertal suppression using gonadotropin releasing hormone (GnRH) analogs is usually reversible and should not impair resumption of puberty upon cessation, though most children who undergo pubertal suppression go on to begin gender-affirming hormone therapy without undergoing natal puberty.

Further discussion of pubertal suppression, and the decision to undergo gonadectomy prior to the legal age of majority, is included in the guidelines for transgender children and adolescents.

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20. General approach to cancer screening in transgender people

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Long term follow up case control studies have not identified differences in cancer rates in trans patients undergoing hormone therapy compared to birth-sex controls, however these studies had many limitations.[1,2] Insufficient evidence exists to determine if transgender people increased or decreased overall as well as organ-specific cancer risk. Primary care providers should conduct an organ based routine cancer screening for all transgender patients in accordance with current guidelines as a component of comprehensive primary care. **As a rule, if an individual has a particular body part or organ and otherwise meets criteria for screening based on risk factors or symptoms, screening should proceed regardless of hormone use (Grading: X C S).** Therefore, an ongoing and thorough medical and surgical history is crucial to determine an individual patient's screening needs.

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21. Screening for breast cancer in transgender women

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Introduction

Adaptation of recommendations for screening in transgender women are complicated by the lack of consensus on breast cancer screening in non-transgender women. Existing recommendations vary widely in each of these critical considerations, and are subject to numerous biases based on the interests of the organization and its constituency.[1–7]

Ideal breast cancer screening recommendations minimize mortality and missed diagnoses, while at the same time avoiding over-screening, with its inherent risks of unnecessary follow-up studies, emotional distress, and potentially invasive biopsies and other procedures. It is noteworthy that the positive predictive value (PPV), defined as the likelihood of a positive screening test representing a true presence of the disease (as opposed to a being a false positive) declines as the prevalence of the disease within a specific population declines.

Breast cancer risk in transgender women

In transgender women, factors that may contribute to a reduced risk of breast cancer include potentially less lifetime overall or cyclical exposure to estrogen and in some cases the absence of or minimal exposure to progesterone. However, transgender women have a high prevalence of dense breasts, an independent risk for breast cancer and also a predictor of increased rates of false negative mammograms; a Dutch study of 50 transgender women found that 60% had "dense" or "very dense" breasts on mammography.[8]

Existing retrospective data on transgender women have mixed findings. Two retrospective population based studies of breast cancer in transgender women have been reported; both reported only on cases of breast cancer which were detected as part of routine clinical care, as opposed to through a structured and broad screening program. A retrospective study of 2,307 Dutch transgender women treated at a single center found an estimated incidence of 4.1/100,000 person-years, in comparison to the incidence of 155/100,000 person-years in the general Dutch non-transgender female population.[9] A retrospective review of 3,566 transgender women receiving care in the U.S. Veterans Administration Healthcare System found 3 cases total, translating to a non-significant standardized incidence ratio (SIR) of 0.7 (95% CI 0.03 to 5.57) in comparison to non-transgender women, and a significant SIR of 33.3 (95% CI 21.9 to 45.1) in comparison to non-transgender men.[10] It is unclear how many cases of breast cancer went undetected in these two populations, and were then otherwise lost to follow-up or to mortality (known to be high in transgender women) from other causes.[11]

Data on breast cancer in transgender women has been limited to the above studies as well as several case reports, and is overall reassuring with regards to risk being not higher, and possibly lower than in the non-transgender female population.

Age to first consider screening

The only large population based study of mammography before age 50 was conducted in the UK on 160,921 women and found no difference in overall breast cancer mortality.[12] Given the equivocal value of screening before age 50 and the likely lower incidence in transgender women, it is recommended that screening mammography in transgender women not begin before age 50.

Length of exposure to feminizing hormones

Transgender women differ from non-transgender women in the length of exposure to estrogens as well as variable exposure to progestagens. As such it is recommended that screening not commence in transgender women until after a minimum of 5 years of feminizing hormone use, regardless of age. Some providers may choose to discuss the risks and unknowns with patients and delay screening until after up to 10 years of feminizing hormone use, regardless of age. Note that transgender women over age 50 do not meet screening criteria until they have at least 5-10 years of feminizing hormone use.

Frequency of screening

Existing recommendations in non-transgender women vary with respect to the frequency of screening. As with the age of onset, given the likely lower incidence in transgender women, **it is recommended that screening mammography be performed every 2 years, once the age of 50 and 5-10 years of feminizing hormone use criteria have been met. Providers and patients should engage in discussions that include the risks of overscreening and an assessment of individual risk factors (Grading: T O W).** Risk score calculators such as the GAIL method may be unreliable when used in transgender women.

Modality of screening

Screening mammography is the primary recommended modality for breast cancer screening in transgender women. Transgender women are often concerned with their breast appearance and development, and may perform frequent unguided self-examinations. Early breast development may be associated with breast pain, tenderness, and nodularity. Transgender women may request breast exams for these symptoms, or may find breast examinations to be gender-affirming. As such providers may consider periodic clinical breast exams, and/or a discussion with patients about general breast awareness and health, however as with non-transgender women,[13] formal clinician or self breast exams for the purpose of breast cancer screening are not recommended in transgender women.

Special considerations

As with non-transgender women, clinicians may choose to reduce the age of onset of screening, number of years of feminizing hormone exposure, or frequency of screening in patients with significant family risk factors. Transgender women with a family history suggestive of (or known) a BRCA mutation should be referred for genetic counseling. No data exists to guide the use of estrogens in transgender women found to have a BRCA mutation. Data on breast cancer risk in non-transgender men with BRCA mutations are limited, with data on BRCA-1 suggesting a lifetime risk of 1.2-5.8%, [14-16] and data on BRCA-2 suggesting a lifetime risk of 6.8%. The risk is much higher for non-transgender women with a BRCA mutation, at 78% lifetime risk. [14, 17] It is unclear if transgender women with the BRCA-1 mutation and using estrogen have a risk above that of non-transgender men, and what role the age at start and total length of exposure to estrogen might play. A single case report of a transgender woman with the BRCA-1 mutation involved the continued use of estrogen under informed consent.[18]

A retrospective cohort study of 1,263 transgender women receiving care at a large urban community health center patients in the United States found that transgender individuals between ages 50 and 74, and with a history of at least 5 years of hormone therapy were significantly less likely than non-transgender individuals to have a mammogram per guidelines (AOR = 0.53; 95% confidence interval = 0.31, 0.91).[19] Further research is needed to understand barriers and other factors which underlie this disparity.

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22. Prostate and testicular cancer considerations in transgender women

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Prostate cancer

Documented cases of prostate cancer in trans women with a variety of hormone use and surgical histories have been reported.[1–3] Most cases of prostate cancer in trans women have been in individuals who started hormones after age 50; such cases may actually represent occult neoplasms, which existed prior to initiation of hormone therapy.[4] In a cohort of 320 transgender women in Belgium who had undergone vaginoplasty, PSAs along with transvaginal ultrasound and digital vaginal examination of the prostate revealed lower PSA and prostate volume than what would be expected in a non-transgender men of corresponding age.[5] Some anti-androgens, such as 5-alpha reductase inhibitors have also been documented to decrease the PSA result.[6] Removal of gonads in addition to estrogen exposure likely reduces risk for prostate cancer and benign prostatic hypertrophy.[4,5]

Regardless, primary care providers should remain aware of the possibility of prostate cancer in transgender women, even those who have undergone gonadectomy. The decision to perform screening for prostate cancer in transgender women should be made based on guidelines for non-transgender men. If a prostate exam is indicated, both rectal and neovaginal approaches may be considered. Transgender women who have undergone vaginoplasty have a prostate anterior to the vaginal wall, and a digital neovaginal exam examination may be more effective.[5] It should be noted that when PSA testing is performed in transgender women with low testosterone levels, it may be appropriate to reduce the upper limit of normal to 1.0 ng/ml.[4]

Testicular cancer

There has been one case of testicular cancer reported in the literature.[7] It is likely that risk decreases with androgen suppression. Routine testicular cancer screening is not recommended in non-transgender men, and there is no evidence to perform screening in transgender women. Transgender women adherent to therapeutic doses of estrogen plus an androgen blocker, and with persistent testosterone elevations, should be evaluated for testicular tumors by physical exam, as well as human chorionic gonadotropin (hCG), alpha-fetoprotein (AFP) and lactic dehydrogenase (LDH) levels, and possibly a scrotal ultrasound.

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23. Breast cancer screening in transgender men

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Transgender men who have not undergone bilateral mastectomy, or who have only undergone breast reduction, should undergo screening according to current guidelines for non-transgender women. No reliable evidence exists to guide the screening of transgender men who have undergone mastectomy. Since most or nearly all breast tissue may have been removed, mammography for the evaluation of a palpable lesion may not be technically feasible, and alternatives such as ultrasound or MRI may be necessary. The risk of breast cancer in residual breast tissues after mastectomy is unknown. It is important to obtain a clear surgical history, as some patients may have undergone only breast reduction. Some surgeons perform routine preoperative mammography. Some guidelines recommend annual chest wall exams in transgender men after mastectomy; however this is not based on evidence, and is in conflict with the move away from clinician exams in general for non-transgender women. Diagnostic physical exams may be appropriate in the case of new complaints. **Clinicians should engage in dialogue with transgender men who have undergone bilateral mastectomy about the unknown risks associated with residual breast tissue, as well as the possible technical limitations of mammography (Grading: X C S).**

24. Screening for cervical cancer in transgender men

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Introduction

Transgender men are at risk for cervical cancer. Cervical cancer is the third most common cancer globally [1]; more than 99% of which are caused by infection with one of several high risk oncogenic strains of the human papilloma virus (hr-HPV).[2] Pelvic exams to obtain pap smears may be challenging for transgender patients. Inadequate screening for cervical cancer is linked to the barriers transgender individuals face in accessing culturally sensitive health care.[3] Transgender men are less likely to be current on cervical cancer screening than non-transgender women.[4] Individuals who have never or have rarely been screened for cervical cancer are at the highest risk for progression of chronic hr-HPV infection to malignancy, morbidity and mortality.[5]

Transgender men who have sex with non-transgender men (trans MSM) report inconsistent condom use during receptive oral, vaginal and anal sex with non-transgender male sexual partners, and are at increased risk for hr-HPV infection and undetected disease progression.[6,7] HPV vaccination between the ages of 9 to 26 has the potential to significantly reduce rates of cervical, oral and anal cancer.[8–10] Adolescent non-transgender males are receptive to HPV vaccination, and 74% of non-transgender men who self-identify as gay or bisexual are willing to get vaccinated for HPV if recommended by their health care provider.[11,12]

Screening recommendations

Cervical cancer screening should never be a requirement for testosterone therapy. Cervical cancer screening for transgender men, including interval of screening and age to begin and end screening follows recommendations for non-transgender women as endorsed by the American Cancer Society, American Society of Colposcopy and Cervical Pathology (ASCCP), American Society of Clinical Pathologists, U.S. Preventive Services Task Force (USPSTF) and the World Health Organization (Grading: X C S).[13–15] As with non-transgender women, transgender men under the age of 21 should not have pap smears regardless of their age of sexual debut.[13] Pap smears on transgender men have a ten-fold higher incidence of an unsatisfactory result compared to non-transgender women, which is positively correlated with length of time on testosterone.[16] If erythema of vaginal and/or cervical tissue is noted, evaluation for usual causes of inflammation is warranted prior to reaching a diagnosis of exclusion of testosterone-mediated atrophic cervicovaginitis. Inflammation may obscure cervical cytological evaluation and result in an unsatisfactory result. In addition, the requisition should indicate any testosterone use as well

as the presence of amenorrhea, to allow the pathologist can accurately interpret cell morphology.

Improving patient experiences

Strategies to promote a more supportive and sensitive setting include using culturally sensitive language, interviewing the patient prior to disrobing, and asking the patient to change from the waist down only. A painful pap smear experience is correlated with non-adherence to future screening and colposcopy.[17] Several anecdotal techniques may reduce pain associated with speculum exams. A pediatric speculum may allow visualization of the cervix and can reduce discomfort with the exam; however it is important to avoid using a speculum so short that it requires excessive external pressure to visualize the cervix. Moving the buttocks past the end of the exam table and encouraging pelvic relaxation may also increase comfort and improve visualization of the cervix. If the examiner notes tension or anxiety, taking time to go through a verbal relaxation exercise can be helpful. Warm water may be used to lubricate a narrow speculum prior to insertion to minimize a patient's discomfort and dysphoria without compromising pap results. Water-based lubricant can reduce discomfort; using a minimal amount of lubricant on the outer portion of a speculum may reduce patient discomfort while minimally increasing the risk of an unsatisfactory sample.[18,19] Excessive lubricant should be avoided; studies have conflicting results on the effect of excessive lubricant on pap results. Some clinicians find inserting a speculum less uncomfortable for patients by first placing a finger or two in the vagina and performing posterior pressure while asking the patient to flex and relax their pelvic floor muscles. A digital (not bimanual) exam may also help identify the location of the cervix and minimize manipulation during the speculum exam. A formal bimanual exam on an otherwise asymptomatic patient may not add clinical value and may add to the patient's discomfort.[20] Other approaches to reduce discomfort might include allowing the patient to insert the speculum themselves or watch the procedure using a mirror, administration of oral benzodiazepines prior to the exam, or the use of vaginal estrogens for 1 week prior to the exam.

Preliminary research on self-collected vaginal samples for HPV compared to clinician obtained samples shows promise, this approach may also be more acceptable to transgender men.[21,22] Future initial HPV screening for transgender men may also utilize non-vaginal sourced specimens; studies supporting concordance of HPV in the urine with HPV in the cervix represent a potential method for a non-vaginal triage algorithm.

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25. Ovarian and endometrial cancer considerations in transgender men

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Endometrial cancer

The administration of exogenous testosterone, which then undergoes aromatization to estrogen, as well as the possible anovulatory state induced by testosterone, may create a hormonal milieu of "unopposed" estrogen. This creates a theoretical risk of endometrial hyperplasia or cancer. Despite this theoretical risk, only one case report of an endometrioid adenocarcinoma exists in the literature.[1] Two studies suggest that the risk of endometrial hyperplasia is low, and that transgender men may commonly have endometrial atrophy when on testosterone: One observational study found endometrial atrophy on histological report in almost half (45%) of trans men on testosterone when histology was performed post routine hysterectomy.[2] Another case control study performed histopathology on samples comparing trans men on androgens for at least one year to pre and post-menopausal women undergoing hysterectomy or histopathology, and found trans men had endometrial atrophy similar to that found in post-menopausal women.[3]

A number of sources have recommended endometrial surveillance with annual pelvic ultrasounds in transgender men who are amenorrheic, however this recommendation is not evidence based. This recommendation may also be unrealistic since transgender men report avoiding gynecologic care due to lack of cultural competency among providers.[4]

As such, routine screening for endometrial cancer in transgender men using testosterone is not recommended. Unexplained vaginal bleeding (in the absence of missed or changed dosing of testosterone) in a patient previously with testosterone-induced ameorrhea should be explored (Grading: X C M). Transgender men should be educated on the need to inform their provider in the event of unexplained vaginal bleeding.

Hysterectomy for primary prevention of endometrial cancer is not currently recommended (Grading: X C M); consideration of hysterectomy for the purpose of eliminating the need for cervical cancer screening may be discussed on a case-by-case basis, in recognition of the role of hysterectomy in reducing gender dysphoria, and in consideration of surgical risks and irreversible infertility.

Ovarian cancer

While there have been several case reports of ovarian cancer among transgender men,[5,6] there is no evidence to suggest that trans men on testosterone are at increased risk.

Testosterone causes the ovaries to develop cortical and thecal thickening similar to that seen in the polycystic ovarian syndrome (PCOS), however histologically there are differences in antral follicle counts.[2,7] Several studies have suggested an increased prevalence of PCOS

in transgender men prior to testosterone therapy.[8–10] While historically concerns have existed about increased risk of ovarian cancer in transgender men using testosterone, these concerns were based mostly on the inaccurate premise that testosterone causes a PCOS-like ovary. Furthermore, recent data refutes the increased risk of ovarian cancer in non-transgender women with PCOS.[11]

From a primary care perspective, no effective screening algorithm is available for ovarian cancer screening in any individuals without a greater than average risk (i.e., known genetic or personal/family risk factors). Transgender men should receive the same recommended counseling and screenings for anyone with ovaries based on history and presentation. While a unilateral or bilateral oopherectomy may be performed in transgender men as part of the management of gender dysphoria or for a pathologic process, routine oopherectomy in for primary prevention of ovarian cancer is not recommended. Transgender men who undergo vaginectomy but retain one or both ovaries/gonads, and who require pelvic imaging, may be evaluated by transrectal or transabdominal sonogram.

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26. Mental health considerations with transgender and gender nonconforming clients

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Mental health in the context of primary care

Mental health is vital to positive physical outcomes and, as for all patients, should be addressed for transgender patients in primary care. Due to pathologization and mistreatment by mental health professionals, transgender people are often reluctant to engage with mental health providers.[1,2] Primary care settings may offer a safer environment for transgender people to bring up mental health concerns and may be easier to access than mental health services. Every intake for care should include a mental health history and an assessment for active mental health concerns. Screening should include primary mental health problems, environmental and social stressors, and gender-related needs. Screening also requires provision of appropriate referrals to transgender-affirming mental health services when needs are identified.

Mental health concerns endorsed by a patient should not be automatically assumed to be related their gender identity.[1] Transgender people may be seeking mental health care for a number reasons; in addition to mental health issues relating to or resulting from one's gender identity, transgender people do experience the background rates of mood disorders and other psychiatric conditions seen in the general population. While some may be seeking specific assistance for gender-related themes, others are seeking assistance with depression, anxiety, or other clinical concerns unrelated to their gender identity.[3]

Primary care should be trauma-informed in its delivery, with an understanding that many patients present with complex trauma histories with interpersonal, social and medical systems-based trauma experiences.[4] Trauma-informed care and training for all staff and providers can enhance care engagement and health outcomes. In a recent publication, Machtinger and colleagues describe a theoretical framework for providing trauma-informed primary care.[5] The model is based on the needs of women who have a history of trauma. The model proposes the need to address the primary care environment, patient screening, provider response to the patient's needs, and a foundation of organizational values that support trauma informed care across all levels of the organization. Machtinger and colleagues address the need for confidential spaces in which to conduct a thorough screening of a patient's history with a special emphasis on trauma and a patient's response. Being able to speak with a provider in a place that ensures privacy is critical.

Primary mental health needs of transgender people

Transgender and gender nonconforming people, in general, have three types of need for mental health.

1. Exploration of gender identity. This includes determining exactly what one's gender identity is, coming to terms with this gender identity, self-acceptance and individuation, and exploring individual – level ways to actualize this identity in the world. This may also include preparation and assessment for various gender-affirming treatments and procedures.
2. Coming out and social transition. This includes coming out to family, friends, and coworkers, dating and relationships, and developing tools to cope with being transgender in a sometimes transphobic world.
3. General mental health issues, possibly unrelated to gender identity. The variety of mental health concerns experienced by transgender people include mood disorders, generalized anxiety, substance abuse, and post-traumatic stress disorder (PTSD).[6]

Transgender people may seek services from mental health providers when they come to realize that their gender identity does not match the sex they were assigned at birth, or when the distress of this incongruence becomes intolerable. The age at which this realization occurs, and the age at which treatment is initially sought, may vary greatly from one person to the next. It should not be assumed that arrival at this realization or seeking treatment late in life indicates that an individual is any "less" transgender.[1]

The coming out process for transgender people can be more challenging than it is for lesbian, gay, and bisexual (LGB) people, primarily because LGB may be able to keep their sexual orientation undisclosed. Due to the nature of social and medical transitions, a transgender person must come out to people with whom they interact unless they relocate and choose to live "in stealth" (i.e. not divulging their transgender identity). The coming out process can be time consuming and emotionally challenging. This process can be gender-affirming when transgender people are supported in doing so. Conversely, a lack of support or experiences of being mistreated, harassed, marginalized, defined by surgical status, or repeatedly asked probing personal questions may lead to significant distress.

Approaches to supporting transgender people during the coming out and exploration process include reinforcing self-identification, and exploration of and integration of individualized identity. This in turn will provide a supportive foundation for interacting with unsupporting partners, friends, relatives or coworkers, as well as provide needed tools to diffuse and deflect potential implicit and unconscious transphobic messaging and rejection in every day life.

Transgender people experience the background rates of common mood disorders, bipolar disorder, schizophrenia etc. that are seen in the general population, as well as a potentially increased rate of some conditions as a result of chronic minority stress and discrimination.[7] Hendricks and Testa have extended Meyer's Minority Stress Model [8] to transgender people.[9] This model addresses the ways that proximal and distal challenges increase the likelihood that a person will experience mental health challenges. Related to this is the work conducted by Nadal addressing microaggressions (e.g., everyday slights).[10] Similar to the

concerns for mental health disorders addressed by Hendricks and Testa, Nadal's work also points to the increased risk of mental health concerns for transgender people.

Routine primary care visits should include screening for co-occurring mental health conditions, past treatments, and history of suicide and self-injurious behaviors, symptoms of posttraumatic stress, and substance use. Primary care providers should be equipped to handle basic mental health needs of transgender patients (e.g., depression and anxiety) just as any other patient. Any primary mental health concerns beyond the scope of the provider's routine practice should be referred to transgender-affirming mental health providers. Referrals should be made when appropriate to substance abuse treatment programs, including dual diagnosis programs for those with co-occurring mental illness. All primary care offices should have a clear suicide response plan for any patient endorsing thoughts of suicide. Trans Lifeline is a crisis hotline staffed by and for transgender people and can be included in safety planning with patients.[11]

Transgender people seeking care for mental health concerns require culturally competent providers.[1] This includes basic knowledge gender identity. Transgender patients should not be placed in the position of training their providers about their mental or physical health care needs.

Environmental and social considerations

Environmental and social stressors greatly impact mental health. Transgender people are more likely to live in poverty, be discriminated against in employment, and be victims of violence than non-transgender people.[12] Transgender people also face higher rates of family loss, and homelessness. Transgender people with intersecting identities such as race, ethnicity, or socioeconomic status face increased likelihood of adverse life events. Transgender women of color face extraordinarily high rates of social and health disparities.[13–16] Routine primary care visits should always assess for housing, food, financial, and safety concerns in living and/or work environments. Case management services should be provided within the primary care setting if available. Due to environmental stressors, transgender people may have secondary adjustment difficulties including depression, anxiety, and trauma reactions. Offering referrals for individual and group therapy and support can bolster protective factors in lieu of the extreme hardships many endure.[17,18]

Diagnosis of gender dysphoria

According the *Diagnostic and Statistical Manual for Mental Disorders* (5th ed.) a person may be diagnosed with a mental health disorder ("Gender Dysphoria") if their gender identity does not match the sex they were assigned at birth, and they are suffering clinically significant distress or social/occupational impairment.[6] A diagnosis may provide an explanation for their gender concerns. However, receiving a Gender Dysphoria diagnosis may be perceived as pathologizing.[19] The issue of diagnosis is further complicated by a lack of a diagnostic code for the care of those with a history of gender transition of some kind who no longer experience significant distress or social/occupational impairment. In some cases patients will have a

carve-out of mental health services from their medical plan. It is possible that in these cases medical benefits may be denied under the medical plan for transition related care, since the only current ICD10 Gender Dysphoria codes are in the mental health section. A process is in place to create an expanded and more relevant set of codes for ICD11. Insurance plans in some states exclude coverage even if the care has been deemed to be medically necessary.[20] In states that ban health insurance exclusions, or if the individual's insurance includes transgender care, a diagnosis of Gender Dysphoria may be required for insurance to pay for necessary medical and surgical treatment.

Gender identity – specific considerations

Different gender identities and differences of gender expression are not pathologies.[21] However, some transgender people seek mental health services related to their gender. Often, distress is present over the extreme social and environmental difficulties transgender people encounter and they are seeking care to assist with these stressors. Transgender people may also seek mental health services with distress that gender does not match the sex they were assigned at birth or to discuss social and medical avenues available to live as a different gender.

Transgender patients frequently access primary care providers to discuss initiation of cross-sex hormones. **Primary care providers who are experienced in working with transgender patients may feel comfortable initiating hormone therapies without an initial mental health assessment using an informed consent model (Grading: T O S).**[22] The informed consent process includes addressing the medical *and* social risks and benefit of hormone treatment. Setting up a separate appointment for this process can be helpful to ensure the patient is given adequate time to review the information and address any questions the patient may have. Informed consent should be reviewed in person to best meet all patients' health literacy needs.

The World Professional Association for Transgender Health (WPATH) publishes the Standards of Care (SOC).[23] The SOC outlines a process for the initiation of cross-sex hormones. Per the SOC, an assessment by an experienced clinician—a primary care provider or mental health professional-- is required for initiation of cross-sex hormones. This assessment establishes the presence of persistent gender dysphoria and the ability to give informed consent. Exploration of risks and benefits of treatment to give informed consent should include not only the medical risks and benefits of treatments, but also possible social risks and benefits (such as the risks to employment, relationships, and housing), and ways to navigate and mitigate these risks. Therapy is not required to initiate a medical transition, but is encouraged to address any concerns that might arise during the process.[23] The SOC are intended to be flexible and taken on a case-by-case basis.[23] Removal of the gatekeeper role from mental health providers allows a more open and therapeutic relationship to be formed with mental health providers.

If mental illness impairs a patient's capacity for informed consent, referrals for further mental health assessment and treatment should be made prior to initiation of treatment. SOC recommends stabilizing co-occurring mental illness prior to initiation of hormones, but in some

cases the medical treatment of gender dysphoria is best done simultaneously with treatment of mental illness and substance use disorders.[24]

Some patients presenting for initial primary care services may already be on hormones. When a physician has previously prescribed these hormones no new mental health assessment is required for continued hormone treatment. Hormones and standard maintenance of physical and laboratory assessments should be continued after a discussion with the patient about their continued goals of care.

Providers are encouraged to review the tasks of the mental health provider as outlined in the SOC.[23] This document outlines the various activities of mental health providers. This might include assessment, counseling, and medication management. The SOC requires one or two evaluations by mental health professionals prior to certain surgeries for transgender people, including chest and genital surgeries. The requirements for each surgery and evaluation letter are listed in the SOC, and mental health providers can access further training online in performing these assessments.[25] See Table 1 for an explanation of the required evaluations and related referral letters. Providers are encouraged to be cautious with psychological assessment tools that were not designed for use with transgender people.

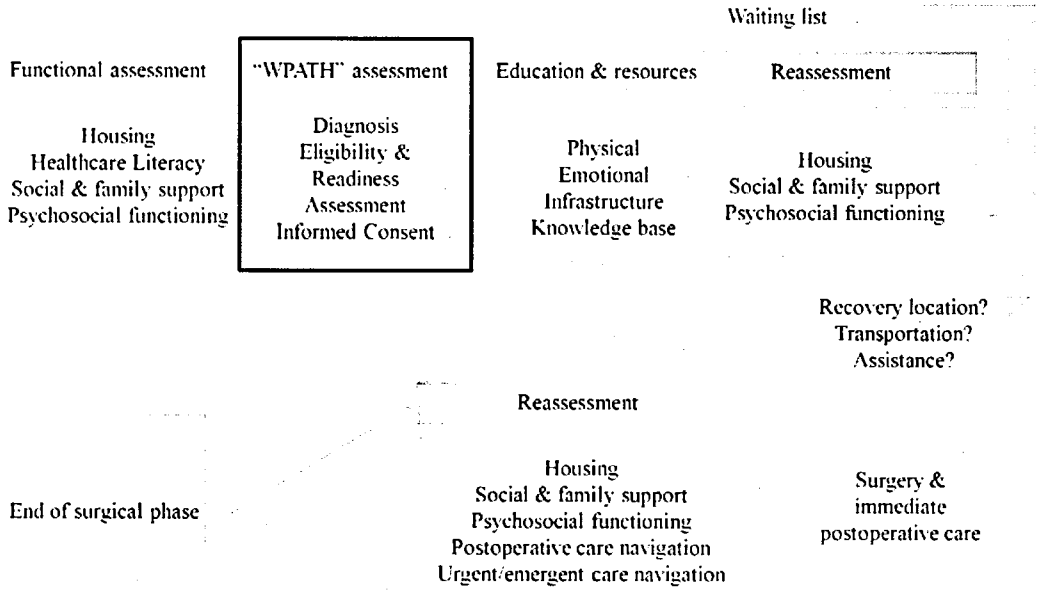
The preoperative assessment process has historically been focused on making a diagnosis of gender dysphoria, determining capacity to provide informed consent, and assessing for certain specific criteria (i.e. length of time taking hormone therapy). However, recovery from gender-affirming surgeries can be complex and involved processes, and there is an additional need for assessment of overall psychosocial functioning and support, health literacy, capacity for self-care, and social support structure in place. There is also a need to provide basic education about the surgical procedure, and provide support to fill in gaps identified during the assessment process. This need has increased with the advent of expanded access to surgery among a broad range of persons, including those who are medically indigent. A framework has been proposed in which this entire process, including the WPATH assessment, should occur (Fig 1).[26] This framework includes an evaluation of psychosocial functioning, housing status, social support system, transportation, health literacy and access to emergency care in the postop period.

Table 26-1. Assessments ("Letters") required for Gender-Affirming Medical Treatment

Procedures other than those listed below do not require a formal assessment process, though in some cases an assessment and preparation may be indicated, as with any surgery. In some cases, an assessment and letter from a medical provider who has initiated hormone therapy using an informed consent approach may be appropriate.

Type of care	One assessment	Two assessments	Time criteria
Breast augmentation	X		12 months of hormones recommended but not required
Mastectomy ("top surgery")	X		
Gonadectomy/hysterectomy		X	12 months of hormones unless contraindicated
Vaginoplasty/phalloplasty		X	12 months of hormones unless contraindicated and 12 months of living in a gender role congruent with one's gender identity, unless contraindicated

Figure 26-1. Framework for perioperative assessment, preparation, and care navigation



Adapted from: Deutsch MB. Gender- affirming Surgeries in the Era of Insurance Coverage: Developing a Framework for Psychosocial Support and Care Navigation in the Perioperative Period. J Health Care Poor Underserved; May 2016.

Counseling can be an important aspect of care for transgender people. For those patients seeking a mental health consultation or psychotherapy prior to the initiation of gender-affirming hormone therapy, there is **no minimum** requirement for number of sessions or period of time in therapy.[23] As stated above, providers must use caution about the reason for clinical services and not assume that care is related only to immediate gender dysphoria. It is important to normalize for patients any experiences related to grief and loss. Any transition a person makes in their life may include experiences of loss, regardless of the reason for the loss.

Finally, some mental health providers are trained and licensed to manage psychotropic medications for transgender people. Similar to counseling, this can be an important part of care when a patient has a co-occurring mental health concern for which medication is indicated. In some states psychologists have prescriptions privileges. In most states though, these services will be offered by psychiatrists, primary care physicians, nurse practitioners, or physician assistants.

Harm reduction

Other transgender patients may have obtained hormones by other means, such as the internet or street sources, without initial or ongoing medical assessment or supervision. The SOC has provisions for physicians to continue the medical treatment of patients who have independently initiated cross-sex hormone therapy, regardless of the patient's ability or desire to receive gender-related psychiatric/psychological evaluation.[23] Physicians may provide treatment based upon the principle of harm reduction. When patients have demonstrated their determination to continue using medication(s) without physician oversight, then it is advisable to assume their medical care and prescribe appropriate hormones. Denial of care will likely result in continued independent treatment and possible harm.

Finding a mental health provider

Making a referral to a provider who is culturally competent can be challenging. This is due, in part, to the lack of training.[27,28] Although this has been changing in recent years, it can still be a challenge. Large cities with LGBT Health Centers and providers known to offer competent care to transgender people have become a reliable source of care. Often there is a network of mental health providers in these cities. For transgender people who live in rural settings or in conservative areas of the country, finding a provider for referral can be more challenging.[16] Some providers will offer tele-mental health services. However, it is important to assure that the provider is licensed in the jurisdiction where the client is receiving services.

Patients should be encouraged to reach out to possible providers and be prepared to ask questions to assure that the provider will be able to meet their needs. Some providers will offer an initial consultation at no cost. This allows an opportunity to determine if the provider will be a good fit. A list of providers by U.S. state can be found through the WPATH website.[29]

Collaborative care

Mental health providers are encouraged to create interdisciplinary relationships.[30] Transgender people, especially those who pursue gender-affirming treatments and procedures, will require care from a variety of providers. This might include primary care physicians, endocrinologists, and surgeons. Providers are encouraged to seek out the names of providers in their area who are known to provide affirmative care with transgender clients and patients.

Summary

Transgender people deserve to receive mental health services from providers who are culturally competent. Trans-affirmative care assumes that the clients understand their own experience and identity. Providers should approach each individual with cultural humility, and avoid making assumptions or projections based on prior patients, experiences, or preconceptions. Providers are reminded to treat all clients with dignity and respect.

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27. Postoperative care and common issues after masculinizing chest surgery

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Introduction

The most common techniques applied to transgender men for masculinizing chest surgery include subcutaneous mastectomy via a periareolar incision and inframammary mastectomy with free nipple grafting. Regardless of approach chosen, the goals of masculinizing chest surgery are to sculpt a natural appearing masculine chest matched to the patient's body habitus with pectoral definition. Unfortunately, there is no consensus approach to surgical planning.[1–5] Surgical technique is dependent not only on the plastic surgeon's individual experience and patient-specific preferences, but also on evaluation of the patient's preoperative body habitus, breast size and shape, and skin quality.

The preoperative chest may be simplified into four components: the breast and subcutaneous tissue, the skin envelope, the nipple and finally the resulting incision.[5] To achieve a masculine chest shape, removal of the breast glandular tissue is required. This is distinctly different in regard to anatomy, goals, and execution from mastectomy performed for breast cancer as well as subcutaneous mastectomy performed for gynecomastia. Depending on breast tissue volume, preoperative ptosis, and skin elasticity, the skin envelope may require significant reduction for a taut, aesthetic male chest. The nipple-areola complex (NAC) likewise requires resizing, reshaping, and repositioning to match masculine proportions within the constraints of its blood supply. Finally, incisions and skin reduction should create scars with the least conspicuous size, position, and orientation.

With the number of considerations and constraints possible, a myriad of technique refinements and algorithms have been proposed; all can fit into two general categories of techniques. In smaller, less ptotic breasts, a single incision per breast designed around or through the NAC can be used to perform a subcutaneous mastectomy with a crescentic or donut-shaped skin excision. However, this approach is more difficult to apply larger ptotic breasts, as it is difficult to anatomically reposition the nipple and also achieve the necessary skin envelope reduction. In these cases, two incisions are necessary per breast. The glandular tissue and subcutaneous fat is removed and recontoured through a primary inframammary incision, and the nipple is brought through a separate oval incision. If it is not possible to transfer the NAC based on a vascular pedicle, free nipple grafting is also an option.

The procedure itself generally takes 2-4 hours, depending on technique used. Most patients require an overnight or short hospital stay.[1] General anesthetic is used. Surgical drains, left in place until a postoperative clinic visit, are the norm. The authors' preference is to use drains and compressive dressing or garment for the duration of 1-2 weeks.

In general, complications are rare for transgender men undergoing masculinizing chest surgery. Early reoperation is required in 4-9% of patients, usually for hematoma evacuation and infection, with a 12% overall complication rate.[1,2] Postsurgical complications are divided into those presenting early (within 2 weeks postoperatively) and late (after two to four weeks). Limited data specific to transgender masculinizing chest surgery are not as robust as data published for reduction mammoplasty and male gynecomastia surgery, so data on surgical complications are supplemented with data abstracted from the more extensive literature available in these fields.

Postoperative care in the primary and urgent care setting

Most early complications, although rarely life-threatening, should be expeditiously directed to the attention and experience of the operative plastic surgeon. Certain early complications (specifically hematoma, seroma, and nipple complications) can cause lasting aesthetic deformities that would be avoidable with timely intervention.

Delayed complications and specific areas of aesthetic dissatisfaction also merit referral to a surgeon. The most common complaints are related to postoperative scarring, contour deformities, and nipple appearance or discoloration. The process of healing and remodeling over the course of a year should be reinforced with patients. Prior to consideration for elective revision, patients should be medically, psychologically, and socially stable, and have realistic expectations.

Skin flap and incisional complications and scarring

Masculinizing chest surgery requires resection of redundant skin and soft tissue through surgical elevation of thin skin flaps. As a result, the blood supply to these skin flaps is tenuous.[6] This results in early complications, presenting as some degree of wound separation, delayed wound healing, or skin flap necrosis, with an estimated incidence of about 5 percent in the breast reduction population.[7]

Risk factors for early incisional and skin flap complications include high BMI (>30), hypertension, prior breast incisions, and amount of breast tissue resected. Perhaps the most important factor and one that is also modifiable for non-emergent surgery is preoperative smoking.[7,8] Patients should be counseled to stop completely for 4 weeks prior to surgery, and given the difficult nature of cessation of smoking, should consider quitting before even being referred for this type of surgery.

Unacceptable scarring, as a delayed complication, is also of concern to transgender men. A goal of surgery is to minimize the appearance of scars and optimizing their placement. Delayed wound healing results in a wide, abnormally pigmented scar that is more noticeable than the ideal fine line scar. In general, scarring from surgical incisions can be improved with some basic tenets of postsurgical wound care. Firstly, reduction of mechanical stress and tension across the wound by following postsurgical activity restrictions is paramount to reducing scar width. Tension across the incision can result in minute wound disruptions, causing excessive or widened scar formation. Patients should be counseled that incisions predictably look the worst in the early stage of healing, up to 10 weeks postoperatively, before

they begin to remodel over the next several months up to one year. Hyper- or hypopigmentation can also result in a more noticeable scar during this time of remodeling. We therefore recommend sun avoidance, or strong sunblock applied over a healed incision for the first year postoperatively. Scar compression has also been found to reduce hypertrophic scarring, although the mechanism is not known. This can take the form of gentle scar massage (beginning no earlier than 2 weeks postoperatively), taping, or silicone gels and sheets.[9] Surgical scar excision and revision is sometimes necessary if scar care fails to improve the appearance to an acceptable level.

Hematoma / seroma

Hematomas occur in approximately 1-2% of all breast reduction patients postoperatively, and usually present early after surgery.[8] The incidence has been reported as high as 5-11% among certain subgroups of transgender patients.[1–3] Hematomas can be prevented with meticulous surgical hemostasis and optimization of medical comorbidities (coagulopathies, hypertension, and stopping ongoing anticoagulation and certain herbal medications). A hematoma presents as asymmetric swelling and pain, sometimes accompanied by ecchymoses. In general, most hematomas need to be evacuated because of the physical pressure they can exert on the taut skin envelope, which can compromise skin flap viability and can also cause postoperative chest deformities. Other complications can include calcification or infection of the hematoma. Usually upon surgical re-exploration and evacuation, no discrete bleeding vessel is ever identified. Small liquefied hematomas can be aspirated or drained percutaneously.

Seromas and oil cysts are fluid collections that occur at the surgical site that are usually preemptively drained by placement of closed suction drains during the operation, combined with adherence to a postsurgical pressure garment. Occasionally, these collections can persist or recur after surgical drains are removed, and need to be drained to prevent skin flap or incisional compromise. Timing of surgical drain removal is dependent on drain output, and should be a decision made in conjunction with the surgeon.

Large oil cysts result from fat necrosis, which can cause contour irregularities and calcifications over time. These are addressed by aspiration and/or surgical revision.

Infection

Infection is a rare early complication after masculinizing chest surgery.[1,8] Usually this will present as localized cellulitis, and can usually be treated with a short course of oral antibiotics. An underlying fluid collection may need to be drained if it is associated with a persistent postsurgical infection.

Nipple-areola-complex and nipple graft complications

Whether the Nipple-Areola-Complex is preserved on a dermal pedicle, as in subcutaneous mastectomy, or it is taken as a free graft, there are associated early and late complications related to nipple healing. Decreased nipple sensitivity, numbness, or parasthesias are expected outcomes for both methods. Patients report varying degrees of sensory recovery

over time with both techniques. Both techniques result in some degree of hypopigmentation, reduction in nipple projection, and the rare complication of nipple loss; with these risks being more pronounced with free grafting. Careful adherence to postoperative instructions and nipple dressings can help assure good results with either technique,[1,2] with described overall nipple loss rates at 1% or less. It is important to distinguish between full thickness nipple necrosis and expected superficial skin slough in these postoperative patients.[6]

Nipple reconstruction and revision procedures may be required to restore the appearance of the nipple. Nipple position and size can also be adjusted during a secondary procedure. Usually these are minor procedures than can be accommodated once the initial healing phase is complete.

Contour irregularities

Minor chest wall contour deformities or asymmetry, including redundant tissue found at the end of incisions (dog ears), represented the most common reasons for patients seeking secondary chest wall surgery in multiple published series.[3,6] These can be excised as an outpatient procedure. Additionally, other contour deformities or asymmetries can be addressed with liposuction or fat grafting.

Overall operative revision rate for aesthetic improvement was reported as high as 32% in large published series of masculinizing chest surgery.[2]

Breast cancer risk

Transgender men should be counseled that androgenic hormonal therapy and chest wall contouring procedures (including subcutaneous mastectomy) do not obviate the risk of breast cancer development, particularly among those patients who are at greater risk for breast cancer due to family history. Chest wall contouring, with inherently different goals and techniques, as well as abundant intersurgeon variability in regard to technique, should not be considered a risk-reducing procedure. The presence of residual breast tissue has been acknowledged independently by various surgical authors describing various techniques.[1,3,6] Since the approaches to cosmetic mastectomy differs from those used in the management of breast cancer, all patients undergoing chest surgery should have baseline mammography to prevent an unexpected intraoperative or surgical pathology finding. Ongoing screening for breast cancer after subcutaneous mastectomy is discussed elsewhere in these guidelines.

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28. Perioperative and postoperative care for feminizing augmentation mammaplasty

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Introduction

As with non-transgender women, breast augmentation in transgender women involves implant-based augmentation mammoplasty. A prosthetic implant comprised of a silicone shell, with saline or cohesive silicone filler, is placed underneath the breast tissue (subglandular implant) or under the pectoralis muscle (subpectoral implant).

Initiation of estrogenic and antiandrogenic therapy stimulates the development of breast tissue in transgender women. In the absence of solid evidence for an optimal length of time on feminizing hormone therapy prior to augmentation, some sources recommend a minimum of 6 months of hormone therapy prior to surgery, to allow hormone-related breast development to progress.[1,2] Realistically, a minimum of 2-3 years is more likely to maximize hormonal breast development.

The choice of implant, type, and position is governed by the woman's preoperative body habitus and wishes, in consultation with a board-certified breast or plastic surgeon. Subglandular implant placement may be preferred when there is adequate breast and subcutaneous tissue to cover the implant, and prevent visible implant seams and rippling. Subpectoral implant placement may be preferred when saline implants are used, or in the absence ofadequate soft tissue to disguise the shape of the implant.[3] There are no objective outcomes data to support the use of saline vs. silicone filler, other than aesthetic considerations and preference on the part of the surgeon and patient.[4] Since many transgender women have inadequate breast development, subpectoral silicone implant placement is the typical approach used.

Breast augmentation procedures are often performed as a "same-day," ambulatory procedure under general anesthesia; operative time is approximately 2 hours. Recovery is fairly rapid over the course of several weeks, though some patients may experience prolonged soreness, swelling, and mild bruising. A small incision is made along the new inframmary crease and a space for the implant is created in the subglandular or subpectoral planes described above. The incisions are closed with several layers of sutures and the patient generally feels well enough to go home the same evening.

In general, results are durable and complications are rare for feminizing augmentation mammoplasty.[2] Complications are typically divided into early (less than two to four weeks) or late complications (more than four weeks). Surgical data on augmentation mammoplasty specific to transgender women [2,5] are limited; some data are extrapolated from data published on non-transgender women undergoing this procedure. In one study, 75% of transgender women reported satisfaction in long-term follow-up with implant-based

augmentation, with the majority of dissatisfaction related to subjective aesthetic outcome (primarily inadequate breast size) rather than technical surgical complications.[5]

Postoperative complications in the primary and urgent care setting

Any concern for an early postoperative complication (as detailed in sections below) should be expeditiously referred to the operative surgeon.

A plastic surgery referral is also appropriate for a patient presenting late after augmentation mammoplasty with new symptomatic or objective breast complaints related to prior breast augmentation (e.g. swelling, pain, erythema, significant deformity/asymmetry, and implant deflation). Benign and malignant breast tumors are always in the differential diagnosis and should be worked up appropriately. Breast cancer screening should be up-to-date prior to referral. If a fluid collection or implant rupture is suspected based on history or exam, it is helpful to confirm this with an ultrasound or MRI prior to seeing the plastic surgeon.

Women who present with subjective dissatisfaction after previous breast augmentation may require a second surgical consultation or referral to another plastic surgeon. Elective secondary revision of augmented breasts is not uncommon. Prior to any referral for breast surgery, patients should be medically, psychologically, and socially stable, up-to-date in regard to breast cancer screening if indicated), and have reasonable postsurgical expectations.

Anesthetic complications particular to gender-affirming feminizing mammoplasty

In addition to standard anesthetic complications, patients undergoing feminizing mammoplasty should be assessed for risk factors for venous thromboembolism,and appropriate mechanical and chemoprophylaxis measures applied based on individual risk factors. Management of perioperative estrogen therapy and estrogenic risks of venous thromboembolism are discussed elsewhere in this protocol.

Hematoma

A hematoma typically presents early (within 1-2 weeks) after augmentation mammoplasty, typically as a localized or unilateral swelling accompanied by pain and bruising at the surgical site. In the absence of breast trauma, delayed hematomas are rare.[6]

Close adherence to postoperative care protocols is necessary to prevent early postoperative hematomas. Specifically, the patient should be counseled to avoid strenuous activity and situations where the chest could be exposed to external trauma. Additionally, strict medical adherence (especially in regard to withholding anticoagulant, antiplatelet, and certain herbal medications and compliance with antihypertensive medications) can decrease incidence of postoperative hematoma.

Hematomas are typically treated with surgical re-exploration, evacuation with identification of the bleeding source, and reclosure, with or without exchange of the prosthetic implant. Small hematomas can occasionally be managed expectantly. An untreated large hematoma can result in secondary complications, such as infection, capsular contracture, or implant malposition.[7]

Seroma

A sterile postsurgical fluid collection is expected to form periprosthetically and typically is resorbed after the early recovery period.[6] Unless there is reason to suspect that there is concomitant infection or that the fluid collection is in danger of causing incisional breakdown and implant exposure, there is no reason for concern or need for further radiographic evaluation with an early postoperative fluid collection. There is no evidence in the plastic surgery literature to support the routine use of drains in augmentation mammoplasty. A delayed seroma is generally abnormal, and should be evaluated by a plastic surgeon.[4]

Infection

Infections are uncommon and typically present as early (1-4 weeks) complications following breast augmentation. The severity of infection can range from a mild incisional cellulitis to a purulent periprosthetic infection. The most common pathogens in periprosthetic infections are skin flora, and as a result, surgeons go to extensive lengths to avoid contamination.[8]

A majority of postoperative infections will respond to medical treatment with antibiotics. However, most authors would advocate for implant removal in cases that fail to resolve, with delayed secondary augmentation performed in 6-12 months, once the patient has time to heal and fully clear the infection.[3]

Incisional complications

Incisional scarring is a late complication of augmentation mammoplasty. Patients should be cautioned on appropriate scar care, including sun avoidance in the early postoperative period. Patients with darker or oily skin types or a prior history of hypertrophic scar or keloid formation should also be aware of their increased risk for these complications.

In general, scarring from surgical incisions can be improved by following some basic tenets of postsurgical wound care. Firstly, reduction of mechanical stress and tension across the wound by following postsurgical activity restrictions is paramount to reducing scar width. Tension across the incision can result in minute wound disruptions, causing excessive or widened scar formation. Patients should be counseled that incisions predictably look the worst in the early stage of healing, up to 10 weeks postoperatively, before they begin to remodel over the next several months to up to one year. Hyper- or Hypopigmentation can also result in a more noticeable scar during this time of remodeling. We therefore recommend sun avoidance, or strong sunblock applied over a healed incision for the first year postoperatively. Scar compression has also been found to reduce hypertrophic scarring, although the mechanism is not known. This can take the form of gentle scar massage (beginning no earlier than 2 weeks postoperatively and after the wound is fully healed), taping, or silicone gels and sheets.[9]

Implant rupture

A break in the silastic shell of a saline [10] implant will be recognized immediately as deflation and loss of breast volume. Implants placed prior to the late 2000s contained a liquid silicone gel which was prone to leakage, both due to shell rupture and leaching. Potential complications include deformity, inflammation, and pain. Currently available silicone breast implants (4^{th} or 5^{th} generation implants, also termed cohesive gel implants), even a break in the outer shell of the implant will not allow free silicone gel to escape the implant. As a result, silicone implant rupture often goes undetected. Suspected rupture can be confirmed by MRI imaging. A long-term MRI study of implant integrity found that more than 90% of the current generation of silicone implants were intact at 10 years.[11]

A 2011 report by the FDA recommended routine MRI screening for asymptomatic silicone implant rupture, initially three years after implantation and biannually thereafter,[12] although there is no evidence base to support such a recommendation and an MRI may not be covered by insurance.[13] Patients should receive preoperative counseling regarding this recommendation, as well the lack of objective evidence to support it.

Implant malposition and capsular contracture

Implant malposition can occur over time as the breast adapts to breast implant placement and aging. Nonpathologic capsule formation over the surface of the implant is expected. Pathologic fibrotic capsule formation, known as capsular contracture, can cause the implant to be hard and palpable, or cause implant displacement, breast deformation, or even breast pain related to the implant. Once symptomatic or disfiguring, implant removal and surgical excision of the capsule is indicated. Capsular contracture rates in modern implants are felt to be less than 10%, although long-term followup is needed.[3] There has not been any link between breast implants or periprosthetic capsule formation and connective tissue diseases.[3] While the U.S. Food and Drug Administration recommends screening for silicone implant rupture with MRI every 3 years, there is no evidence to support this practice in the absence of symptoms (pain, deformity), since the recommended approach to an incidental and assymptomatic implant rupture is non-operative observation.

Inadequate size and aesthetic deformities

A long-term study of transgender women who underwent augmentation mammoplasty found that 16% of the patients underwent a second augmentation procedure for breasts that were too small.[5] These patients accounted for the majority of dissatisfaction related to augmentation.

A number of aesthetically unappealing complications can occur and result in dissatisfaction requiring revisional surgery and secondary augmentation. These complications are generally a result of a combination of technique and patient anatomy. Some of these complications can include a visible implant and implant folding or rippling, which occurs in saline implants or when the patient has inadequate soft tissue covering the implant. Other patients can develop asymmetry related to scar formation or displacement over time by the action of the pectoralis

muscle (in the case of submuscular implants). These deformities will need to be addressed with secondary revision breast augmentation procedures.

Breast masses

Breast cancer epidemiology and screening in transgender women is covered elsewhere in this protocol. For those transgender women requiring screening or diagnostic mammography or breast ultrasound, both are possible with breast implants. However, mammography cannot detect implant-related complications, such as ruptures.[14]

Breast soft tissue injections

Although autologous fat grafting is gaining acceptance in plastic surgery,[15] its use in transgender women has not been widespread or well-described. Injection of silicone and other non-medical substances by unlicensed providers is covered in detail elsewhere in this protocol.

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29. Vaginoplasty procedures, complications and aftercare

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Introduction

The most common vaginoplasty technique is some variation of the penile inversion procedure. In this technique, a vaginal vault is created between the rectum and the urethra, in the same location as a non-transgender female between the pelvic floor (Kegel) muscles, and the vaginal lining is created from penile skin. An orchiectomy is performed, the labia majora are created using scrotal skin, and the clitoris is created from a portion of the glans penis. The prostate is left in place to avoid complications such as incontinence and urethral strictures. Furthermore, the prostate has erogenous sensation and is the anatomic equivalent to the "g-spot." Great care is taken to limit the external scars from a vaginoplasty by locating the incisions appropriately and with meticulous closure. Typical depth is 15 cm (6 inches), with a range of 12-16cm (5-6.5 inches); in comparsion, typical vaginal depth in non-transgender females is between 9-12cm (3.5 to 5 inches). In the case of prior circumcision a skin graft, typically scrotal in origin, may be required. If there is insufficient skin between the penis and the scrotum to achieve 12cm (5 inches) of depth, a skin graft from the hip, lower abdomen or inner thigh may be used. Resultant scarring at the donor site may be minimized or hidden using standard techniques. Because the penile inversion approach does not create a vaginal mucosa, the vagina does not self-lubricate and requires the use of an external lubricant for dilation or penetrative sex.

Scrotal skin has abundant hair follicles and it is possible to transfer skin with sparse hair growth into the vagina unless hair is removed in advance. Some surgeons rely on treating all the visible hair with aggressive thinning of the skin and cauterization of visible hair follicles at the time of surgery. However, since hair grows in stages this approach might not adequately address dormant follicles. The most reliable method of preventing hair growth in the vagina is to perform scrotal electrolysis, at least three full clearings 8-12 weeks apart, depending on electrolysist preference and hair type and distribution. Surgeons should provide a diagram of the specific area for clearance.

A common outcome of penile inversion vaginoplasty performed in a single stage (a "one-stage" vaginoplasty), with penile skin positioned between scrotal skin, is labia majora that are spaced too far apart. There may also be minimal if any clitoral hooding (except in heavier patients) and the labia minora may be insufficient after one operation. Although there are different variations of the one-step procedure, it has been the author's experience that these previously mentioned deficiencies are common. This constraint is due to factors inherent to the penile inversion approach and the limitations of the blood supply. From the standing position and with the legs together, most results appear acceptable; however, upon direct examination or intimate view, the deficiencies discussed above will be apparent. In order to

adequately address these deficiencies, the author believes that a second operation is required. A secondary labiaplasty provides an opportunity to bring the labia majora closer to the midline in a more anatomically correct location, provide adequate clitoral hooding, and define the labia minora. In addition, there are many variables that can affect healing and the final result. Specifically, this secondary procedure also allows the surgeon to deal with differences in healing, such as revision of the urethra, correction of any vaginal webbing or persistent asymmetries, or revise scars that are unsatisfactory. These revisions will improve functionality and the final outcome for the patient and might not otherwise be addressed.

Immediate postoperative considerations

Gauze packing or a stenting device is placed in the vagina intraoperatively and remains in place for 5-7 days. Once removed, the patient is instructed in vaginal dilation, with dilators generally provided by the surgeon; dilation schedules vary between surgeons. Table 1 shows sample postoperative instructions, and Table 2 shows dilation instructions and a sample dilation schedule.

Table 29-1. Vaginoplasty Postoperative Instructions

Focus area	Instructions
Activity	Avoid strenuous activity for 6 weeks. Avoid swimming or bike riding for 3 months.
Sitting	For the first month post-op, sitting may be uncomfortable, but not unsafe. Recommendation to use donut ring to relieve pressure at surgical site.
Bathing	Resume showering following first postoperative visit, patting incisional areas dry. Do not take baths or submerge in water for 8 weeks post-op.
Swelling	Labial swelling is normal and will gradually resolve 6-8 weeks postoperatively. Swelling may be aggravated with long-term sitting or standing. For the first week post-op, applying ice on the perineum for 20 minutes every hour can assist in relieving some swelling.
Sexual intercourse	You may resume sexual intercourse 3 months after surgery, unless you have been instructed otherwise.
Hygiene	Wash hands before and after any contact with the genital area. Shower or wash daily. When washing, wipe from front to back to avoid contamination by bacteria from the anal region. Avoid tight clothing; friction may facilitate bacteria transfer.
Vaginal	Vaginal discharge that is brownish yellow should be expected in the first 4-6 weeks postoperatively. Bleeding and spotting should be

Focus area	Instructions
discharge	expected in the first 8 weeks postoperatively. Soap and water douche should help reduce this. Chamomile or lavender liquid soap can help cleanse the neo vagina as well.
Tobacco/ smoking	Avoid tobacco use or smoking 1 month postoperatively, as this can interfere with the healing process.
Diet/nausea/ constipation	Begin with a liquid diet and increase to your usual diet as tolerated. Anti-nausea medication may be prescribed. Narcotic pain medication may cause constipation; a stool softener such as Colace can help prevent constipation.
Pain medication	Postoperative pain is normal, and pain medication may be prescribed. Pain medication is to be taken as prescribed, and can be switched for Extra Strength Tylenol at any time.
Dilation	Dilation is an important part of recovery. Dilators may be provided to patient with instructions regarding dilation in the post-op period.

Source: Brownstein & Crane Surgical Services

Dilation Instructions

Source: Brownstein & Crane Surgical Services

Please be aware that each person's dilation schedule may vary.

- Prior to insertion into the vagina, ensure the dilator is clean.
- Clean the dilator with warm water and antibacterial soap. Rinse well and dry with a clean paper towel or cloth.
- Apply Surgilube or KY Jelly to the dilator prior to insertion. Only use water based lubrication.
- Avoid silicone-based lubricants.
- Gently insert dilator into the vagina at an angle of 45 degrees until under the pubic bone, and then continue inserting straight inward.
- Expect to feel a small amount of resistance and tenderness. Stop immediately if there is too much resistance or severe pain.
- Insert the dilator into the full depth of the vagina (until you feel moderate pressure or resistance) and leave in place for 10 minutes. You should be inserting until only one or two white dots remain outside of the vagina.
- Start dilating three times daily for three months on the day the vaginal packing is removed.
- You may start using the next size dilator after three months of dilating. You should use the next size for three months.

- Dilation frequency: 0-3 months after surgery 3 times/day for 10 minutes each time, 3-6 months after surgery 1/day for 10 minutes each time, more than 6 months after surgery 2-3/week for 10 minutes each time, more than 9 months 1-2x/week.
- If the vagina begins to feel tight, increase the frequency of the dilation schedule.
- You should use soap and water to cleanse the vaginal canal after each dilation.

Table 29-2. Dilation Sample Schedule

Months Since Surgery	Color of Dilator	Diameter of Dilator	Frequency
0-3	**VIOLET**	1-1/8"	3X per day
3-6	BLUE	1-1/4"	Once daily
6-9	GREEN	1-3/8"	Every other day
9-12	ORANGE	1-1/2"	1-2x per week

Source: Brownstein & Crane Surgical Services

Immediate risks include bleeding, infection, skin or clitoral necrosis, suture line dehiscence, urinary retention or vaginal prolapse. Fistulas from the rectum, urethra or bladder usually present early on.

Acute bleeding usually originates from the urethra and most often can be controlled with local pressure. If local pressure is unable to achieve hemostasis, then placing a larger catheter (20F) in the urethra alone may stop the bleeding. If necessary, placing a suture around the bleeding site (with the catheter in place) will stop the bleeding in almost all cases. It is not unusual for localized hematomas to spontaneously drain through the vagina or suture line. This usually occurs a week or greater after surgery as the hematomas liquefy. The blood characteristically appears dark and old, and is not accompanied by clots. Although frightening to the patient, no treatment is indicated.

The genitalia and perineum have an excellent blood supply, so infections should be rare and seldom require more than a broad-spectrum antibiotic. Skin slough or loss is also rare, and should be treated conservatively. Separation of the suture line can occur, most often at the posterior perineum due to the pressure and stretching that occurs with dilation. Separations should be treated conservatively with antibiotic ointment, most will heal without consequence. Dilation should not be discontinued, and is critical at this stage. Failure to adequately dilate in the immediate postoperative period will likely result in severe vaginal stenosis. No attempt at immediate secondary closure of the dehiscence is indicated since it is a contaminated wound and would likely fail. In some cases, dehiscence may result in the development of a posterior web, which can be easily revised at a later stage.

Partial or complete clitoral necrosis may occur and should be treated conservatively with antibacterial ointments. In the majority of cases, the neurovascular bundle and a portion of the clitoris is still present and will usually maintain good sensitivity.

Urinary retention due to swelling and/or temporary peripheral nerve injury (neuropraxia) should be treated with replacement of a catheter for 5-7 days. Flomax is helpful, and this is almost always temporary. Early strictures are very rare.

A patient may lose a portion of the added skin graft and pass it out through the vagina. This usually occurs at least 2 weeks from surgery, and typically due to excessive skin grafting into the vagina. It is not accompanied with bleeding and the sloughed skin appears nonviable. Recovery is uneventful and patients should continue to dilate. A more severe scenario is expulsion of the entire vaginal skin lining, which occurs earlier (usually within the first postoperative week) and is frequently accompanied with at least some bleeding. While uncommon, in most cases it is a disastrous complication and the patient will require surgical intervention, typically one year later to re-line the vagina.

Delayed / long-term postoperative maintenance and considerations

Adherence to the dilation regimen is critical to healing and maintaining vaginal depth and girth. After the initial healing period, dilation must continue regularly for at least one year postoperatively. The depth and the width of the vagina should be checked regularly as one tapers down the dilation schedule. If it is noticed that vaginal depth or width are diminishing either by patient report or in-office examination, the dilation schedule should be increased. If the patient experiences difficulty with dilation due to discomfort, instillation of lubricant ahead of the dilator with either a 3cc syringe, or the applicator device supplied with vaginal antifungals may be helpful. Patients may develop a sensitivity to the preservative in the water based lubricant; simply changing the brand of lubricant is often an effective solution.

Loss of vaginal girth due to inadequate dilation can often be remedied by increasing dilation frequency; loss of vaginal depth is more difficult to address by dilation alone. Persistent pain or otherwise problematic dilation should be discussed with the surgeon. Other possible causes of painful or inadequate dilation include a small pelvic inlet or muscle spasm and vaginismus. Approaches may include but are not limited to botulinum toxin injections, removal of webbing at the entry of the vagina, and/or a referral to a physical therapist that specializes in pelvic pain and pelvic floor issues.

The vagina is skin-lined and under normal conditions is colonized with a combination of skin flora as well as some vaginal species; a study of vaginal flora in a mix of transgender women with and without symptoms of odor and discharge found Staphylococcus, Streptococcus, Enterococcus, Corynebacterium, Mobiluncus, and Bacteroides species to be most common. Lactobacilli were found in only 1 of 30 women, and candida was not found. There was no correlation between the presence of vaginal symptoms and any one particular species.[1] These findings suggest that vaginal discharge and odor in transgender women is unlikely to due to common causes in non-transgender women such as bacterial dysbiosis or candida; indeed the lack of a mucosa or low pH are consistent with this study's findings of rare lactobacilli and no candida. In most cases discharge is most likely due to sebum, dead skin or keratin debris, or retained semen or lubricant.

Since the vagina does not contain a mucosa, routine cleaning or douching with soapy water should be adequate to maintain hygiene. Initially the patient should douche daily during frequent dilation. Douching can be reduced to 2-3 times a week when dilation is less frequent. If odor or discharge persists, an examination for lesions or granulation tissue should be performed. Use of a solution of vinegar or 25% povidine iodine in water for 2-3 days may help in cases of flora overgrowth or imbalance, after which the patient can return to regular soap and water cleaning. If the drainage and odor persist, an empiric 5-day course of vaginal metronidazole is reasonable.

It is reasonable to consider a yearly visual pelvic exam to screen for lesions, granulation tissue, or undesired loss of depth and girth, though no evidence exists to support this recommendation. Since the vagina is skin lined, there is a risk of developing the same skin cancers that occur on the penile and scrotal skin (squamous cell, basal cell, melanoma). Other skin disorders such as psoriasis can also affect the vagina and should be treated similarly. If indicated, a prostate exam may be performed endovaginally since the rectal approach may be obscured by the new presence of the vaginal walls in between the rectum and the prostate.

A far less common approach to vaginoplasty is the use of either colon or small bowel to line the vaginal vault. This technique has the advantages of diminished need for dilation, greater depth and is naturally self-lubricating. However, this approach requires abdominal surgery with a risk of serious or even life-threatening complications. The primary indication for an intestinal approach is the revision of prior penile-inversion vaginoplasties. Since the secretion is digestive there is a risk of malodor and frequent secretions, and secretions are constant rather than only with arousal. Wearing panty liners or pads may be necessary for the long term. Bacterial overgrowth (diversion colitis) is common and may present with a greenish discharge, treatment includes. The bowel lining is also not as durable as skin. Use of intestinal tissue also places the vagina at risk of diseases of the bowel including inflammatory bowel disease, arterio-venous malformations (AVM) or neoplasms; screening or diagnostic evaluations for these conditions should be performed as indicated.

Fistulas

The most common fistula is a rectovaginal fistula. These usually occur at the midline within 5 cm of the vaginal opening, and are almost universally the result of a surgical injury to the rectum. Small fistulas may only pass flatus, while larger fistulas can allow stool to drain through the vagina. A temporary diverting colostomy may be required for hygiene. Dilation should continue to avoid closure of the vagina, with the plan to repair the fistula in a minimum of 6 months.

Urethrovaginal fistulas present with urine leakage from the vagina. The majority of cases do not need or require immediate intervention, and in most cases the patient will still be continent. The patient should be counseled that they will be more susceptible to urinary tract infections--particularly after intercourse. Voiding promptly after intercourse and/or acidifying the urine with juices or cranberry pills is usually adequate preventive care. Fistulas between the bladder and vagina are the least common, but are the most difficult to manage. A foley

catheter in the bladder will divert a majority, but not all of the urine; in general surgical intervention will be required.

Granulation tissue

Granulation tissue in the vagina is the result of delayed healing and is common. The need for frequent dilation in the early post-operative period exacerbates the problem by causing repeated trauma to the area of granulation. The typical complaint is of mildly blood-streaked yellowish discharge. In most cases this will heal as the need for frequent dilations diminishes over time. If persistent, regular silver nitrate treatments and topical treatment of steroid cream (triamcinolone) or medical grade honey (Medihoney) will speed the healing. Silver nitrate can be applied to granulation areas until cautery is observed with resultant grey scabbing and coagulation. Steroid creams or honey can be applied on the tip of the dilator. Long term, the penile skin lined vagina should be very durable.

Urinary tract infections (UTIs)

Urinary tract infections are not uncommon, since the urethra is shortened during a vaginoplasty. Proper hygiene and hydration are generally adequate preventive measures. A patient who has recurrent urinary tract infections should be evaluated for a urethral stricture. A simple diagnostic test is to attempt to pass a 16F catheter into the bladder to rule out strictures, including post-bulbar or meatal stenosis. Patients with a mucosal flap causing a large meatus will require meticulous hygiene and possibly prophylaxis. Most patients will see a reduction in their ability to hold larger volumes of urine over longer times as a consequence of the involution of the prostate. Rarely some may even experience urgency incontinence. Bladder relaxants like tolterodine or darifenacin are helpful in these cases.

Sensation and orgasm

No major sensory nerves should have been divided during surgery, so sensitivity should not be adversely affected after vaginoplasty. In an outcome study published in 2002, 86% of the author's patients were orgasmic.[2] Pre-operative functionality is an important indicator, though it is possible that a previously anorgasmic patient will be orgasmic following vaginoplasty. The combination of prolonged estrogen/anti-androgen therapy and orchiectomy during surgery may result in a reported decline in libido for some patients, which is discussed elsewhere in these guidelines.

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30. Phalloplasty and metaoidioplasty – overview and postoperative considerations

Primary author: Curtis Crane, MD

Introduction

Phalloplasty in transgender men involves the creation of a penis using any one of a number of procedures; either a free flap or pedicled flap of skin, usually taken from the arm (radial forearm free-flap, RFF) or anterior lateral thigh (anterior lateral thigh pedicled flap phalloplasty, ALT). In a free flap procedure, tissue is completely removed from the donor site along with its blood supply. The blood supply is then anastomosed to a recipient blood supply at the site of transfer. In a pedicled flap procedure, the tissue is never severed from its blood supply. Using either procedure, the donor skin is rolled into a tube like structure and grafted to the inguinal area. In order to minimize the risk of fistula, most commonly this procedure is performed after a hysterectomy and vaginectomy (or vaginal mucosal ablation) is performed. Scrotoplasty may also be performed using skin flaps. Scrotoplasty may be performed with or without testicular implants. A urethral hookup may be performed using cheek or vaginal mucosa, and an erectile implant may be placed. Often the entire phalloplasty procedure involves multiple staged surgeries, with earlier stages allowing skin grafts to develop local blood supply prior to cosmetic procedures to complete the phalloplasty. Depending on the surgical approach, the penis may or may not have intact erotic sensation.

Risks associated with phalloplasty

There are general risks associated with any surgery, including infection, bleeding, damage to surrounding tissues, and pain. Specific to phalloplasty in transgender men, there is risk of flap loss, urethral complications, wound breakdown, pelvic bleeding or pain, bladder or rectal injury, lack of sensation, prolonged need for drainage, or need for further procedures. Donor site risks include unsightly scarring, wound breakdown, granulation tissue formation, decreased mobility, hematoma, pain and decreased sensation. If patients are discharged from their surgeon's care and are not local, they should see their primary care provider every three months during the first year.

Some of the most common complications are listed below. Different techniques and approaches can have varying levels of complexity. Different surgeons may also have different complications rates; understanding what procedures different surgeons perform, their experience, frequency with which they perform these procedures, and complication rates is helpful.

Immediate/early (within one month) complications after free or pedicled flap phalloplasty

Wound infections typically occur within the first few weeks after surgery and can present as cellulitis, fungal infection or both. Antibiotics and antifungal cream are usually sufficient for treatment. In some cases intravenous antibiotics may be required.

Wound breakdown is common and typically occurs at points where multiple suture lines meet (i.e. perineal-scrotal junction and base of phallus). Most wound breakdown issues can be managed with local wound care (wet to dry dressing changes) as the wounds heal by secondary intention. Some wound breakdowns may require debridement(s), and fewer may require skin grafting or further surgical procedure(s) to close the wound.

Urinary catheter difficulties present as a clogged catheter or bladder spasms. This is managed by making sure there are no kinks or twists in the tubing, flushing the catheter, and antispasmodic medications (anticholinergics). Urinary tract infections (UTIs) in the setting of a urinary catheter can develop and present with a constellation of symptoms including cloudy urine, odorous urine, increased bladder spasms or leakage around catheter. These symptoms may or may not present with fever or other systemic symptoms. If a patient does not have a constellation of these symptoms, it is unlikely to be a true UTI even if the urinalysis (UA) and urine culture (UCx) demonstrate laboratory findings consistent with infection.

Flap loss is rare and typically occurs due to technical error (misplaced microsurgical suture or vascular pedicle kinking/compression). Flap loss typically presents within the first 72 hours, and if recognized early (within hours) can be salvaged by emergent return to the operating room. On return to the OR, drainage of a hematoma compressing the vascular pedicle, revision of the arterial or venous anastomosis, or in some cases mechanical thrombectomy with balloon catheters or instilling tissue plasminogen activator (tPA) into the flap can save a flap from loss. Even with these measures, partial or complete flap loss is possible. Hypercoagulable states can predispose a patient to clotting after surgery and flap loss. Undiagnosed clotting disorder such as Factor V Leiden, antiphospholipid syndrome, prothrombin gene mutation G20210A, antithrombin III deficiency, Protein C and S deficiency, and hyperhomocysteinemia should be considered in the case of flap thrombosis.

Pelvic or groin hematomas can occur, and may be managed by drains, or may require surgical drainage. While medical deep vein thrombosis prophylaxis with unfractionated heparin or lovenox may place the patient at higher risk of hematoma formation, this risk must be weighed against the risk of deep vein thrombosis and pulmonary emboli. Risk assessment models exist to help determine individualized perioperative anticoagulation modalities.[1] While these risk assessments will generally be performed by surgeons, primary care providers with knowledge of an individual patient's increased risk for thromboembolism or perioperative bleeding should notify surgeons pre-operatively.

Rectal injury is a rare but serious complication. The vaginectomy portion of the procedure involves developing a plane between the posterior wall of the vagina and the anterior wall of the rectum. Laceration with scissors or cautery can cause this injury. Inadvertent injury to the rectal wall can present acutely (immediately known and repaired) or subacutely (days to

weeks later). Recognition of a rectal injury in the subacute period can be based on constitutional symptoms of fever, chills, malaise, or more overt symptoms of sepsis. The portion of the rectum in the surgical field is extraperitoneal, so abdominal pain or peritoneal signs would be unusual. Drainage of stool from the perineal incisions, scrotum or base of the phallus indicates formation of a fistula between the rectal wall and the skin. Such wounds require hospitalization and general surgical involvement in the care plan. A short-term colostomy may be required to divert the fecal stream and allow the fistula to close. Washout of a pelvic abscess and closure of the rectal fistula, with secondary wound healing may be required.

Long-term complications after free or pedicled flap phalloplasty

Urethral strictures typically present 6-12 months after surgery with symptoms of a weak stream, straining with urination, and sometimes concomitant fistulas secondary to distal obstruction from the stricture. This will require surgical intervention with either dilation or urethroplasty.

Wound contraction and scarring are complications that occur any time the skin is cut, but the degree to which they occur is highly variable between patients. Some patients form scar more robustly than others. All scars contract with time as myofibroblasts within the wound become active in the first 2-9 days.[2] Wound contracture is a natural mechanism to decrease the defect size, decreasing the effective surface area that must be healed. However, wound contracture can lead to distortion of surrounding tissues and contour defects. Wounds that close by secondary intent show more contracture than primary closure.

Scars can be thin lines, or can widen or become "proud" (hypertrophic), or even pass beyond the borders of the scar (keloid). Hypertrophic scars can successfully be revised by excision and reclosure with skin tension reducing measures to decrease recurrence. Keloids occur infrequently, often in people predisposed to keloid formation. The recurrence of keloids after simple excision and closure is very high (at least 70%). Steroid injections, silicone and compressive dressings, and radiation therapy have been offered as treatment modalities, with limited improvements in recurrence rates.

Granulation tissue is common at the donor site around and within the skin graft. Its appearance represents an over exuberant proliferation of fibroblasts and small blood vessels. Most granulation tissue can be treated with topical application of silver nitrate applied periodically over several office visits, as needed. Silver nitrate can lead to dark discoloration of the treated tissues, which can persist for weeks to months. However, granulation tissue rarely requires more involved treatment.

Corona flattening can occur on occasion and may require revision surgery done at the same time of the 2nd stage surgery (typically penile and testicular implantation)

Erectile implants

Roughly nine months after the penis is created, the patient can have a penile implant placed to allow rigidity for penetration. Currently there are no FDA approved implants specifically

created for transgender patients. As such, implants created for non-transgender males with erectile dysfunction are rigidly fixed to the pubic bone. Complications can include infection and erosion.

Infection is the most common complication of the penile implant. Pre and post op antibiotics reduce the risk, as well as intraoperative sterile technique. If an implant becomes infected, it typically has to be removed. A new implant may be replaced six months later.

Erosion is when the implant protrudes through the skin of the phallus or the urethra. The presence of sensation in the phallus, and avoiding an excessively large implant reduce the risk of erosion. As with infection, erosion of an implant necessitates surgical removal.

Dysuria

Should a recently postop phalloplasty patient have dysuria, the best approach is to obtain a urine culture. Urinalysis is of little value as white and red cells can be detectable in normal post op patients for months after reconstruction. If a urine culture is positive, the infection should be treated with culture specific antibiotics. If it is negative, the most likely culprit is a urethral stricture, which should be evaluated by the surgeon who performed the phalloplasty, or if unavailable, a local urologist.

Metoidioplasty

Metoidioplasty (metaoidioplasty) is a Greek word that means "towards male genitalia." Testosterone causes growth of the clitoris; metoidioplasty uses only local tissue (no grafting) to create a smaller, 1 to 3 inch phallus with girth approximately the size of someone's thumb. Patients may opt to have a urethra placed in the phallus, but not all patients choose to do this. A scrotum can also be created from the labia majora and a vaginectomy may be performed. Because metoidioplasty is a shorter procedure, occasionally hysterectomy is performed at the same time as metoidioplasty. Some surgeons may use tissue expanders to create the scrotum, while others do not find this necessary. Testicular implants are typically placed at a second stage approximately 4 months later. While the phallus is not large enough to accept a penile implant, erections are possible since the procedure involves the use of natal clitorial and other genital tissues.

Complications associated with metoidioplasty are very similar to free flap phalloplsaty, except for flap loss since no flap is used. Wound breakdown, infection, urethral stricture and fistula are all seen in similar anatomic sites to that of free flap phalloplasty, although the incidence is lower in metoidioplasty. Risks such as coronal flattening do not occur in metoidioplasty, as the corona does not require sculpting in metoidioplasty. Management of complications similar to as is detailed in the phalloplasty section.

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31. Hysterectomy

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Introduction

Hysterectomy with and without salpingectomy/oophorectomy is considered by WPATH to be a medically necessary component of gender-affirming surgical therapy for those transgender men who choose to seek this procedure.[1] It is unknown how many transgender men desire and obtain hysterectomy for the purposes of gender affirmation or in the context of gender dysphoria. In the National Transgender Discrimination Survey, 21% of trans men surveyed had undergone hysterectomy.[2] 58% desired a hysterectomy at some time in the future, and 21% had no desire for a hysterectomy, It is unclear what differentiated individuals who had already undergone hysterectomy from those who desired the procedure in the future, though access to care and financial considerations are likely contributors. Also unclear is how reproductive desires may play into decisions about hysterectomy and or oophorectomy. Furthermore, it is unclear from this study what proportion of these hysterectomies were due to a medically pathologic condition rather than gender dysphoria, since hysterectomy is one of the most common non-obstetrical surgical procedures.

A study of 134 transgender men reported a diversity of indications for hysterectomy, though most procedures were performed for gender affirmation. In that study, 58% underwent hysterectomy because organs were incongruent with current gender identity, 47% for further physical masculinization, 43% to facilitate a change in legal documents, and 37% to avoid future gynecological appointments. However, this same study also noted that for many this procedure was seen as "preventive" in 59%, was performed because of pre-existing medical problems in 26%, specifically for "tumors, cysts, fibroids or endometriosis" in 22% or to stop extreme bleeding and cramping in 22%.[3] Since widespread explicit insurance coverage for hysterectomy for purposes of gender affirmation is both recent and evolving, it is possible that some of the decisions to perform hysterectomy in the setting of pathologic conditions may have been hastened by coexisting gender dysphoria.

Surgical approaches

Best practice for the surgical approach to hysterectomy in transgender men has not been studied. Hysterectomy may be performed abdominally, laparoscopically, or vaginally. Based on existing evidence, the American Congress of Obstetricians and Gynecologists has stated that for patients in whom the approach is appropriate, a vaginal approach has the fewest complications and blood loss, quickest recovery, and is the most cost-effective.[4] For transgender men, vaginal hysterectomy has the added benefit of leaving no abdominal scars. Initial data [5,6] support the notion that vaginal hysterectomy is appropriate for transgender men. Many other studies have noted that laparoscopic hysterectomy, the second least invasive form of hysterectomy, is also possible and can successfully be accomplished without additional complications.[7–11]

Hysterectomy has been successfully combined with other gender-affirming surgeries performed on the same day in the same operating suite including vaginectomy, mastectomy, and genital reconstruction including metoidioplasty and phalloplasty.[10,12] Hysterectomy itself does not largely differ, however some modifications in concurrent surgeries and extent of dissection may differ depending on the goals of the transgender patient. For example if a transgender man undergoing hysterectomy has no plans for penetrative vaginal intercourse in the future, the vaginal cuff closure could be much more exterior, such that less of a vaginal orifice remains. Similarly, vaginectomy (removal of vaginal mucosal tissue) and colpocleisis (closure of the vaginal canal) could be performed if no vaginal orifice is desired, as long as there is no desire for future genital reconstructive surgery that would make use of the vaginal mucosa (for urethral lengthening etc). Finally, consideration of whether to retain or remove the ovaries and fallopian tubes at the time of surgery is also a personal decision and will be based on considerations of patient desire, future fertility, plans for exogenous (steroid) hormone administration, and other pathology that may be aided or exacerbated by ovarian removal (e.g., endometriosis).

While the WPATH Standards of Care require two mental health assessments prior to hysterectomy, this has been challenged academically [13] and in practice [7] given that non-transgender women may undergo a hysterectomy for equally or less compelling complaints without similar restrictions.

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32. Binding, packing, and tucking

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Tucking allows a visibly smooth crotch contour. In this practice, the testicles (if present) are moved into the inguinal canal, and moving the penis and scrotum posteriorly in the perineal region. Tight fitting underwear, or a special undergarment known as a *gaffe* is then worn to maintain this alignment. In some cases, adhesive or even duct tape may be used. In addition to local skin effects, this practice could result in urinary trauma or infections, as well as testicular complaints, which are covered elsewhere.

Packing is the placing of a penile prosthesis in one's underwear, giving both an outward appearance as well as reducing gender dysphoria.

Binding involves the use of tight fitting sports bras, shirts, ace bandages, or a specially made *binder* to provide a flat chest contour. In some people with larger breasts, multiple garments may be used, and breathing may be restricted. Prolonged binding may result in breast pain, local skin irritation, or fungal infections.

33. Hair removal

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Introduction

The management of unwanted hair is often a challenge for transgender people, for many reasons. Barriers include access to trans-experienced aesthetic providers, transportation, affordability, and confusion regarding the options, risks and benefits.[1,2] While insurance coverage for hair removal in transgender persons is expanding, it remains inconsistent and can be a significant source of frustration and anxiety for both patient and provider.[3,4]

Transgender men, transgender women, and other gender nonconforming individuals may seek services; a care plan for each patient is best individualized according to their personal needs and transition goals. Transgender woman typically seek hair removal on the face, neck, as well as in the genital area in the case of pre-operative preparation for vaginoplasty.[5,6] Transgender men typically seek hair reduction on forearm or thigh future graft sites in preparation for phaloplasty.[5,7] While epilation (plucking, waxing, or Epi-Lady type devices) and the use of depilatories (chemicals) offer temporary measures, many seek one of several modalities that offer permanent hair reduction/removal: light amplification by stimulated emission of radiation (laser) hair removal (LHR) and electrolysis hair removal (EHR).[8,9] As with any referral for care, it is ideal to establish relationships with experienced, accessible practitioners with a positive reputation in the transgender community.

Methods: pros and cons of each

The hair growth cycle consists of three successive stages that include the anagen (growth) phase, the catagen (transitional) phase, and the telogen (resting) phase. Each strand is at its own stage of development. Time in each phase can vary by location, from an anagen phase of one to two months on the body, to two to six years on the scalp. Patterns of hair growth may also vary based on gender and ethnicity.[10] The effectiveness of both methods rely to some extent on the timing of the hair growth cycle, with the ideal response being when hairs are in the active (anagen) growth phase. Both require multiple sessions, and since effectiveness is approximately 85-90%, combined LHR and EHR may offer the best result for many. Lifelong treatment is often required for sustained effect.[10–12]

Laser Hair Removal: The use of lasers is considered a 'medical procedure' and offers the use of light to selectively target dark, coarse hairs.[13] The pigment in dark hairs absorbs the light to create heat that is transmitted down the shaft to destroy the follicle. It treats larger surface areas and is less time consuming than EHR. Treatments are typically every 4-8 weeks, depending on the treatment location, as the hair growth cycles vary by area. Safety and effectiveness may vary depending on the platform used (diode, ruby, neodymium-doped yttrium aluminum garnet; [Nd: YAG], etc.), patient skin type and hair characteristics. LHR is generally ineffective on thin, light, red, blonde or gray hairs. A wavelength of 1064 (Nd: YAG)

is the only wavelength considered safe for dark-skinned individuals (Fitzpatrick skin types 5 or 6).[9,11]

LHR is FDA approved for permanent hair *reduction.* Patients are required to be evaluated by a medical provider (NP/PA/MD, etc.) prior to being treated; regulations on the qualifications and licensure of the laser operator vary by U.S. state, with some states requiring registered nurses.[10]

As with any light-based treatment that uses selective photothermolysis, overheating can result in redness, blisters, burns, and subsequent hyper or hypo-pigmentation.[14–16] The majority of these are infrequent and temporary; however care should be taken with any patient with a history of keloids (test spot on low visibility area) and LHR is contraindicated in conditions that might flare in reaction to light exposure, such as lupus erythematous [17] It is suggested that patients with a history of herpes simplex outbreaks be aware of the potential for a light-stimulated outbreak (in treatment area) and have antivirals available for self-treatment. Treatments should be avoided when photosensitizing medications are being used (see table [18]). Do not treat areas of active infection. Flashing lights have been known to induce seizures in susceptible patients, so patients should be screened for this risk.[19] Treatments on the face require occlusion of both eyes to protect from retinal exposure and damage. Protective, wavelength specific, eye-ware is used during non-facial body treatments.[20]

Relative CONTRAINDICATIONS to laser hair removal:

- History of melanoma, raised moles, suspicious lesions, keloid scar formation, healing problems, active infections, open lesions, hives, herpetic lesions, cold sores, tattoos or permanent make-up in area of treatment, recent use of isoretinoin, tetracycline, or St. John's wort in the last year, autoimmune diseases such as lupus, scleroderma, vitiligo.[17,18]
- While not a contraindication to treatment, the following drugs may cause increased hair growth: penicillin, cyclosporins, corticosteroids, haldol, phenytoin, thyroid medications.[18]

Electrolysis involves use of an electric current with a very fine needle–shaped probe to destroy the root of individual hair follicles. There are three types of electrolysis; galvanic (direct electrical current produces a chemical reaction), thermolysis (diathermy: short-wave which produces heat) and blend (combination of galvanic and thermolysis).[21] Since electrolysis involves direct mechanical destruction of the root, it can be used on all hair colors and skin types. Treatments are typically weekly and lasting up to 1 hour, based on patient pain tolerance. Targeting individual hairs may be time consuming and costly, however is very effective when used to treat hairs that have not or will not respond to LHR. Newer technologies/epilators (27MHz frequency) offer a more comfortable treatment and may be safer than older model machines (14MHz frequency). As the frequency is increased, so is the heat produced, resulting in improved effectiveness.[22] Electrolysis is FDA approved for permanent hair *removal.* In the U.S., electrologists are licensed in their state of practice and practice independently.

Some of the same risks associated with LHR also apply: redness, pigment changes, and avoiding areas of active dermatitis or infection.[23] Patients with pacemakers are most safely

treated with thermolysis, but should discuss with their cardiologist prior to treatment. Home laser or electrolysis devices have not demonstrated effectiveness and may cause harm.[24]

Managing pain during the procedure

At least some discomfort can be expected during either procedure.[25] Each patient is best assessed individually to determine the optimal approach for pain control. The response to each treatment can vary based on the location of treatment, level of hydration, anxiety and stress. Creating a soothing environment, the use of reassurance, deep-breathing, thoughtful orientation to the device, use of a 'test-spot,' pre-treatment with a cold compress and over-the-counter pain medication (acetaminophen) may all be helpful. It is best to avoid NSAIDS immediately prior and after treatments to minimize the risk of bruising. The use of narcotics is typically not needed, but may be appropriate in some cases.

Topical anesthetics

Lidocaine-containing products (alone or in compounded form) should be provided to the patient initially and then as requested. Topical anesthetics reduce procedure-related pain with minimal side effects. Careful attention must be paid to the particular anatomic location, the total surface area covered, and the duration of anesthetic skin contact. Topical anesthetics can be applied 15-45 minutes prior to treatment and are typically removed during or after the procedure(s).[26–30] The use of EMLA (lidocaine 2.5% and procaine 2.5%) may have limited effect, primarily due to the prolonged onset of action and need for an occlusive barrier during the pre-treatment phase. The combination of benzocaine 20%, lidocaine 8% and tetracaine 4% (BLT) is a common and effective combination. This preparation should only be applied by a licensed medical provider or nurse, as application of excessive amounts can result in toxicity.

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34. Transgender voice and communication - vocal health and considerations

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Introduction

Voice and communication are crucial aspects of daily life for all humans. Within the transgender community voice and communication are often brought to the forefront when the incongruence between gender identity and voice/communication style are greatest. Aspects of voice and communication are highly related to gender [1] and culture.[2] These include pitch, intonation, loudness and stress patterns, voice quality, resonance, articulation, speech rate, language, and nonverbal communication.[3,4] Altering the aspects of voice and communication related to gender have been reported to reduce gender dysphoria while improving mental health and quality of life.[1]

There are many resources to help trans people identify communication characteristics that may be targeted to develop more gender specific communication style. These may include vocal coaches, theater professionals, singing teachers, and movement experts.[3] **Specialty trained speech language pathologists (SLPs) are best equipped to facilitate overall vocal health and efficiency,** in addition to behavioral changes related to voice and communication for transgender people.[1–3,5] Otolaryngologists with subspecialty training in laryngology are skilled in vocal fold surgery techniques (phonosurgery) which may act as an adjunct to voice therapy.

Approach to voice complaints

Transgender people may present with voice complaints related to quality change or fatigue that are unrelated to gender transition.[2] This could be non-organic, organic, iatrogenic, or idiopathic in nature (Table 1). It is important that a comprehensive voice evaluation is completed, including voice and communication needs related to gender transition, by a laryngologist and voice trained speech pathologist prior to initiating voice treatment. Evaluation should include a thorough laryngeal examination including videostroboscopy to assess the anatomy and physiology of structures related to voice production.

Table 34-1. Common Voice Complaints and Diagnosis

Origin	Diagnosis	Voice Complaints
Organic	Nodules, Polyp(s), Cyst(s) Granuloma Scar	Roughness, breathiness, pitch breaks Voice fatigue Increased vocal effort
Non-Organic	Muscle Tension Dysphonia	Roughness Voice fatigue Increased vocal effort
Iatrogenic	Vocal Fold Motion Impairment Scar	Breathiness, roughness, increased pitch Voice Fatigue Increased effort
Idiopathic	Vocal Fold Paralysis/Paresis	Breathiness Voice Fatigue Increased effort

The overarching treatment goal for transgender people who present with voice and communication complaints is to aid in achieving a gender congruent voice in an efficient and safe manner. Treatment should be patient specific and can be accomplished through behavioral and medical/surgical intervention.

Voice feminization

In a study of self-perceptions of trans females, it was found that the strongest contributor to communication satisfaction was voice.[6] The components of voice production include pitch, resonance, intonation and intensity.

Pitch

Pitch may be perceived as the most important factor for voice and subsequently gender identification.[2,7,8] A strong marker for the perception of female voice is an average speaking pitch of 180 Hz in a range of approximately 140 to 300 Hz.[9,10] The average non-transgender female pitch is approximately 225Hz while the average non-transgender male pitch is approximately 125Hz. A pitch range that is considered gender neutral generally falls between 155-185Hz.[11] It has been demonstrated that increasing speaking pitch impacts the degree of voice feminization.[9,12,13] However, increasing pitch into the female range does not necessarily result in listener perception of the speaker as female.[7,14] Research indicates that other voice characteristics such as speaking pitch range, intonation, resonance, and voice quality play varying roles in the perception of femininity.[5] Similarly, pitch floor (the bottom of the pitch range) and the proximity of the usual speaking pitch to this floor is thought to influence the perceived maleness of voice, rather than the speaking pitch alone.[14]

Resonance

There is some discrepancy in the literature on the role of resonance, as studied through formant (harmonic) frequencies. Harmonic frequencies are multiples of the root speaking pitch; the combination and configuration of formant frequencies for any given sound determine its "tone." Contributors to vocal resonance include the length of the pharynx and size of the sinuses, which in transgender women who have undergone a male puberty are fixed in a larger size than with non-transgender women. One report suggests a primary role of resonance in perceptual identification of the speaker's gender.[10] However, another study reports that a combination of both pitch and resonance are found to contribute to perceived femininity and should be addressed.[4,15]

Intonation

Intonation, or variability in pitch during speaking, is a recommended component of behavioral intervention for voice feminization. In one study, there were no significant differences in overall intonation patterns observed between genders. Transgender participants who were identified as female had a larger number of upward intonation patterns and larger semi-tone range within utterances than other groups. Transgender women who were misidentified as male had fewer upward and more downward intonation patterns than females and transgender females who were correctly identified.[16]

Intensity and other voice characteristics contributing to perception of gender

Increasing breathiness [9,17] using lower vocal intensity [13,17] and avoiding vocal fry [13] can contribute to voice feminization.

Behavioral Intervention

The components of voice production are primarily addressed through behavioral voice therapy. It is thought that the total number of voice therapy sessions, in addition to living full time as female might be predictive of response to behavioral intervention.[18]

Two common voice therapy techniques include flow phonation and resonant voice therapy. Flow phonation targets balanced exhalation of airflow during voice production to achieve vocal efficiency and may aid in altering breathiness and intensity. Resonant voice therapy focuses on achieving easy phonation while experiencing the energy or vibration of sound in the oral cavity therefore altering resonance.[19] When used with transgender women, oral resonance therapy is reported to increase femininity by altering resonance to more closely approximate female resonance with a spontaneous increase in pitch.[4] Vocal function exercises, a systematic program of physiologic voice exercises that are designed to strengthen and balance the laryngeal musculature and to achieve balance between airflow and muscular effort,[20] do not seem to improve therapy outcomes in trans women.[18]

Long-term gains have been reported related to listeners' perception of gender following voice therapy that targeted primarily pitch and resonance.[15] Voice therapy has also been shown to generate changes that significantly impact listener's perception of femininity; however femininity is perceived as higher immediately following therapy than 15 months later.[21] Trans women having varying voice goals and may choose to use feminine communication

patterns all of the time or situationally.[1,17] The decreased perception of femininity over time, mentioned above, and the variable application of feminine voice may indicate the place for a maintenance program following voice therapy. While research is required in this area, intermittent 'checking-in' and recalibration of voice components may be warranted.

Studies indicate that trans women attain improvement in voice following voice therapy and most are satisfied with the outcome.[17,21] If, after a course of behavioral therapy the desired outcome is not achieved, surgical intervention may be considered.[22] At this time, surgical intervention primarily targets alteration in pitch. Pitch change alone has been shown to be insufficient for listeners to accurately identify gender [7,14] and should not be considered the initial or only treatment for voice feminization.

Effects of hormone therapy on voice

Hormone therapy in trans women, while resulting in reduction of testosterone levels and increases in levels of progesterone and estrogen, has not been perceived to have a significant effect on voice or the perception of feminine voice.[23] Vocal pitch is a function of the overall size and mass of the vocal folds, and there are few if any formal studies in the English literature that support that hormonal manipulation in post pubescent males will significantly alter vocal pitch. During male puberty, exposure to testosterone results in hypertrophy of the laryngeal muscles, cartilage and mucosa. This results in the characteristic voice changes that occur in pubescent males.

While withdrawing testosterone result in a modest degree of mucosal and muscle thinning, this effect takes years and cannot reverse the significant hypertrophy caused by the previous exposure. Thus pitch, which is related to vocal fold mass and size remains lowered, and the overall effect on voice from withdrawal of androgens is minimal once these changes have occurred. This is consistent with what is seen in females who have been exposed to androgens for the treatment of medical conditions. Once the exposure has occurred and the vocal pitch is lowered, the withdrawal of androgens is not generally associated with a significant re-elevation of pitch. Therefore, if behavioral interventions do not result in a sustained improvement in patient satisfaction with the characteristics of voice, then surgery may be considered.

Surgical considerations

As previously stated, pitch of voice is related to overall vocal fold mass and the tension of the vocal fold while the patient is producing voice. We can all voluntarily increase the tension in our vocal folds to elevate pitch. This, however, requires continuous muscular effort. With attention, training and time, this increased effort may become habitual. However, even successful patients often complain of a sensation of vocal effort and/or fatigue at the end of the day. Therefore, surgeries have been designed to elevate pitch by either altering vocal fold tension, mass, or both. The tendency of biological structures to relax when artificially stretched or tensed represents a significant challenge to surgical approaches to voice modification. Furthermore, procedures which attempt to alter the tension by scarring the vibratory portion of the vocal fold, or reducing the overall vocal fold mass, risk inducing

negative alteration in the delicate tissue of the vocal folds, which must vibrate at high frequencies to produce normal vocal quality.

Surgical attempts to elongate the vocal folds

One of the earliest procedures reported for elevation of vocal pitch is a criothyroid approximation, or type 4 thyroplasty, initially developed in the 1970s. In this surgery, the vocal folds are placed under permanent increased tension, using sutures that approximate the front aspect of the thyroid cartilage to the cricoid ring. A year-long longitudinal report of 11 patients (only 1 of whom was transgender) who underwent this procedure showed initial promise immediately postop.[24] However, while pitch did remain elevated at one year, it was lower in comparison to the postop pitch, and it was theorized that the vocal chronic vocal tension resulted in stretching of the tissue with relaxation or that the sutures pulled through the cartilage. This has led to proposed modifications to the originally described procedure, either by altering the method of suture placement,[25] or by scarifying the thyroid to the cricoid.[26] Other case series have found similar results of initial improvement with benefits that wane over time.

Other attempts to permanently elongate the vocal folds to increase tension have resulted in similar outcomes.[27,28] These modifications have proposed pulling the anterior aspect of the vocal folds forward without fixing the cricoid to the thyroid. The theorized advantage is that the patient would be able to further modulate pitch. However, this has not been the outcome and the results are variable when the patients are followed long-term.

Surgeries to reduce vocal fold mass and length

In 1982, Donald et al [29] proposed surgery to reduce the size of the vocal folds, and create a web between the anterior portion of the vocal folds, by opening the larynx, removing the front third of the vocal folds and suturing the larynx closed. This surgery has the advantage of being able to be combined with procedures to reduce the prominence of the larynx in the neck.[30] Though the length of follow-up is not noted, Donald reported on successful pitch elevation and patient satisfaction in 3 patients. The procedure has been modified by other surgeons, and combined with shortening of the pharynx by bringing the larynx and the hyoid bone closure together. In a series of 94 patients (74 of whom were followed for approximately 1 year or more), these authors reported an average elevation of pitch from 139 Hz preoperatively to 196 Hz postoperatively. Complications were relatively rare and transient.[31] While promising, the results were somewhat unpredictable in terms of overall vocal quality and vocal range. In addition, while the surgery is generally well tolerated, it does place the airway at risk and require an external incision in the anterior neck skin.

Surgeries to increase tension by producing scar on the vocal folds

As previously mentioned, vocal fold vibration rate, which determines the pitch of the voice, is affected by vocal fold mass (as the mass decreases, the vibration rate or pitch increases) and tension (as the tension increases the vibration and pitch increases). This has led surgeons to attempt to elevate pitch by increasing tension through scarring the surface of the vocal folds or scarring the front portion of the vocal folds together to shorten the portion available for vibration. The main advantage of these types of procedures is that they can be done through

the mouth without an incision in the neck, are well tolerated, and do no place the patient's breathing at significant risk. The main disadvantage is that healing and scar production can be unpredictable and results variable.

The initial reports of this type of surgery were present by Wendler in 1989.[32] The procedure, which has come to be known as the Wendler glottopasty, is relatively easy to perform. The mucosa or skin from the front aspect of the vocal folds is removed. This can be done with either a CO2 laser, or with traditional non-powered instruments; the front aspect of the vocal folds is then sutured together. Variations on this procedure have replicated results in multiple small patient series from other centers.[12,22,33,34] In general, the vocal fold pitch is significantly elevated, but the overall pitch range and vocal loudness levels are reduced. In all patients, there is a modest increase in degree of vocal roughness postoperatively, and this is more noticeable when the procedure is performed in patients over 50 years of age. The procedure can also be repeated if healing does not result in as much scar as desired, and can be performed in patients who have failed other types of surgery.[35]

Finally, some surgeons have attempted to create scar on the top/superior surface of the vocal folds, either as a separate procedure [36] or as an adjunct to Wendler Glottoplasty.[37] These attempts have not been shown to produce reliable results or benefits over glottoplasty alone, and are likely best avoided.

Voice masculinization

Far fewer transgender males present for voice evaluation and treatment than transgender females. This may be related to the reduction in pitch that transgender males experience as a result of hormone therapy.[38,39] As a result, the need for voice therapy for transgender men may be underestimated.[40] The hormone induced pitch change is not always without problems and it remains unclear if it is in all cases sufficient for the speaker to be identified as male.[38,39] Research supports that voice and communication should be targeted in voice therapy.[2,5,40–42]

Pitch

With hormone therapy, final lowered pitch is achieved sometime after 1 year. Following response to this treatment, it is reported that about 75% of trans men are identified as male by telephone.[42] This leaves 1 in 4 transgender men who may not be perceived vocally as male. The perceived masculinity of voice is related not only to pitch but also to the proximity of the habitual speaking pitch to the pitch floor, or lowest pitch.[5] Following behavioral intervention with a speech pathologist, it was demonstrated that speaking pitch decreased by an additional 35Hz and pitch instability and voice fatigue resolved.[40]

Resonance

Increased 'chest resonance' is suggested as a goal in voice therapy.[2] Achieving balanced resonance during voice production contributes to overall vocal efficiency and may play a role in the reported improvement in voice complaints for trans men following voice therapy. These changes in resonance are further supported by data showing a change in formant frequencies

(the acoustic correlate of resonance) during the first year of hormone treatment in conjunction with behavioral intervention.[5]

Intonation

In one study, there were no significant differences in overall intonation patterns observed between 4 gender groups (12 non-transgender males, 12 non-transgender females, 6 transgender men, 14 transgender women). However, transgender women who were misidentified as male had fewer upward and more downward intonation patterns than females and transgender females who were correctly identified.[16] Decreasing pitch variation, while avoiding monotonicity is suggested for trans men.[2]

Intensity

Vocal intensity in trans males is not well documented in the research literature. However, if increasing breathiness [9,17] and using lower vocal intensity [13,17] contributes to voice feminization, it may be considered that reducing breathiness and avoiding a soft voice may be perceived as more masculine.

Behavioral intervention

While pitch is primarily addressed through hormone therapy and secondarily by voice therapy, the other components of voice production are primarily addressed through behavioral voice therapy.

Flow phonation and resonant voice therapy are two common voice therapy techniques. Flow phonation targets the balanced exhalation of airflow during voice production using respiration as the power source to achieve vocal efficiency. Resonant voice therapy focuses on achieving easy phonation while experiencing the energy or vibration of sound in the oral cavity.[19] The combination of these techniques can work to maximize voice production targeting pitch, resonance, intonation and intensity for trans men; efficacy data is needed to support this.

Some transmasculine spectrum people seek only some voice masculinization, and desire flexibility with their voice and communication.[5] While the literature supports the role of voice therapy for voice masculinization,[40,41] this is an area that needs further attention. With this in mind, voice therapy should be patient specific and physiologically based to achieve patient and therapy goals in a vocally efficient and safe manner.

Effects of testosterone hormone therapy on voice

90% of trans men will achieve acceptable voice results, lowering of pitch into a gender neutral or male range, after 4 to 5 months of taking exogenous androgens.[38] In multiple reports of small series, the average speaking pitch dropped for a female range of 190- 200 Hz to an acceptable male range of 100 to 140Hz.[5,43] However, while lowered pitch occurs as a consequence of thickening of the tissues due to the effects of androgens, in some cases male speaking patterns must be learned through behavioral therapy. 10% of patients or more will have some difficulty during transition either due to inability to produce efficient vocalizations with the altered laryngeal apparatus, or an inability to naturally adopt male speaking

patterns.[44] These patients usually respond to counseling with a certified speech-language pathologist who has experience in managing individuals with transgender voice issues.

Surgical consideration

As hormonal therapies and behavioral therapies are effective in helping 90% of transgender men achieve acceptable voice, surgical intervention is rarely indicated in this group. If needed, however, relaxation thyroplasty, designed to reduce the tension of the vocal folds can be performed. This same surgery is used in male patients with inappropriately elevated pitch and results in a reduction of pitch if performed in the original method [45] and an even greater reduction if modified as described by other authors. Typical pitch reduction is in the range of 100 Hz and usually results in the patient attaining an acceptable male vocal pitch. However, as the vocal cord tension is less controllable after the intervention, the voice is often perceived as more rough and with less volume.[46]

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35. Health insurance coverage issues for transgender people in the United States

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Introduction

Insurance plans issued in the United States since the 1980s routinely contained broadly written exclusions prohibiting payment for care related to "transsexualism," "sex change treatments," "gender identity disorders," or "transgender care." In some cases providers or clinic administrators, as well as claims administrators within insurance companies, would interpret these exclusionary statements in the broadest possible terms, assuming that transgender people could not receive medical care. The burden of fighting against this level of adversity when people are physically ill or injured represents a significant barrier to care. This adversity has contributed to the high incidence of transgender people avoiding seeking needed health care.[1]

Complexities of insurance and health benefits plans

Insurance policies are regulated by each of the 50 U.S. states; therefore, for example, an Anthem Blue Cross policy issued in one state may be very different in content from a policy issued by the same carrier in another state, though the plans may appear at first to be equivalent. Further, many people with private insurance in the U.S. receive coverage through their employer, and many large employers are able to negotiate their coverage to include or exclude specific care. These are "health benefits plans" and are not "insurance plans" strictly speaking, although they may appear the same to the enrolled member. Often referred to as "ERISA plans," (in some cases referred to as "self-insured" plans) such health benefits plans are usually regulated under the federal Employee Retirement Income Security Act of 1974), These ERISA plans are issued and administered by the same insurance companies that offer individual or small group plans, but the employer pays the direct costs of all care. As such ERISA plans have greater flexibility in what is covered, depending on the mission and intentions of the employer. In non-ERISA plans (in some cases referred to as a "fully funded" plan), the insurance company assumes the risk that the individual or group will not cost them more than the premium and co-pays will bring in. Being further removed from an incentive (i.e. covered employee recruitment and retention), non-ERISA plans may be less nimble in adding coverages or responding to case-by-case scenarios.

Although plans insured by or administered by a given carrier (e.g., Aetna, United Health, Anthem BCBS, et cetera) are often very different from each other, there are also often similarities in approach as carriers strive to standardize internal processes. Most carriers have now issued their own internal guidelines specific to transgender-related healthcare, especially surgical interventions. These guidelines (called by various names such as medical policies or coverage positions) spell out what services will be covered for a specific medical condition

and usually apply to all insurance products issued by a carrier. However, they may not apply to some ERISA-regulated health benefits plans since large employers have the ability to negotiate medical guidelines specific to their own employee health plans.

Thus, what is covered by a given health plan will vary not only by state but also by employer. Some large companies choose to offer transgender health benefits under their ERISA plan in order, for example, to maximize their talent recruitment, to provide a just and equitable workplace, or to control healthcare costs by providing the services people need. These large employers have chosen to implement medical guidelines that offer increased access, such as coverage of a greater range of medically necessary services. Smaller businesses, which depend on the insurance company to assume the risk (and whose risk is combined with other small employers), may not have the leverage to negotiate inclusion of transgender health benefits. However, smaller employers can inquire with their carrier representative as to feasibility and per-member, per-month costs of doing so, since coverage is becoming increasingly common across the country.

Gaining coverage: changing the paradigm

From the 1960s through the 1990s, some very persistent Individuals, often with support from their health care providers, were able to secure benefits payments, in certain instances. However, systemic reform did not begin until the 2000s, after advocates were able to convince the City & County of San Francisco to eliminate exclusions in at least one of the five plans City & County employees could select from for their health care coverage. Utilization data from the first five years showed that there was little or no increase in plan cost when medically necessary gender-affirming care was included in a large group plan. These results were used to inform the inclusion of transgender health benefits in the Human Rights Campaign's Corporate Equality Index, an instrument devised to grade companies on their approach to LGBT employee and customer relations.[2]

Private and public insurance reform

As of 2015, an increasing number of employers are offering transgender-inclusive health benefits plans, and insurance Commissioners in numerous states and the District of Columbia have issued regulations prohibiting the sale of insurance plans that discriminate against transgender people.[3] Further, on May 30, 2014, the U.S. Department of Health and Human Services issued a ruling that Medicare's longstanding exclusion of "transsexual surgical procedures" was no longer valid, leaving the provision of services up to local coverage determinations.[4] Following suit, some states have begun to revise their Medicaid plans to offer transgender-inclusive health care.[5] Specific Medicaid policies can be obtained from individual state Medicaid regulatory agencies. Currently (as of 2015) the Center for Medicare and Medicaid Services (CMS) is in the process of developing a new National Coverage Determination with regards to inclusion of gender-affirming care in the Medicare program. Private health insurance products are often regulated by the State Department of Insurance or Department of Managed Care (department nomenclature may differ by state); specific policies and coverage details can be obtained from individual state agencies

Claim denials for sex-specific procedures

In some automated systems, if for example the patient is designated as "female" in the electronic record (EMR), and a treatment or procedure code is entered for care that is exclusively covered for bodies designated male [e.g., prostatic ultrasound]), that claim may be automatically rejected. The reverse would be true for someone designated as "male" in the EMR but who requires care that is exclusively covered for bodies designated "female." If the patient's plan document or individual state regulations provide that transgender care is covered (or that care may not be restricted on the basis of sex), then the patient may need support from the physician's office to inform the carrier or administrator that the patient is transgender, and that this claim cannot be rejected. If there is no provision for transgender care in this instance, it will be necessary for the provider to appeal to the carrier for coverage of the specific treatment or diagnosis.

Overriding a "sex mismatch": condition code 45

All federally-funded health institutions (e.g., most hospitals) have received instruction on the use of Code 45 (and the KX modifier) in their coding practices and all Medicare Administrative Contractors are required to process this code,[6] which is an override for a sex mismatch. However, the code may not have been implemented by all hospitals or carriers' systems; in these cases using Code 45 may result in a returned claim for correction, or outright denial of the claim.

Discrimination claims

The Office for Civil Rights of the U.S. Department of Health and Human Services (HHS) has already issued guidance that preventive services may not be denied simply on the basis of sex, resulting for example in CDC coverage of mammograms for transgender women. In May 2015, CMS issued sub-regulatory guidance clarifying that preventive services are available under the Affordable Care Act (ACA) regardless of an individual's gender identity, sex assigned at birth, or recorded gender. Section 2713 of the Public Health Service Act, as amended by the ACA, requires most health plans to cover certain preventive services, regardless of gender.[7,8] Over time resolution of other sex-gender "mismatch" problems is expected to evolve as a result of new regulations guiding the implementation of non-discrimination provisions based on sex, contained in Section 1557 of the Affordable Care Act (forthcoming from the U.S. Department of Health and Human Services, HHS).[7] In the meantime, those who experience denials on the basis of sex-gender mismatches for sex-specific services are encouraged to file complaints with HHS Office for Civil Rights.[8]

Claims denials and discrimination

Many transgender people experience denials of their claims for transgender transition-specific services. Many more never receive a formal denial because their plan contains transgender-specific exclusions and the physician never files paperwork for prior authorization for such services. Many call their insurance carrier and are told services will not be covered, and on that basis never attempt to file a claim. Transgender individuals and their health providers

should be aware that unless a denial is in writing, it is not a denial and cannot be appealed. More importantly, transgender individuals with well-documented claims are increasingly achieving success in their appeals. Individuals are encouraged to work proactively with their medical providers to ensure that appeals documents include individualized, extensive documentation of the necessity and appropriateness of services. Such appeals should also include a comprehensive and detailed overview of the process of gender transition, including the role of and evidence in support of the specific services requested. In addition to providing a background to uninformed reviewers, such comprehensive documentation conveys the individual's intent to pursue the appeals to the final stages, which can be quite persuasive.

Over time resolution of these problems is expected to evolve as a result of new regulations guiding the implementation of non-discrimination provisions based on sex, which will be issued by HHS in the coming months.[9] In the meantime, individuals whose health plans contain provisions which discriminate on the basis of sex, including transgender-specific exclusions, are encouraged to file complaints with the HHS Office for Civil Rights.[8] While not every health plan in the U.S. is currently regulated under Section 1557 of the ACA, the ACA does specify that the Essential Health Benefits they are required to provide must also not discriminate on the basis of sex.

Table 35-1. Available health coverage in the U.S.

Coverage Type	General Characteristics and Caveats
ACA/Exchange Plans	Affordable Care Act coverage for individuals and families who are not eligible for Medicaid or Medicare, and who do not have insurance coverage through their employer, or may be self-employed. Until HHS implements Section 1557, only states with laws forbidding discrimination against transgender people in insurance products are likely to have transgender-inclusive plans available. To see if your state is one of these, check for the latest information on health coverage at www.transequality.org [10] or www.transgenderlawcenter.org.[11] However, even in several states currently prohibiting transgender exclusions in insurance plans, some or all marketplace plans may still retain exclusions.
Employer Plans, Fully-Funded (ERISA)	These are group plans available to small businesses, and sometimes may include plans offered to qualified individuals. Fully-funded means that purchaser of the plan pays a premium to fund the cost of services provided by medical providers and by the insurance company. Insurance companies often aggregate these plans to reduce their risk by pooling similar customers; if a small employer could find out who else was in their "pool," they might be able to convince the other companies to also ask for a policy change to make their plan transgender-inclusive. However, aggregate group composition is not public information, allowing insurers to control variables to maintain

Coverage Type	General Characteristics and Caveats
	profit margins. These plans are subject to state regulation, so their terms may vary by state. To see if your state is one of these, check for the latest information on health coverage at www.transequality.org or www.transgenderlawcenter.org.
Employer Plans, Self-Insured (non-ERISA)	These are group plans that are administered by insurance companies, using the same kind of provider networks and claim processing mechanisms as their other plans, but the employer pays ALL the costs themselves, and thus the employer bears all the risk. These plans are exempt from state regulation by the federal ERISA regulations, which give the employer/customers of the plans much more leeway to request the features and coverage levels that they want, including transgender-specific care. Some of these plans have their own internal medical guidelines that provide for coverage of all services medically necessary for transition.
Health Maintenance Organizations (HMO)	These state-regulated organizations provide both the insurance coverage and the medical services that they cover. In some cases, available services may not include transgender-specific care, but many HMOs are working hard to provide competent trans-sensitive care. As of December 2015, thirteen states including the District of Columbia have prohibitions on transgender exclusions (note a prohibition on exclusions is not the same as mandated inclusion) in these health plans, with implementation varying by state. Individual state information is available at www.transequality.org or www.transgenderlawcenter.org.
Medicaid	These are state-run (partially funded by federal money) safety net programs that provides payment to providers who will accept the amount the program is willing to pay (usually much less than private insurance will pay). Medicaid provides coverage for qualified low-income people, families and children, pregnant women, the elderly, and people with disabilities. Some states are starting to remove exclusions for trans-specific care from their Medicaid plans. To see if your state is one of these, check for the latest information on health coverage at www.transequality.org or www.transgenderlawcenter.org.
Medicare	This is the federal program that covers people over 65 years old, and disabled people under age 65. HHS ruled in May 2014 that blanket exclusions for "transsexual surgery" are no longer appropriate because the medical evidence exists to show that such care, when delivered appropriately, is effective, and it is no longer experimental surgery, nor is it "simply cosmetic." Currently coverage is available through Local Coverage Determination on a case-by-case basis.
Railroad Medicare	Under this program, people who worked for railroads for at least 10

Coverage Type	General Characteristics and Caveats
	years may access Medicare Part B services at favorable rates through the railroad-specified administrator. Transgender-specific services may be available according to Local Coverage Determinations (LCDs) through the Center for Medicare and Medicaid Serves (CMS).
TRICARE	This is the health benefit administration program for U.S. active duty military service members and their dependents and retirees who are not eligible for Medicare. Transgender-specific services are not available while transgender people are not permitted to serve openly in the military. This policy may change in mid-2016.
Union Plans	Some labor unions, in some states, may have transgender-inclusive policies available; check with the union's benefits office/department. Several labor unions have resolutions at the national level calling for the elimination of transgender exclusions. Although not binding on member unions, these may help union members fight for benefits equity.
Veteran's Administration	Transgender Veterans may obtain regular medical care, including hormone therapy. Transgender-specific surgical procedures are currently restricted or prohibited, although this may change as the U.S. military considers the role of transgender service members.

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36. Legal and identity documents

Primary author: Dan Karasic, MD

The concept of a "legal sex" is complex, though for simplicity the term will be used in this discussion. The World Professional Association for Transgender Health advocates a simple administrative procedure to change legal identity documents to match experienced gender.[1] While self-determination of legal gender is the law in a small (but growing) number of countries, including Argentina, Denmark, Malta, and Ireland, most countries require the involvement of health professionals, if legal "change of sex" is possible at all.[2]

Under United States federal law, and in some states, surgery is not required to change legal sex, but a health professional must certify that their patient has undergone "necessary" medical or psychological treatment for transition.[3] In completing this paperwork, the health professional should be aware that there is no particular clinical treatment (such as hormones or surgery) that is "necessary" for all trans people, and that legal documents reflecting a sex congruent with one's gender identity contribute to a patient's health, by supporting employment, safe travel, and other necessities of daily living, as well as facilitating access to medical care.

In some jurisdictions, there is a surgical requirement to change legal sex. The health provider may have leeway, depending on the law, as there is no particular surgery that is "necessary" for all trans people. Some trans people are unable to change their birth certificate in their home state or country, but may still change their gender markers on their U.S. passport, Social Security card, and driver's license.[4]

Transgender people may encounter a conflict between their legal sex and sex-specific medical care, such as screening for cervical cancer or prostatic disease. While state laws may vary, in some cases it may be necessary for the provider to contact the insurance company and explain the specific circumstances in the case of a sex-specific denial. Once legal documents have been changed, patients should be sure to update their legal name and sex with their insurance company and medical provider to prevent a denial based on a mismatch of information.

Legal change of name is not a gendered process in many, but not all jurisdictions; in most jurisdictions the name change process for transgender people is identical to that for non-transgender people.

U.S. Department of State guidelines for passports [5]:

http://travel.state.gov/content/passports/en/passports/information/gender.html

U.S. Social Security Administration guidelines [6]:

https://secure.ssa.gov/apps10/poms.nsf/lnx/0110212200

The National Center for Transgender Equality maintains a resource center with links to guidelines for changing identification documents in each U.S. state [3]: http://www.transequality.org/documents

Information on changing gender identity documents in Europe can be found at tgeu.org.[7]

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37. Sex-segregated systems

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A guiding principle in sex-segregated systems is to give people the autonomy to use the facilities and programs most aligned with their gender identity. This includes using restroom facilities, inpatient and residential beds, and locker rooms concordant with experienced gender (Grading: X C S). When available and preferred by the individual, non-gendered facilities can be utilized, but services should not be dependent on their availability.

The legal right to access to programs according to gender identity has expanded with recent state and federal regulation. Schools are required to allow students to use facilities and programs concordant with their gender identity, under the laws of some states, including California.[1] Under California law, students should be able to choose facilities according to their gender identity, or to use a private facility. Students should be able to participate in athletic programs and facilities according to gender identity. Students should be referred to according to preferred name and pronoun, and be listed according to gender identity in data systems. The Department of Education, under Title IX, has ruled that the students must be able to use programs and facilities according to their identity.[2]

The U.S. Department of Health and Human Services now requires shelters and other housing programs to provide housing and other accommodations and services to trans people according to their gender identity.[3]

WPATH SOC 7 addresses the care of people in institutional environments, stating that all aspects of transition care should be available to people living in institutions, and states that sex segregation by external genitalia may be inappropriate and place trans people at risk for victimization.[4]

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38. Homeless transgender individuals

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Introduction

One fifth of transgender people surveyed in the National Transgender Discrimination Survey reported experiencing homelessness. Homelessness frequently resulted from fleeing intolerant family, being forced out by family, by losing a job due to discrimination, or not being able to be employed due to discrimination and disability. In the same survey, of those who experienced homelessness, the majority of those trying to access a homeless shelter were harassed by shelter staff or residents (55%), 29% were turned away altogether, and 22% were sexually assaulted by residents or staff.[1] Many transgender individuals have found health care and social service providers to be ignorant about transgender issues and needs. It is essential that homeless service providers are well educated in this area as they are likely to encounter trans individuals.[2] The National Healthcare for the Homeless Clinicians Network has offered high quality trainings in this area.[2–4]

Assault and discrimination in public settings, especially homeless shelters, are frequently reported by homeless trans people.[5] While federal and other policies forbid discrimination,[6] many individuals are still unable to express their felt gender due to this discrimination, and best practices start with the collection of gender identity data in a confidential non-discriminatory manner, followed by an inquiry of housing preference if the shelter is sex segregated. Most individuals will prefer to be housed according to the gender in which they live or identify, however in some instances individuals may prefer to be housed based on their birth sex due to safety or other concerns. Best practice guidelines for shelters are now available.[7,8]

Functional disability is very common in homeless transgender individuals. Many homeless transgender individuals are unable to work due to disabilities. Gender dysphoria itself may lead to severe depression, anxiety, and suicidality.[9] Adverse childhood experiences, losses, and traumas may result in PTSD and other persistent problems. Physical assaults, alcohol and drug use may result in chronic physical conditions. Loss of educational opportunities and lack of job opportunities may result in poor capacity to learn and acquire new skills. These problems often cause long-term loss of capacity to work. Individuals may be eligible for social security disability, which may be their only way out of homelessness. Careful documentation of disability will be helpful for these individuals.[10]

Homelessness and gender-affirming care

Hormone therapy and transgender surgeries are considered medically necessary (when desired) for the treatment of gender dysphoria. Homelessness has in some cases been used as a blanket exclusion for these medical services. In most cases individuals who need hormone therapy are highly motivated, and despite the stresses of homelessness are able to adhere to treatment and monitoring. Healthcare for the Homeless providers have successfully

treated many patients with hormone therapy.[3] Homelessness is also not a contraindication for planning surgery for those patients who seek chest, breast, genital or other gender confirming procedures. The degree of housing stability required for successful outcomes for each of these surgeries will vary with the procedure and individual. Medical respite programs may have the capacity to allow some patients to recuperate from some surgeries. Since there is often a year or more waiting period from referral to surgery, this period is a time to intensively work on stabilization of housing status. The hope and promise of surgery is often a very strong motivator for individuals who were previously hopeless. Some patients may have unrealistic ideas about the rigor of surgery, recovery and aftercare or the possibility of their being stably housed. These individuals require intensive work with primary care providers, mental health providers, care navigators, and others to develop the stability needed for successful surgery outcomes. Care should be taken during the education and preparation process prior to surgery to avoid creating the perception of caregivers' concerns about housing instability as discriminatory or as arbitrary "hoops to jump through."[11]

Prevention

Prevention of homelessness is dependent upon decreasing discrimination in family, work, and other social settings, and providing transgender individuals with equal opportunities. Assisting people who are unable to work to obtain disability entitlements is an important way out of homelessness. Prevention of the harms of homelessness can be accomplished by implementing best practices and educating homeless service providers. While substantial research has been initiated in this area [12,13] more research is needed to inform the development of best practices for implementing these changes.

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39. Health considerations for gender non-conforming children and transgender adolescents

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Introduction

Care for transgender and gender non-conforming (TGNC) youth is a rapidly expanding field of medicine, and lends itself to controversy among professionals. It stands to reason that transgender adults started as transgender youth, and if identified in childhood or adolescence may benefit from early access to hormone blockers and/or gender-affirming hormones. While sparse data exist regarding the impact of puberty suppression and gender-affirming hormones administered during adolescence, there have been promising results from the Netherlands indicating that this approach in adolescents results in improved quality of life and diminished gender dysphoria.[1] The principle challenge in determining best practice for transgender youth lies in the fact that development is different for each individual. While there are standard ranges of pubertal initiation in children,[2] the age at which children begin to articulate their experience of gender dysphoria or assert a gender identity that is distinct from their assigned sex at birth is highly variable. Providers of transgender youth care should be skilled at meeting the needs of young people presenting for care at any stage in their process. The care of transgender youth does not need to be limited to pediatric endocrinologists. General pediatricians, specialists in adolescent medicine, family medicine, medicine/pediatrics, as well as nurse practitioners, physician assistants and others are all potentially qualified to provide high quality care for transgender youth.

Creating affirming spaces for youth

Cultural sensitivity and awareness begins with front office staff, and other staff that are initial points of contact for parents and patients. Staff and provider inquiry about, and consistent use of appropriate pronouns and name is the first, and potentially most important step toward creating a culturally sensitive and welcoming environment. Professionals can model appropriate use of names and pronouns in the presence of parents and caregivers.

Increasing numbers of young people are presenting with nonbinary or gender queer identities, preferring gender-neutral pronouns as a more accurate way to be described. It is not uncommon for providers, parents, friends and family members to struggle with gender-neutral pronouns, and inadvertently invalidate nonbinary identities. Regardless of whether nonbinary identities are a stepping stone to a more binary identity, or are landing spots, they are valid and need to be honored.

Mental health support

Mental health professionals have a critical role in the care of TGNC youth. Even prior to disclosure of an authentic gender identity that differs from assigned sex at birth, transgender youth commonly experience symptoms of depression, anxiety, social isolation, behavioral problems, school struggles, and suicidal ideation.[3] Often young people are engaged in mental health services long before presenting for care related to phenotypic gender transition. Unfortunately, because so few mental health providers are experienced in the care of TGNC youth, inaccurate recommendations are not uncommon. Mental health support should not be sought in order to convince TGNC youth into accepting a gender identity that aligns with their assigned sex at birth, but rather, to provide a safe and welcoming space for young people to discuss and explore their gender, and any mental health challenges that may exist. While historically mental health professionals have been charged with authenticating the gender of their TGNC clients, this approach is rapidly falling out of favor, and is being replaced by a support model, rather than a gatekeeper model of accessing care.[4] Mental health professionals play an important role in helping youth learn to articulate their gender experience, and identify their needs around a gender that is not aligned with their sex assigned at birth. Therapists should spend time with young people gathering historic information from youth about their experience of their gender, and how that has been handled by the young person's support system. Additionally, therapists can help youth develop strategies around disclosure, self-acceptance, integration of transgender identity, intimate partnerships, and social transition if that is desirable. Therapists can help youth clarify what they are hoping to gain from pubertal suppression, gender-affirming hormones, and/or surgery.

Mental health providers also play a major role in educating parents, family members, schools and others about the needs of TGNC youth, as well as advocating for the young person across multiple domains. Therapists also can work closely with parents to help them understand what their child is experiencing, and will likely need from their parents and/or caregivers. Many TGNC adolescents, like most people of any age undergoing a significant life change, will benefit from ongoing therapy during both pubertal suppression, and the first few years of gender-affirming hormone administration, and perhaps, beyond. Despite increasing visibility and acceptance, TGNC youth are likely to experience transphobia and its negative consequences, and may benefit from ongoing support. Requiring participation in therapy in order to access medical care related to physical gender transition is neither successful, nor does it promote honest communication between young people and therapists. Therapy should be strongly recommended, and discussed routinely with youth, though due to an ongoing lack of skilled gender mental health professionals it is not always feasible, financially or geographically, for TGNC youth or families to access this resource. Increasingly, therapists skilled in supporting TGNC youth are offering online or telephonic therapy to assist in these difficult situations. Additionally, youth are often accessing mental health care for reasons not related to gender, such as social anxiety, depression, self-harm, and others. While these symptoms overlap with gender dysphoria, there are plenty of mental health professionals who are familiar with these particular challenges. Issues addressed by mental health providers can also be addressed by medical providers who are experienced, comfortable and have the time

to have such discussions with youth. This is often necessary in geographic locations without available or accessible mental health professionals.

Pre-pubertal gender non-conforming (GNC) children

Over the past five years, it has become increasingly common for families with young children to request advice about the best way to approach their gender non-conforming child. Children as young as 18 months old have articulated information about their gender identity and gender expression preferences. Most parents are at a loss as to how to best help their child, and may seek the advice of a professional; commonly a psychiatrist or pediatrician. At this stage of development, no medical intervention is warranted or necessary. For young children, decisions must be made to create safe environments that promote healthy growth and development. For some children this may include a social transition – changing of external appearance (clothing, hairstyle) and possibly name and pronouns to match one's internal gender.

While there still exists uncertainty as to which GNC children will continue into adolescence and adulthood with transgender identities and/or gender dysphoria and which will not, it is been noted in prior studies that increased intensity of gender dysphoria is a predictor of a future transgender identity. This finding is subject to confounding, as youth who repress gender dysphoria due to safety or lack of basic language to express ones feelings may be no less likely to persist into adulthood, yet not present at an early age. Clinical experience has shown that it is those children who are the most dysphoric who seek social transition – the opportunity to live and be seen as a gender other than their assigned sex. Social transition has become more common, and a recent research endeavor reported good mental health among transgender children supported in their asserted gender.[5] Social transition for children can be logistically complicated and is best facilitated by a support team that includes the family, medical providers, mental health therapists and even lawyers. This team can work together to advocate for the child in school, sports, and other places so that GNC children can participate safely in these activities. Mental health therapists can play a significant role in the education of parents and other family members about GNC children, and their need for support and love.

Medical care for transgender youth

The approach to care may be simplified by defining two distinct cohorts of youth: those in the peri-pubertal, or early pubertal stages of development (Tanner 2-3), and those who are well along, in the final stages of, or completed with pubertal development (Tanner 4-5). These two cohorts often require different medical interventions; suppression of endogenous puberty, and/or the use of gender-affirming hormones for the development of masculinizing or feminizing features.

Suppression of endogenous puberty in early pubertal youth

Youth with gender dysphoria often experience significant trauma at the onset of their endogenous pubertal process.[6] Not uncommonly, gender dysphoria first emerges with the

onset of puberty. The development of secondary sexual characteristics can be the solidification of an undesired physical developmental process for those with a gender identity that is incongruent with their assigned sex at birth. With the high frequency among transgender youth of mental health challenges including anxiety, depression, social isolation, self-harm, drug and alcohol misuse, many providers view early treatment as life-saving.

For those youth on a transmasculine spectrum, puberty begins with the development of breast buds at approximately age 10, though a large cross-sectional study demonstrated that 10% of caucasians, 23% of black non-Hispanics, and nearly 15% of hispanics had Tanner 2 breast development by 7 years of age.[7] For those youth who identify on the transfeminine spectrum, the first sign of puberty is enlargement of the testicles to beyond 4 mL in volume, with an approximate average age of onset of 11 years. Development of undesired secondary sex characteristics related to natal puberty can have profound negative psychosocial effects and for many, are a source of great distress.

A team of experts in the Netherlands at the Gender Identity Clinic at the VU University Medical Center in Amsterdam was the first to develop a protocol that presented the possibility of delaying, or avoiding altogether, the development of undesired secondary sex characteristics resulting from an unwanted endogenous pubertal process.[8] This model of care includes the use of gonadotropin releasing hormone (GnRH) analogues, most commonly in the United States, leuprolide acetate or histrelin, medications that have been used for decades to delay pubertal development in children with central precocious puberty.[9] GnRH analogues offer a reversible intervention that allows youth temporary relief from an undesired, and potentially traumatic endogenous puberty. While data are sparse, preliminary results from the Netherlands indicate that behavioral problems and general psychological functioning improve while youth (age 12 and older) are undergoing puberty suppression.[10]

In order to avoid the development of undesired secondary sexual characteristics, GnRH analogues ideally are initiated at the earliest stages of puberty (Tanner 2-3).[11] There is a role for using GnRH analogues in youth who are in the later stages of pubertal development, either for induction of amenorrhea, or to halt ongoing development of undesired secondary sex characteristics. In addition, GnRH analogues are an effective complement to estrogen treatment in transfeminine youth, given that estrogen alone, at physiologic doses, is typically insufficient to adequately suppress testosterone production (see below). Youth cannot remain on GnRH analogues alone indefinitely, as bone mineralization relies on the presence of sex steroids. While clinically becoming increasingly common, the impact of GnRH analogues administered to transgender youth in early puberty and < 12 years of age has not been published. While rare, reported side effects from the use GnRH analogues may include diminished bone mineral density acquisition, weight gain, abscesses at the site of injection (if injectable form is used), irregular vaginal bleeding, and emotional lability.

Obtaining consent for treatment

Additional challenges arise when parents have discordant opinions about their TGNC child, or if a youth is in the custody of the courts. If both parents maintain medical decision-making for the youth then it becomes the task of the medical and mental health providers to help both

parents understand the necessity of medical interventions. This process is not always straightforward, can take a lot of time, and sometimes necessitates involvement of legal assistance. For youth in the child welfare system, judges can order that medical intervention, including the administration of gender-affirming hormones, be undertaken.

Dosing of GnRH analogs

Leuprolide acetate can be delivered via injection anywhere from daily, to every 3 to 4 months.[12] Histrelin is delivered via a time-release implant that is surgically inserted in the underside of the upper arm. The implant lasts between 12 and 36 months.

The physical exam for children beginning an unwanted puberty can be extremely stressful. Providers should work on developing clinical rapport with children in order to foster trust prior to carrying out to a genital exam. Providers should discuss the importance of genital exams (for those with testicles) and chest exams (for those with ovaries) in assessing pubertal progress. Using techniques to distract children during these exams with phones, devices, books and other things can make the exam tolerable. Significant genital and chest dysphoria are common among youth, and aversion to an examination of secondary sex characteristics should not be a barrier to moving forward with suppression of puberty. In fact, the provider should consider deferring a genital or chest exam until a follow-up visit, after a positive rapport has hopefully been established. In extreme cases, providers should consider creative approaches such as obtaining labs first to confirm initiation of puberty, and following up with the genital and/or chest exam after the relationship is better established.

Monitoring youth on GnRH analogues

Blood tests to determine if the hypothalamic-pituitary-gonadal axis is suppressed with GnRH analogues should occur 6-8 weeks after starting monthly doses, or 8 weeks after starting the 3-month dosing. For those with implants, blood levels assessing efficacy should be obtained 8 weeks after the implant is placed. Blood tests include ultrasensitive LH/FSH/total testosterone (in those with testes) or estradiol (in those with ovaries). There is some evidence that LH/FSH levels are not necessarily reliable indicators of suppression in those with GnRH analogue implants, therefore more accurate assessment of adequate suppression might require gonadotropin response to a subcutaneous leuprolide acetate stimulation test.[13]] While current guidelines recommend laboratory tests every three months to assess adequate suppression of the hypothalamic-pituitary-gonadal (HPG) axis,[11] repeated blood draws can be expensive and traumatizing for TGNC children. Suppression of the hypothalamic-pituitary-gonadal (HPG) axis should be assessed with clinical evaluation including height and weight, every three to four months, with blood serum ultrasensitive LH, FSH, estradiol/testosterone levels, renal and liver function, lipids, glucose, insulin, glycosylated hemoglobin considered annually, as clinically deemed appropriate while patients are on GnRH analogues. If there are clinical concerns regarding the efficacy of the puberty blocker, ultrasensitive pediatric FSH/LH, and sex steroid levels may be considered more frequently. More comprehensive and frequent laboratory tests will occur if the child is involved in a clinical or research trial.

There are potential benefits of baseline information about bone density, although no consensus about the necessity of obtaining bone densitometry prior to, and during GnRH analogue administration exists. If there is a family history of non-traumatic bone fractures, or osteoporosis, baseline screening is recommended. To optimize bone health, providers should ensure adequate dietary intake of calcium and should monitor vitamin D levels (25-OH) and supplement if indicated. Weight-bearing activity should also be encouraged. Physical changes of puberty should be assessed at follow up visits.

Follow-up conversation with youth who are undergoing pubertal suppression should include an assessment of an ongoing desire for endogenous puberty suppression. While extraordinarily rare, some youth may want to discontinue GnRH analogues and experience their endogenous puberty. For young people who remain gender dysphoric, and are interested in moving forward with masculinization or feminization, gender-affirming hormones can be added to GnRH analogues.

Gender-affirming hormones

Gender-affirming hormones may be added to GnRH analogues to assist in the development of feminizing or masculinizing features in transgender youth. **While the current Endocrine Society guidelines recommend starting gender-affirming hormones at about age 16,**[11] **some specialty clinics and experts now recommend the decision to initiate gender-affirming hormones be individually determined, based more on state of development rather than a specific chronological age. (Grading: X C S).**[12] Factors which support consideration of hormone initiation prior to age 16 include:

1. Length of time on GnRH analogues – for those youth whose endogenous puberty is suppressed in the earliest stages of puberty, waiting until age 16 to add hormones means a potential 5-7 year gap, during which bone mineral density is only accruing at a pre-pubertal rate. This could potentially impact peak bone mineral density, and place youth at risk for relative osteopenia/osteoporosis.
2. Experiencing puberty in the last years of high school or early college years presents multiple potential challenges. The emotional upheaval that occurs for youth undergoing puberty happens normally at 11 or 12 years of age. For those youth who struggle with emotional lability at that age, they do so in a relatively protected environment, regulated by parents/caregivers, and without access to potential dangers such as motor vehicles, drugs, alcohol and adult (or almost adult) peers and sexual partners. Having the physical appearance of a sexually immature 11 year old in high school can present emotional and social challenges that are amplified by gender dysphoria.
3. Available data from the Netherlands indicates that those youth who reach adolescence with gender dysphoria are unlikely to revert to a gender identity that is congruent with their assigned sex at birth.[10]

Awareness of one's gender identity **does not** require cognitive capacity acquired in adolescence or early adulthood, nor does it require a fully myelinated frontal lobe. Gender studies in non-transgender participants have found that children are aware of their gender by the age of five or six, and often earlier.[14]

Induction of amenorrhea in post-pubertal youth

Commonly, trans-masculine youth are either not yet ready for, or are not yet at an appropriate age to begin testosterone therapy, but are interested in induction of amenorrhea. GnRH analogues may be used in this situation, however access is often difficult for financial and other reasons, and these medications cannot be used without hormone replacement indefinitely. Other mechanisms for inducing amenorrhea include continuous administration of oral contraceptive pills, and progestagen-only long acting reversible contraceptives (LARC) such as depo-medroxyprogesterone acetate injections, a levonorgestrel intrauterine device (IUD), or etonorgestrel rod implants (Grading: NT R M). Progesterone releasing intrauterine devices may result in amenorrhea in approximately half of all users.[15] Note that some trans-masculine youth are uncomfortable using "female" hormones, even for induction of amenorrhea. Youth can be informed that the administration of progestagens alone have little if any feminizing effect. Careful consideration of the individual's needs is critical in this decision making process.

Preparing for gender-affirming hormone use in transgender youth

Prior to the initiation of gender-affirming hormones, providers should review the expectations that patients have about the use of hormones in their phenotypic gender transition. It is important for young people to have realistic expectations about gender-affirming hormones, and have an understanding about what hormones can and cannot achieve. Both GnRH analogue and gender-affirming hormone administration require parental/legal guardian consent if a youth is under the age of 18. Side effects, risks, and benefits should be reviewed during the consent process, as well as addressing the possibility of unknown long-term risks. The consent process for hormones should include a conversation about fertility. While options are being explored to preserve future fertility for transgender youth, the current reality is that cryopreservation is very expensive, in many cases prohibitively so for those with ovaries. For youth whose pubertal process has been suspended in the earliest stages, followed by administration of gender-affirming hormones, development of mature sperm or eggs is unlikely at the present time, although it is noteworthy that there is active research developing gametes in vitro from the field of juvenile oncology. The issue of future infertility is often far more problematic for parents and family members than for youth, especially at the beginning stages of discussing moving forward with gender-affirming hormones. Youth who determine that future genetic contribution to offspring is more important than avoiding the development of unmatched secondary sex characteristics can choose to stop GnRH analogues, and progress through endogenous puberty in order to cryopreserve sperm, or harvest eggs.

Administration of gender-affirming hormones in youth undergoing concurrent GnRH analogue puberty suppression

For those youth who are on GnRH analogues for puberty suppression, providers have the opportunity to create a more natural puberty with exogenous hormones. Because there is no need to use exogenous sex hormones to suppress endogenous secretion of sex hormones,

an escalating dose of either testosterone (for transmasculine youth) or estradiol (for transfeminine youth) can be used.

Transmasculine youth – hormone therapy with GnRH analogs

For those youth assigned female at birth who identify on the transmasculine spectrum, testosterone is used for the development of masculine secondary sexual characteristics. Testosterone can be delivered by injection, or topically via gel, compounded cream or a patch. Most adolescents are not enthusiastic about using gels or patches for a variety of reasons including necessity of daily application, potential of absorption for others in close proximity, and high incidence of local skin irritation in when a patch is used. Although injectable testosterone has historically been given intramuscularly, many practices have moved toward the less painful, and equally effective subcutaneous delivery mechanism.[16] Some patients note a surge of hormone with subcutaneous dosing, as serum testosterone levels may rise rapidly. Subcutaneous dosing must be weekly as the testosterone level decreases significantly by a weeks' time, whereas intramuscular testosterone lasts longer and may be dosed either weekly or every other week.

Subcutaneous dosing of testosterone with concurrent GnRH analogue use:

Dosing schedules may start with 12.5 mg SC weekly for 8-12 weeks, increase to 25 mg SC weekly. Check levels after three months and adjust in 12.5 mg intervals accordingly. Practitioners may decide to mimic total testosterone levels that correspond to Tanner stages, and increase at 6-month intervals. Most patients achieve a normal male range of total testosterone and good clinical results at 50-75mg of testosterone delivered subcutaneously each week. Providing or prescribing 1 mL syringes for achieving these small doses is helpful. Providers should also prescribe 18 gauge 1-inch needles for drawing up medication, and 25 gauge 5/8-inch needles for injecting subcutaneously. Youth can learn to self-inject into the subcutaneous space in the flank or thigh, switching sides each week. A common side effect is induration in the area of injection that can be minimized if the area is massaged liberally after injection.

Intramuscular dosing of testosterone with concurrent GnRH analogue use:

Intramuscular dosing of testosterone weekly or bi-weekly with an escalating schedule that is similar; 25 mg IM every week for 8 weeks, then increase to 50 mg IM every week. If dosing is every two weeks, the dose is doubled, but it is not uncommon for patients to experience fatigue, irritability and overall lack of energy toward the end of the second week of the cycle; weekly injections helps minimize these issues. Dosing is adjusted in 25 mg increments as guided by hormone level monitoring. Most patients do well on a final dose 50-100mg IM every week, or 100-200 mg every two weeks. Practitioners should provide or prescribe 1 mL syringes, 18 g 1-inch needles for drawing medication, and 21, 22, 23 or 25 g 1-inch needles (most commonly 23 or 25 gauge) for injecting intramuscularly. Youth can be taught to self-inject into the thigh, switching sides each time.

Injectable testosterone is suspended in oil, commercially in cottonseed oil, but often compounded for a less expensive form in sesame oil. Clinicians should be aware that some

youth may have an allergic reaction to either of these oils, and usually switching to another oil is successful in alleviating the problem.

Topical dosing of testosterone with concurrent GnRH analog use:

Occasionally there are youth who prefer testosterone delivery be topical, rather than injectable. Testosterone is available as a patch, gel or cream. Testosterone patches and gel are commercially available, cream can be compounded by specialty pharmacies. Testosterone patches come in 2mg and 4mg strengths, testosterone gel is available in 1% and 1.62% concentrations. There are no consensus dosing schedules for testosterone patches or testosterone gel in the induction of male puberty, only cited case examples of hypogonadal cisgender boys who's puberty was induced by topical testosterone.[17] Testosterone patches only come in two strengths and are difficult to titrate because of this, but testosterone pumps make titration a more feasible option.[18]

Monitoring

Monitoring for safety of testosterone is outlined elsewhere in these guidelines (link to testosterone administration), and the Endocrine Society have also published guidelines for testosterone administration.[11] Dosing adjustments should be made according to clinical response, and testosterone levels. Depending on the patient's age, providers may want to aim for testosterone levels that correspond to Tanner stages as doses are escalated.

Transfeminine youth – hormone therapy with GnRH analogs

For those youth assigned male at birth who identify on the transfeminine spectrum, 17 β estradiol is used for induction of feminizing secondary sex characteristics: breast development, fat distribution in the hip and chest area, and softening of the facial features. Estradiol will also help suppress the production of testosterone, which is unnecessary if youth are on GnRH analogues. Estrogen alone is not typically sufficient to fully inhibit testosterone production, and a second agent—either a GnRH analog or an antiandrogen such as spironolactone should be used (see below). As outlined in a recent review by Rosenthal [12] escalation of estrogen can be achieved in the following manner:

a. Transdermal: twice weekly patches (6.25 μg [achieved by cutting a 25-μg patch] with gradual increase to full adult dose of 400μg);
b. Oral/sublingual: daily (0.25 mg with gradual increase to full adult dose of 6 – 8 mg/d);
c. Parenteral IM (synthetic esters of 17β-estradiol): estradiol valerate (5–20 mg up to 30 – 40 mg/2 wk) or estradiol cypionate (2–10 mg/wk).

Monitoring for safety of estradiol is outlined elsewhere in these guidelines (link to testosterone administration), and the Endocrine Society have also published guidelines for estrogen administration.[11] Dosing adjustments should be made according to clinical response, and safety.

Timing for discontinuation of GnRH analogues

No consensus exists on the length of time GnRH analogues should continue after youth begin gender-affirming hormones. The Dutch Model follows a protocol in which simultaneous GnRH analogues and gender-affirming hormones continues until transgender individuals have their gonads removed. This model is appropriate in the Netherlands, where gonadectomy is easier to access at the age of 18 years old, and both gonadectomy as well as GnRH analogs are paid for by health insurance. In the United States, genital surgeries related to phenotypic gender transition are often not covered by insurance, and pose significant access issues. Additionally, gonadectomy is not necessarily desirable for all transgender persons, especially if future fertility is desired. Continuation of GnRH analogs in tandem with gender-affirming hormones into late adolescence or even early adulthood may be beneficial. Continued suppression of the HPG axis will permit use of lower doses of estradiol, and antiandrogens may not be necessary.

Administration of gender-affirming hormones without concurrent GnRH analogue administration

Many transgender youth accessing services are well beyond the early stages of puberty, and many are not able to get GnRH analogues covered by insurance. Because the cost of GnRH analogues is prohibitive for most families, gender-affirming hormones (in combination with other agents such as hormone blockers) are used to both suppress endogenous hormone production and masculinize or feminize bodies.

Hormone dosing in youth will vary based on the age, health, and other factors specific to the young person. In order to achieve amenorrhea with testosterone alone, masculinization will likely occur, which may or may not be desirable. In these cases, there may be a role for using other methods of suppressing menstruation such as continuous delivery of combined or progestin-only oral contraceptives, injected depo-medroxyprogesterone acetate, levonorgestrel containing-IUD, or etonorgestrel rod implants.

Transmasculine youth – hormone therapy without GnRH analogues

Similar to those transmasculine patients on GnRH analogues, testosterone is used for the induction of masculinizing features including body and facial hair growth, increased muscle mass, deepened voice, and body fat redistribution. Testosterone can be delivered via injections (subcutaneous or intramuscular), or topical (via gels, compounded creams or patches) for those youth not using GnRH analogues to suppress the HPG axis.

Subcutaneous dosing:

Dosing schedules may start with 25 mg SC weekly for 8-12 weeks, increase to 50 mg SC weekly. Check levels after three months and adjust in 25 mg intervals accordingly. Practitioners may decide to mimic total testosterone levels that correspond to Tanner stages, and increase at 3-6-month intervals. Most patients will experience normal male ranges of total

testosterone and good clinical response at 50-75 mg delivered subcutaneously each week. Providing or prescribing 1 mL syringes for achieving these small doses is helpful. Providers should also prescribe 18 gauge 1-inch needles for drawing up medication, and 25 gauge 5/8-inch needles for injecting. Youth can learn to self-inject into the subcutaneous space in the flank or thigh, switching sides each week. A common side effect is induration in the area of injection that can be minimized if the area is massaged liberally after injection.

Intramuscular dosing:

If intramuscular dosing is preferential, some experts recommend doubling the above doses for IM administration. Intramuscular dosing can be done every one or two weeks with an escalating schedule that is similar; 25 mg IM every week, or 50 mg IM every two weeks for 8-12 weeks, then increase to 50 mg every week or 100 mg IM every two weeks. Check levels, and adjust in 25 mg increments accordingly. Most patients do well on a final dose 50-100mg IM every week, or 100-200 mg every two weeks. It is not uncommon for patients to experience fatigue, irritability and overall lack of energy toward the end of the second week of the cycle. Some patients prefer to dose at other intervals such as every 10 days with adjusting of the dose. Practitioners should provide or prescribe 1 mL syringes, 18 g 1-inch needles for drawing medication, and 21, 22, 23 or 25 g 1-inch needles for injecting intramuscularly. Youth can be taught to self-inject into the thigh, switching sides each time.

It is noted that for older youth who are well past endogenous puberty, the value of a very slow escalation is unclear, and may cause undue distress if masculinization takes years to achieve.

Regardless of technique used, injectable testosterone cypionate is suspended in oil, commercially in cottonseed oil. Clinicians should be aware that some youth may have an allergic reaction to either of these oils, and usually switching to another oil is successful in alleviating the problem. For those youth that are allergic to cottonseed oil, testosterone enanthate is suspended commercially in sesame oil. Additionally, some compounding pharmacies suspend testosterone cypionate in sesame oil for a less expensive option.

Transfeminine youth - hormone therapy without GnRH analogues

17 β estradiol is used for induction of feminizing secondary sex characteristics: breast development, fat distribution in the hip and chest area, and softening of the facial features. Estradiol will also help suppress the production of testosterone, but usually is administered in conjunction with an antiandrogen such as spironolactone. Estradiol is available in oral, injectable and topical delivery via patch and compounded creams.

Approaches for estrogen delivery vary based on the age of the young person. Slower escalation of estradiol may be beneficial for breast development, although is often unbearably slow for patients. For younger patients, smaller starting doses may be more advisable. As outlined in a recent review by Rosenthal [12] escalation of estrogen can be achieved in the following manner:

a. Transdermal: twice weekly patches (6.25 μg [achieved by cutting a 25-μg patch] with gradual increase to full adult dose of 400μg);
b. Oral/sublingual: daily (0.25 mg with gradual increase to full adult dose of 6 – 8 mg/d);
c. Parenteral IM (synthetic esters of 17β-estradiol): estradiol valerate (5–20 mg up to 30 – 40 mg/2 wk) or estradiol cypionate (2–10 mg/wk).

Because there is no concomitant use of GnRH analogues, dosing may need to be started higher than the schedule outlined above. Initial doses and escalation of dosing quantity should be individually tailored to each young person. For example, a youth who has experienced endogenous male puberty and enters care at age 16 or 17 may follow a dosing schedule such as:

Oral 17β–estradiol: start at 2 mg/day for 4-8 weeks, and increase by 1 mg increments depending on clinical response.

Parenteral IM (synthetic esters of 17β-estradiol): estradiol valerate 10-15 mg IM Q 14 days for 8-12 weeks, then increase by 5 mg as needed based on clinical and monitoring results.

It is noted that for older youth who are well past endogenous puberty, the value of a very slow escalation is unclear, and may cause undue distress if feminization takes years to achieve.

The utility of escalating doses of spironolactone (to decrease side effects including blood pressure instability or dizziness) is unclear, but because of the diuretic effect, it may be useful to start at 25 mg bid and taper up each week to a final dose of 200 mg BID.

The use of progesterone in transfeminine individuals does not have consensus among providers. It may be advisable when using progesterone to choose bio-identical micronized progesterone, as some experts have concerns of side effects with synthetic progesterone such as exacerbation of underlying depression or weight gain. A detailed discussion on the role and dosing of progestagens are included in the adult guidelines.

Surgical interventions for transgender youth

Transmasculine youth who have undergone endogenous puberty commonly experience significant chest dysphoria, and may engage in inappropriate methods of chest binding. Binding with duct tape, ace bandages and plastic wrap can all lead to serious medical complications. Even well fitted chest binders are hot, uncomfortable and make exercising difficult. Male chest reconstruction is a medically necessary part of phenotypic gender transition for many trans-masculine individuals. While increasing numbers of insurance companies are covering the cost of male chest reconstruction, there are often arbitrary barriers to surgery citing that youth need to be at least 18 years of age prior to undergoing this procedure. Providers should participate in appeal processes so that patients can undergo chest surgery. There are currently no available data that report the positive impact of male chest reconstruction in minors, although a study is underway now.

Despite advances in youth care that include the use of puberty blockers and hormones in adolescence, many transgender youth (particularly transfeminine youth) often experience genital dysphoria that results in significant anxiety and depression, and has been reported by

many youth as a barrier to quality of life. The ability to develop skills and experience in social relationships is negatively impacted in those youth with genitals that do not correspond to their gender. High school is a time when young people begin to explore intimacy, as well as experience their own, and each other's physical bodies. For transgender adolescents, the very idea of sharing intimate space with a potential partner is often overwhelmingly terrifying, since their transgender status can be disclosed in an instant if their bodies are inadvertently exposed. For many transgender women, this disclosure has resulted in physical assault and all too often, death, at the hands of an angry partner. For many youth, social situations and dating are foregone, and the opportunity to learn necessary social skills during this stage of development is lost. Both the Endocrine Society Guidelines and the World Professional Association of Transgender Health (WPATH) Standards of Care version 7.0 recommend deferring genital surgery for both transmasculine and transfeminine youth until the age of 18 years. As youth are transitioning at increasingly younger ages, genital surgery is being performed on a case-by-case basis more frequently in minors, in order to address the issues mentioned above.

Editor's note: Gender-affirming care for transgender youth is a young and rapidly evolving field. In the absence of solid evidence, providers often must rely on the expert opinions of innovators and thought leaders in the field; many of these expert opinions are expressed in this youth guideline. The four primary authors for this youth protocol represent many years of expertise in clinical care and research, in both academic and community practice settings, and within the disciplines of adolescent medicine, pediatric endocrinology, family medicine, and advanced practice nursing.

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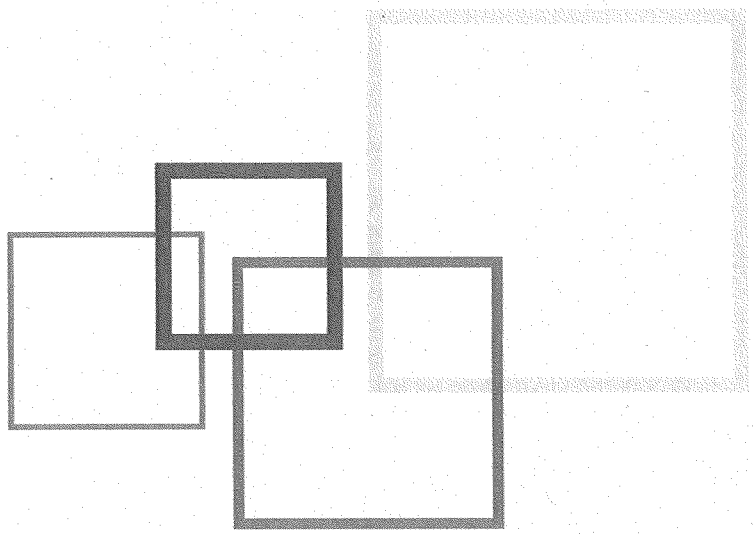

THE REPORT OF THE

2015 U.S. TRANSGENDER SURVEY

National Center for TRANSGENDER EQUALITY

About the National Center for Transgender Equality

The National Center for Transgender Equality (NCTE) is the nation's leading social justice policy advocacy organization devoted to ending discrimination and violence against transgender people. NCTE was founded in 2003 by transgender activists who recognized the urgent need for policy change to advance transgender equality. NCTE now has an extensive record winning life-saving changes for transgender people. NCTE works by educating the public and by influencing local, state, and federal policymakers to change policies and laws to improve the lives of transgender people. By empowering transgender people and our allies, NCTE creates a strong and clear voice for transgender equality in our nation's capital and around the country.

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The Report of the
2015 U.S. Transgender Survey

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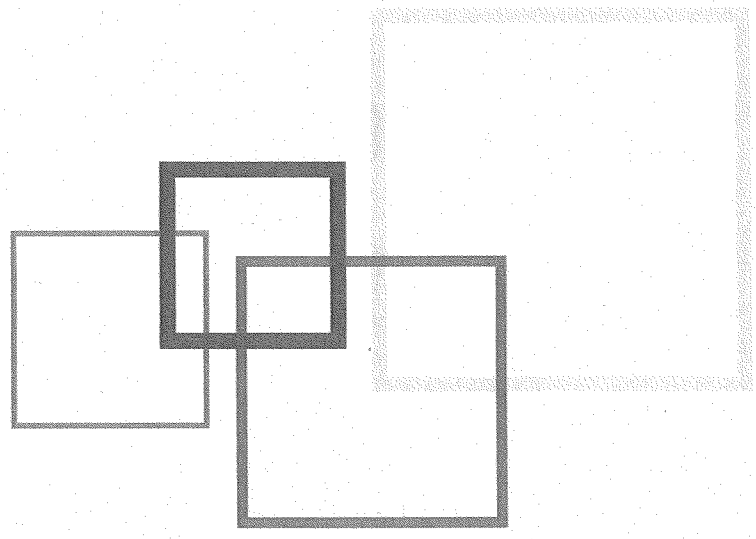


EXECUTIVE SUMMARY

USTS Executive Summary

The 2015 U.S. Transgender Survey (USTS) is the largest survey examining the experiences of transgender people in the United States, with 27,715 respondents from all fifty states, the District of Columbia, American Samoa, Guam, Puerto Rico, and U.S. military bases overseas. Conducted in the summer of 2015 by the National Center for Transgender Equality, the USTS was an anonymous, online survey for transgender adults (18 and older) in the United States, available in English and Spanish. The USTS serves as a follow-up to the groundbreaking 2008–09 National Transgender Discrimination Survey (NTDS), which helped to shift how the public and policymakers view the lives of transgender people and the challenges they face. The report of the 2015 USTS provides a detailed look at the experiences of transgender people across a wide range of categories, such as education, employment, family life, health, housing, and interactions with the criminal justice system.

The findings reveal disturbing patterns of mistreatment and discrimination and startling disparities between transgender people in the survey and the U.S. population when it comes to the most basic elements of life, such as finding a job, having a place to live, accessing medical care, and enjoying the support of family and community. Survey respondents also experienced harassment and violence at alarmingly high rates. Several themes emerge from the thousands of data points presented in the full survey report.

Pervasive Mistreatment and Violence

Respondents reported high levels of mistreatment, harassment, and violence in every aspect of life. One in ten (10%) of those who were out to their immediate family reported that a family member was violent towards them because they were transgender, and 8% were kicked out of the house because they were transgender.

The majority of respondents who were out or perceived as transgender while in school (K–12) experienced some form of mistreatment, including being verbally harassed (54%), physically attacked (24%), and sexually assaulted (13%) because they were transgender. Further, 17% experienced such severe mistreatment that they left a school as a result.

In the year prior to completing the survey, 30% of respondents who had a job reported being fired, denied a promotion, or experiencing some other form of mistreatment in the workplace due to their gender identity or expression, such as being verbally harassed or physically or sexually assaulted at work.

In the year prior to completing the survey, 46% of respondents were verbally harassed and 9% were physically attacked because of being transgender. During that same time period, 10% of respondents were sexually assaulted, and nearly half (47%) were sexually assaulted at some point in their lifetime.

Severe Economic Hardship and Instability

The findings show large economic disparities between transgender people in the survey and the U.S. population. Nearly one-third (29%) of respondents were living in poverty, compared to 14% in the U.S. population. A major contributor to the high rate of poverty is likely respondents' 15% unemployment rate—three times higher than the unemployment rate in the U.S. population at the time of the survey (5%).

Respondents were also far less likely to own a home, with only 16% of respondents reporting homeownership, compared to 63% of the U.S. population. Even more concerning, nearly one-third (30%) of respondents have experienced homelessness at some point in their lifetime, and 12% reported experiencing homelessness in the year prior to completing the survey because they were transgender.

Harmful Effects on Physical and Mental Health

The findings paint a troubling picture of the impact of stigma and discrimination on the health of many transgender people. A staggering 39% of respondents experienced serious psychological distress in the month prior to completing the survey, compared with only 5% of the U.S. population. Among the starkest findings is that 40% of respondents have attempted suicide in their lifetime—nearly nine times the attempted suicide rate in the U.S. population (4.6%).

Respondents also encountered high levels of mistreatment when seeking health care. In the year prior to completing the survey, one-third (33%) of those who saw a health care provider had at least one negative experience related to being transgender, such as being verbally harassed or refused treatment because of their gender identity. Additionally, nearly one-quarter (23%) of respondents reported that they did not seek the health care they needed in the year prior to completing the survey due to fear of being mistreated as a transgender person, and 33% did not go to a health care provider when needed because they could not afford it.

The Compounding Impact of Other Forms of Discrimination

When respondents' experiences are examined by race and ethnicity, a clear and disturbing pattern is revealed: transgender people of color experience deeper and broader patterns of discrimination than white respondents and the U.S. population. While respondents in the USTS sample overall were more than twice as likely as the U.S. population to be living in poverty, people of color, including Latino/a (43%), American Indian (41%), multiracial (40%), and Black (38%) respondents, were up to three times as likely as the U.S. population (14%) to be living in poverty. The unemployment rate among transgender people of color (20%) was four times higher than the U.S. unemployment rate (5%). People of color also experienced greater health disparities. While 1.4% of all respondents were living with HIV—nearly five times the rate in the U.S. population (0.3%)—the rate among Black respondents (6.7%) was substantially higher, and the rate for Black transgender women was a staggering 19%.

Undocumented respondents were also more likely to face severe economic hardship and violence than other respondents. In the year prior to completing the survey, nearly one-quarter (24%) of undocumented respondents were physically attacked. Additionally, one-half (50%) of undocumented respondents have experienced homelessness in their lifetime, and 68% have faced intimate partner violence.

Respondents with disabilities also faced higher rates of economic instability and mistreatment. Nearly one-quarter (24%) were unemployed, and 45% were living in poverty. Transgender people with disabilities were more likely to be currently experiencing serious psychological distress (59%) and more likely to have attempted suicide in their lifetime (54%). They also reported higher rates of mistreatment by health care providers (42%).

Increased Visibility and Growing Acceptance

Despite the undeniable hardships faced by transgender people, respondents' experiences also show some of the positive impacts of growing visibility and acceptance of transgender people in the United States.

One such indication is that an unprecedented number—nearly 28,000—of transgender people completed the survey, more than four times the number of respondents in the 2008–09 NTDS. This number of transgender people who elevated their voices reflects the historic growth in visibility that the transgender community has seen in recent years. Additionally, this growing visibility has lifted up not only the voices of transgender men and women, but also people who are non-binary, which is a term that is often used to describe

people whose gender identity is not exclusively male or female, including those who identify as no gender, as a gender other than male or female, or as more than one gender. With non-binary people making up over one-third of the sample, the need for advocacy that is inclusive of all identities in the transgender community is clearer than ever.

Respondents' experiences also suggest growing acceptance by family members, colleagues, classmates, and other people in their lives. More than half (60%) of respondents who were out to their immediate family reported that their family was supportive of them as a transgender person. More than two-thirds (68%) of those who were out to their coworkers reported that their coworkers were supportive. Of students who were out to their classmates, more than half (56%) reported that their classmates supported them as a transgender person.

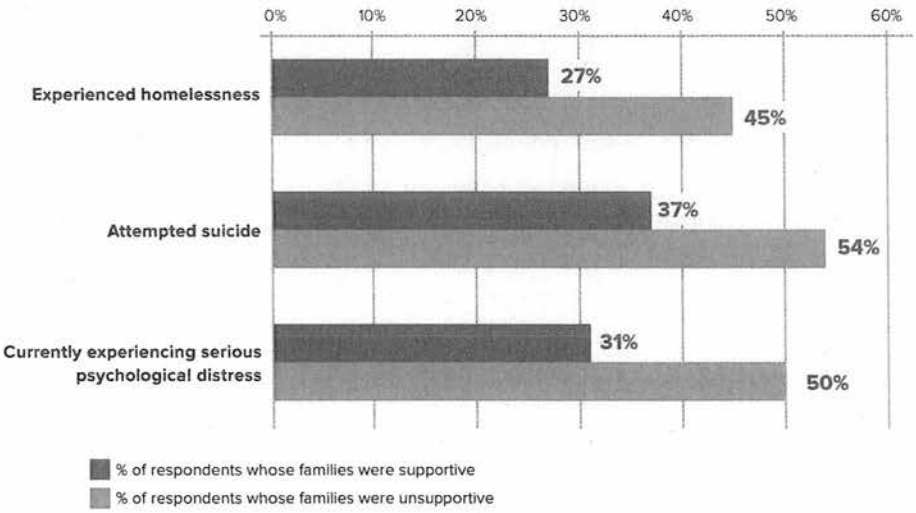
Overall, the report provides evidence of hardships and barriers faced by transgender people on a day-to-day basis. It portrays the challenges that transgender people must overcome and the complex systems that they are often forced to navigate in multiple areas of their lives in order to survive and thrive. Given this evidence, governmental and private institutions throughout the United States should address these disparities and ensure that transgender people are able to live fulfilling lives in an inclusive society. This includes eliminating barriers to quality, affordable health care, putting an end to discrimination in schools, the workplace, and other areas of public life, and creating systems of support at the municipal, state, and federal levels that meet the needs of transgender people and reduce the hardships they face. As the national conversation about transgender people continues to evolve, public education efforts to improve understanding and acceptance of transgender people are crucial. The rates of suicide attempts, poverty, unemployment, and violence must serve as an immediate call to action, and their reduction must be a priority. Despite policy improvements over the last several years, it is clear that there is still much work ahead to ensure that transgender people can live without fear of discrimination and violence.

Overview of Key Findings

Family Life and Faith Communities

- **A majority of respondents (60%) who were out to the immediate family they grew up with said that their family was generally supportive of their transgender identity,** while 18% said that their family was unsupportive, and 22% said that their family was neither supportive nor unsupportive.
- **Those who said that their immediate families were supportive were less likely to report a variety of negative experiences related to economic stability and health,** such as experiencing homelessness, attempting suicide, or experiencing serious psychological distress.

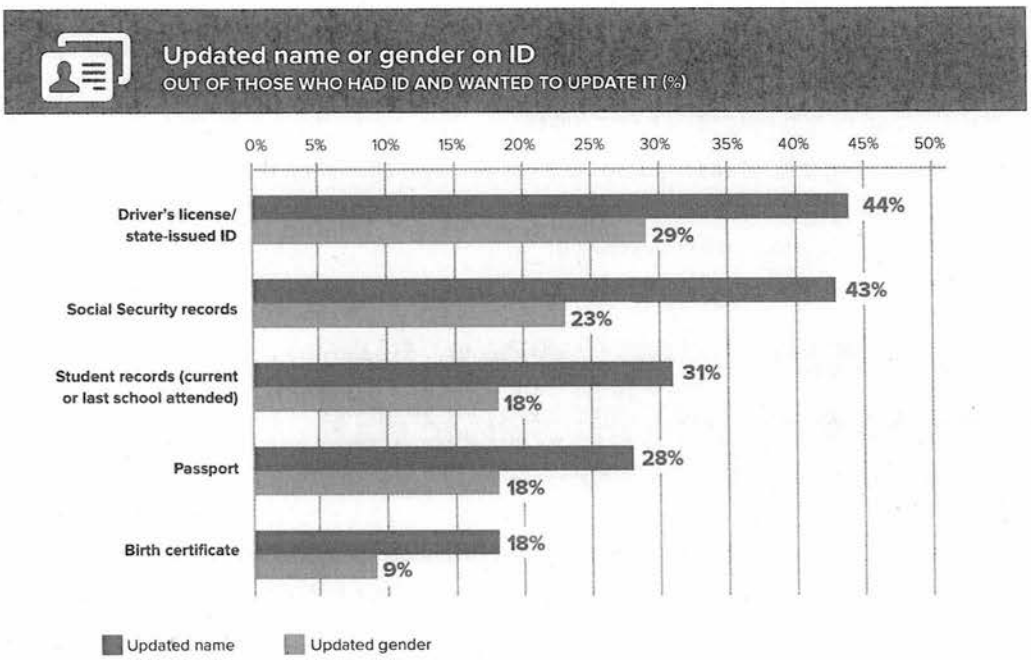
Negative experiences among those with supportive and unsupportive families



- **One in ten (10%)** respondents who were out to their immediate family reported that **a family member was violent towards them** because they were transgender.
- **One in twelve (8%)** respondents who were out to their immediate family **were kicked out of the house**, and one in ten (10%) ran away from home.
- **Nineteen percent (19%) of respondents who had ever been part of a spiritual or religious community left due to rejection**. Forty-two percent (42%) of those who left later found a welcoming spiritual or religious community.

Identity Documents

- **Only 11% of respondents reported that *all* of their IDs had the name and gender they preferred, while more than two-thirds (68%) reported that *none* of their IDs had the name and gender they preferred.**



- **The cost of changing ID documents was one of the main barriers respondents faced**, with 35% of those who have not changed their legal name and 32% of those who have not updated the gender on their IDs reporting that it was because they could not afford it.
- Nearly **one-third (32%)** of respondents **who have shown an ID with a name or gender that did not match their gender presentation were verbally harassed, denied benefits or service, asked to leave, or assaulted.**

Health Insurance and Health Care

- **One in four (25%) respondents experienced a problem in the past year with their insurance related to being transgender,** such as being denied coverage for care related to gender transition or being denied coverage for routine care because they were transgender.
- **More than half (55%) of those who sought coverage for transition-related surgery in the past year were denied**, and 25% of those who sought coverage for hormones in the past year were denied.
- **One-third (33%) of those who saw a health care provider in the past year reported having at least one negative experience related to being transgender**, such as being refused treatment, verbally harassed, or physically or sexually assaulted, or having to teach the provider about transgender people in order to get appropriate care, with higher rates for people of color and people with disabilities.
- In the past year, **23% of respondents did not see a doctor when they needed to because of fear of being mistreated as a transgender person**, and 33% did not see a doctor when needed because they could not afford it.

Psychological Distress and Attempted Suicide

- **Thirty-nine percent (39%) of respondents experienced serious psychological distress** in the month before completing the survey (based on the Kessler 6 Psychological Distress Scale), compared with only 5% of the U.S. population.
- **Forty percent (40%) have attempted suicide *in their lifetime*, nearly nine times the rate in the U.S. population (4.6%).**
- **Seven percent (7%) attempted suicide *in the past year*—nearly twelve times the rate in the U.S. population (0.6%).**

HIV

- Respondents were **living with HIV (1.4%) at nearly five times the rate in the U.S. population (0.3%).**
- **HIV rates were higher among transgender women (3.4%)**, especially transgender women of color. **Nearly one in five (19%) Black transgender women were living with HIV**, and American Indian (4.6%) and Latina (4.4%) women also reported higher rates.

Experiences in Schools

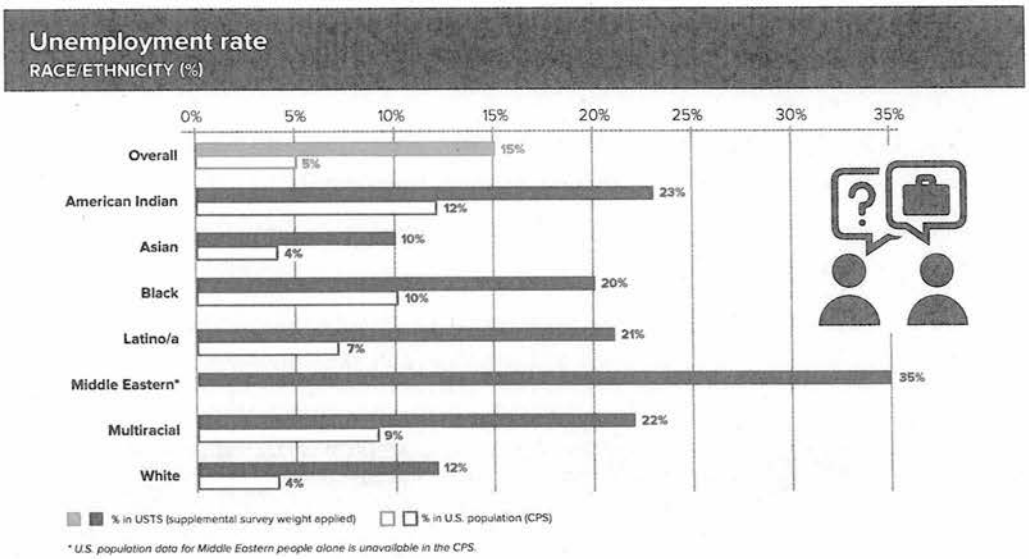
- **More than three-quarters (77%)** of those who were out or perceived as transgender at some point between Kindergarten and Grade 12 (K–12) **experienced some form of mistreatment**, such as being verbally harassed, prohibited from dressing according to their gender identity, disciplined more harshly, or physically or sexually assaulted because people thought they were transgender.
- **Fifty-four percent (54%)** of those who were out or perceived as transgender in K–12 **were verbally harassed, nearly one-quarter (24%) were physically attacked, and 13% were sexually assaulted in K–12 because of being transgender.**
- **Seventeen percent (17%) faced such severe mistreatment as a transgender person that they left a K–12 school.**
- **Nearly one-quarter (24%)** of people who were out or perceived as transgender in college or vocational school **were verbally, physically, or sexually harassed.**

Experiences of people who were out as transgender in K–12 or believed classmates, teachers, or school staff thought they were transgender

EXPERIENCES	% OF THOSE WHO WERE OUT OR PERCEIVED AS TRANSGENDER
Verbally harassed because people thought they were transgender	54%
Not allowed to dress in a way that fit their gender identity or expression	52%
Disciplined for fighting back against bullies	36%
Physically attacked because people thought they were transgender	24%
Believe they were disciplined more harshly because teachers or staff thought they were transgender	20%
Left a school because the mistreatment was so bad	17%
Sexually assaulted because people thought they were transgender	13%
Expelled from school	6%
One or more experiences listed	**77%**

Income and Employment Status

- **The unemployment rate among respondents (15%) was three times higher than the unemployment rate in the U.S. population (5%),** with Middle Eastern, American Indian, multiracial, Latino/a, and Black respondents experiencing higher rates of unemployment.



- **Nearly one-third (29%) were living in poverty, more than twice the rate in the U.S. population (14%).**

Employment and the Workplace

- **One in six (16%)** respondents who have ever been employed—or 13% of all respondents in the sample—**reported losing a job because of their gender identity or expression** in their lifetime.
- **In the past year, 27%** of those who held or applied for a job during that year—19% of all respondents—**reported being fired, denied a promotion, or not being hired for a job they applied for because of their gender identity or expression.**
- **Fifteen percent (15%) of respondents who had a job in the past year were verbally harassed, physically attacked, and/or sexually assaulted** at work because of their gender identity or expression.
- **Nearly one-quarter (23%) of those who had a job in the past year reported other forms of mistreatment** based on their gender identity or expression during that year,

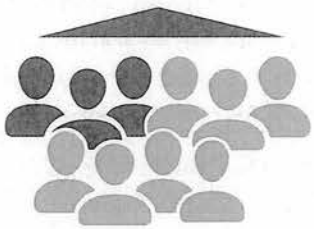
such as being forced to use a restroom that did not match their gender identity, being told to present in the wrong gender in order to keep their job, or having a boss or coworker share private information about their transgender status with others without their permission.

- **Overall, 30% of respondents who had a job in the past year reported being fired, denied a promotion, or experiencing some other form of mistreatment related to their gender identity or expression.**
- **More than three-quarters (77%)** of respondents who had a job in the past year **took steps to avoid mistreatment in the workplace**, such as hiding or delaying their gender transition or quitting their job.

Housing, Homelessness, and Shelter Access

- **Nearly one-quarter (23%) of respondents experienced some form of housing discrimination in the past year**, such as being evicted from their home or denied a home or apartment because of being transgender.
- **Nearly one-third (30%) of respondents have experienced homelessness at some point in their lives.**
- **In the past year, one in eight (12%) respondents experienced homelessness** because of being transgender.
- **More than one-quarter (26%) of those who experienced homelessness in the past year avoided staying in a shelter because they feared being mistreated as a transgender person**. Those who did stay in a shelter reported high levels of mistreatment: **seven out of ten (70%)** respondents who stayed in a shelter in the past year reported some form of mistreatment, including being harassed, sexually or physically assaulted, or kicked out because of being transgender.

Seven out of ten respondents who stayed in a shelter in the past year reported being mistreated because of being transgender.



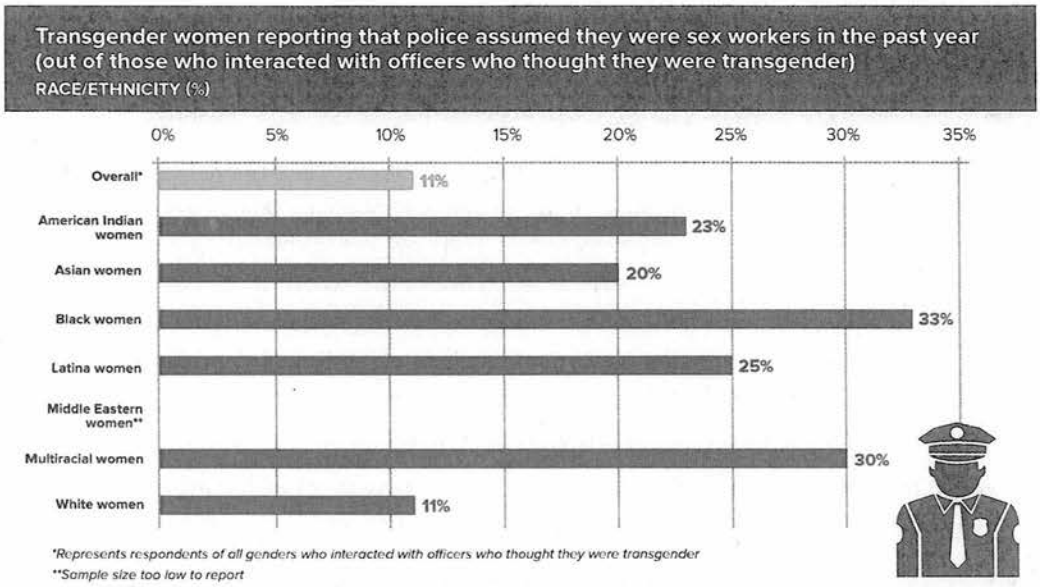
- Respondents were nearly **four times less likely to own a home (16%) compared to the U.S. population (63%)**.

Sex Work and Other Underground Economy Work

- Respondents reported high rates of experience in the underground economy, including sex work, drug sales, and other work that is currently criminalized. **One in five (20%) have participated in the underground economy** for income at some point in their lives—including 12% who have done sex work in exchange for income—and 9% did so in the past year, with higher rates among women of color.
- Respondents who interacted with the police either while doing sex work or while the police mistakenly thought they were doing sex work reported high rates of police harassment, abuse, or mistreatment, with **nearly nine out of ten (86%) reporting being harassed, attacked, sexually assaulted, or mistreated in some other way by police**.
- **Those who have done income-based sex work were also more likely to have experienced violence.** More than three-quarters (77%) have experienced intimate partner violence and 72% have been sexually assaulted, a substantially higher rate than the overall sample. Out of those who were working in the underground economy at the time they took the survey, nearly half (41%) were physically attacked in the past year and over one-third (36%) were sexually assaulted during that year.

Police Interactions and Prisons

- **Respondents experienced high levels of mistreatment and harassment by police.** In the past year, of respondents who interacted with police or law enforcement officers who thought or knew they were transgender, **more than half (58%) experienced some form of mistreatment.** This included being verbally harassed, repeatedly referred to as the wrong gender, physically assaulted, or sexually assaulted, including being forced by officers to engage in sexual activity to avoid arrest.
- **Police frequently assumed that respondents—particularly transgender women of color—were sex workers.** In the past year, of those who interacted with law enforcement officers who thought or knew they were transgender, one-third (33%) of Black transgender women and 30% of multiracial women said that an officer assumed they were sex workers.
- **More than half (57%)** of respondents said they would feel **uncomfortable asking the police for help** if they needed it.
- Of those who were arrested in the past year (2%), **nearly one-quarter (22%) believed they were arrested because they were transgender**.



- Respondents who were held in jail, prison, or juvenile detention in the past year faced **high rates of physical and sexual assault by facility staff and other inmates**. In the past year, nearly one-quarter (23%) were physically assaulted by staff or other inmates, and one in five (20%) were sexually assaulted. Respondents were over **five times more likely to be sexually assaulted by facility staff** than the U.S. population in jails and prisons, and over **nine times more likely to be sexually assaulted by other inmates**.

Harassment and Violence

- **Nearly half (46%) of respondents were verbally harassed** in the past year because of being transgender.
- **Nearly one in ten (9%) respondents were physically attacked** in the past year because of being transgender.
- **Nearly half (47%) of respondents were sexually assaulted** at some point in their lifetime and **one in ten (10%) were sexually assaulted in the past year.** Respondents who have done sex work (72%), those who have experienced homelessness (65%), and people with disabilities (61%) were more likely to have been sexually assaulted in their lifetime.
- **More than half (54%) experienced some form of intimate partner violence**, including acts involving coercive control and physical harm.
- **Nearly one-quarter (24%) have experienced severe physical violence by an intimate partner, compared to 18% in the U.S. population.**

Places of Public Accommodation

- Respondents reported being denied equal treatment or service, verbally harassed, or physically attacked at many places of public accommodation—places that provide services to the public, like retail stores, hotels, and government offices. Out of respondents who visited a place of public accommodation where staff or employees thought or knew they were transgender, **nearly one-third (31%) experienced at least one type of mistreatment in the past year in a place of public accommodation**. This included 14% who were denied equal treatment or service, 24% who were verbally harassed, and 2% who were physically attacked because of being transgender.
- **One in five (20%) respondents did not use at least one type of public accommodation** in the past year because they feared they would be mistreated as a transgender person.

Denied equal treatment or service, verbally harassed, or physically attacked in public accommodations in the past year because of being transgender

LOCATION VISITED	% OF THOSE WHO SAID STAFF KNEW OR THOUGHT THEY WERE TRANSGENDER
Public transportation	34%
Retail store, restaurant, hotel, or theater	31%
Drug or alcohol treatment program	22%
Domestic violence shelter or program or rape crisis center	22%
Gym or health club	18%
Public assistance or government benefit office	17%
Department of Motor Vehicles (DMV)	14%
Nursing home or extended care facility	14%
Court or courthouse	13%
Social Security office	11%
Legal services from an attorney, clinic, or legal professional	6%

Experiences in Restrooms

The survey data was collected before transgender people's restroom use became the subject of increasingly intense and often harmful public scrutiny in the national media and legislatures around the country in 2016. Yet respondents reported facing frequent harassment and barriers when using restrooms at school, work, or in public places.

- **Nearly one in ten (9%) respondents reported that someone denied them access to a restroom in the past year.**
- In the past year, **respondents reported being verbally harassed (12%), physically attacked (1%), or sexually assaulted (1%)** when accessing a restroom.

- **More than half (59%)** of respondents **avoided using a public restroom** in the past year because they were afraid of confrontations or other problems they might experience.
- **Nearly one-third (32%)** of respondents **limited the amount that they ate and drank** to avoid using the restroom in the past year.
- **Eight percent (8%)** reported having a **urinary tract infection, kidney infection, or another kidney-related problem** in the past year as a result of avoiding restrooms.

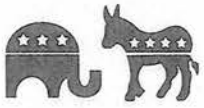
More than half (59%) of respondents **avoided using a public restroom** in the past year because they were afraid of confrontations or other problems they might experience.

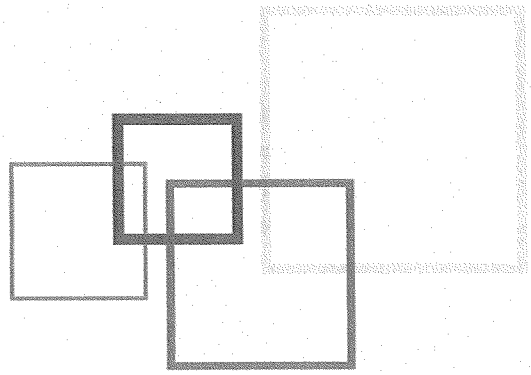
Civic Participation and Party Affiliation

- **More than three-quarters (76%) of U.S. citizens of voting age in the sample reported that they were registered to vote in the November 2014 midterm election**, compared to 65% in the U.S. population.
- **More than half (54%)** of U.S. citizens of voting age **reported that they had voted in the midterm election,** compared to 42% in the U.S. population.
- **Half (50%) of respondents identified as Democrats, 48% identified as Independents, and 2% identified as Republicans**, compared to 27%, 43%, and 27% in the U.S. population, respectively.

Political party affiliation

POLITICAL PARTY	% IN USTS	% IN U.S. POPULATION (GALLUP)
Democrat	50%	27%
Independent	48%	43%
Republican	2%	27%





CHAPTER 1
Introduction

This report presents the findings of the 2015 U.S. Transgender Survey (USTS), a study conducted by the National Center for Transgender Equality (NCTE). With 27,715 respondents, it is the largest-ever survey examining the lives of transgender people in the United States. The USTS provides a detailed portrait of the experiences of transgender people across many areas, including health, family life, employment, and interactions with the criminal justice system.

The USTS serves as a follow-up to the National Transgender Discrimination Survey (NTDS), which was developed by NCTE and the National LGBTQ Task Force and conducted in 2008–09. The NTDS was the first comprehensive survey examining the lives and experiences of transgender and gender nonconforming people in the United States. With 6,456 respondents reporting on a range of experiences throughout their lives, the NTDS was a groundbreaking study. The results were published in the 2011 report, *Injustice at Every Turn*, and showed that discrimination against transgender people was pervasive in many areas of life, including education, employment, health care, and housing. The report also highlighted the resilience of transgender people in the face of such discrimination and found that family and peer support could have a substantially positive impact on a transgender person's quality of life. The report quickly became a vital source of information about transgender people and continues to serve as an important resource for advocates, policymakers, educators, service providers, media, and the general public.

Much has changed since the NTDS was conducted in 2008–09 and results were published in 2011, including increased visibility of transgender people in the media and in society in general. Despite making significant strides in the five years since the report was published, there is still a substantial amount of work to be done to address critical needs in transgender communities throughout the United States. Transgender people continue to experience discrimination and anti-transgender bias in virtually all areas of life.

The 2015 U.S. Transgender Survey was developed by the National Center for Transgender Equality to provide updated and more detailed data to inform a wide range of audiences about the experiences of transgender people, how things are changing, and what can be done to improve the lives of transgender individuals in the United States. It is the largest survey of transgender people conducted to date, far surpassing the previous survey, with 27,715 respondents. This study explores a wider range of topics than the previous survey and more deeply examines specific issue areas where transgender people are disparately impacted, such as health care, HIV/AIDS, housing, workplace discrimination, immigration, sex work, and police interactions. Additionally, by closely mirroring questions from federal and other existing surveys, this study seeks to fill in the gaps left by the lack of data collected about transgender people in national surveys. Since federal survey data is often used by government agencies to make key determinations about policies and programs that affect individuals in many areas of life, such as employment and health, it is important to provide specific data on the potential impact of such policies on transgender people. This report on the U.S. Transgender Survey data draws comparisons between transgender people and the U.S. population and examines disparities across multiple issue areas.

This report demonstrates that transgender people continue to face discrimination in numerous areas that significantly impact quality of life, financial stability, and emotional wellbeing, including employment, education, housing, and health care. Furthermore, many respondents experienced discrimination in multiple areas of their lives, the cumulative effect of which leads to severe economic and emotional hardship and can in turn have devastating effects on other outcome areas, such as health and safety.

Although issues impacting transgender people have become more visible in the years since the NTDS was published, the data overwhelmingly demonstrates that there is still a long way to go towards eliminating harmful discrimination and providing sustainable systems of support for transgender people throughout their lives. These findings are presented with the recognition that advocates, researchers, and transgender communities will greatly benefit from additional research conducted using this extensive data source. The authors encourage subsequent analyses to delve into areas of the data that this report is unable to address, and as before, will strive to make the data set available for such analyses.

Report Roadmap

The next chapter of the report will give an overview of the study's methodology, which will be followed by a guide to this report, including information about terminology used throughout. These will be followed by chapters discussing respondents' experiences across a range of areas that impact transgender people's lives:

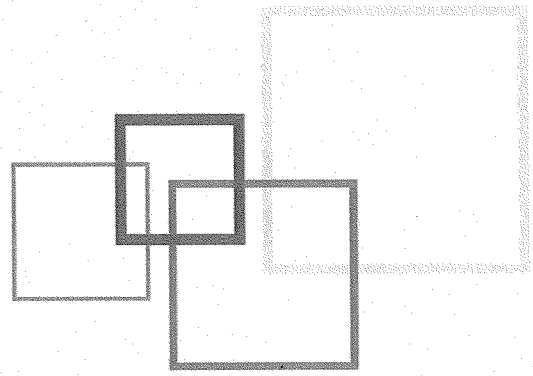
- Portrait of USTS Respondents
- Family Life and Faith Communities
- Identity Documents
- Health
- Experiences at School
- Income and Employment Status
- Employment and the Workplace
- Sex Work and Other Underground Economy Work
- Military Service
- Housing, Homelessness, and Shelter Access
- Police, Prisons, and Immigration Detention
- Harassment and Violence
- Places of Public Accommodation and Airport Security
- Experiences in Restrooms
- Civic Participation and Policy Priorities

The report also contains three appendices, which offer more detailed information related to the study:

Appendix A: Characteristics of the Sample

Appendix B: Survey Instrument (Questionnaire)

Appendix C: Detailed Methodology



CHAPTER 2
Methodology

The U.S. Transgender Survey is the largest survey ever conducted to examine the experiences of transgender people in the United States. The survey instrument was comprised of thirty-two sections reflecting 1,140 distinct variables that covered a broad array of topics, such as health and health care access, and experiences around employment, education, housing, law enforcement, and public accommodation.[1] The survey was developed by a team of researchers and advocates and administered online to transgender adults residing in the United States.[2] The survey was accessible via any web-enabled device (e.g., computer, tablet, netbook, smart phone), accessible for respondents with disabilities (e.g., through screen readers), and made available in English and Spanish. Rankin & Associates Consulting hosted the survey on several secure servers. The survey was accessed exclusively through a website created specifically for the promotion and distribution of the survey.[3] Data was collected over a 34-day period in the summer of 2015,[4] and the final sample included 27,715 respondents from all fifty states, the District of Columbia, American Samoa, Guam, Puerto Rico, and U.S. military bases overseas. The survey contained mainly closed-ended questions, but respondents were also offered the opportunity to provide write-in responses in fifty-three of the survey questions. Over 80,000 write-in responses were provided by respondents.

I. About the U.S. Transgender Survey

The U.S. Transgender Survey (USTS) was developed as the follow-up to the groundbreaking National Transgender Discrimination Survey (NTDS), which was the first study to comprehensively measure experiences and life outcomes of transgender people in the United States. Fielded in late 2008 to early 2009 by the National Center for Transgender Equality (NCTE) and the National LGBTQ Task Force ("the Task Force"), the NTDS provided data that has informed policymakers, advocates, and educators since its publication in 2011. However, the NTDS report acknowledged that the study had "just scratched the surface of this extensive data source" and encouraged advocates and researchers to conduct additional research to continue collecting data aimed at identifying and addressing the needs of transgender people.[5] The NTDS authors also examined the survey instrument and concluded that there were "imperfections" in the manner in which several questions had been posed.[6] The authors addressed areas for potential improvement with respect to both survey question design and substantive content in an "issues and analysis" section of the report.[7] These recommendations were considered in the development of the U.S. Transgender Survey.

In subsequent years, researchers have performed additional analyses using the NTDS public use dataset provided by NCTE and the Task Force. These analyses provided further insight into the experiences of transgender people, but also increased awareness of the questions that remained unanswered after the NTDS report was published. In some instances, there was insufficient information to draw nuanced comparisons between life outcomes of transgender people collected in the NTDS and the U.S. general population. In other cases, the ability to form additional conclusions was limited due to a lack of follow-up questions. For example, the NTDS asked a single question about suicide attempts, which did not allow for a clear examination of suicidal thoughts and behaviors.[8] Additionally, given the deficiency of longitudinal data on outcomes specific to transgender people, there remained a need to collect data that could speak to the experiences of transgender people over time and how outcomes may have changed in the years since the NTDS was published. In these respects, the NTDS provided an important platform upon which to build the USTS to address identified areas for improvement and collect data that would enable new insights to be drawn about transgender people in the United States.

The study was renamed the U.S. Transgender Survey for several reasons. One was to clarify the geographical location of the intended study sample both during the data collection period and following report publication. The use of "U.S." signaled that this study was developed with the unique needs of transgender people in the United States and U.S. territories in mind, considering relevant policies, procedures, and practices applicable to residents of the United States at the time of the study in areas such as health care and insurance, income, employment, housing, and education. Recognizing the contextual differences between the experiences of transgender people in the U.S. and in other parts of the world, the research team sought to dispel any confusion arising from the use of "national" in the title. The new name was also intended to reflect the depth and breadth of the experiences of transgender people in the U.S. and elevate a variety of narratives beyond discrimination, including the resilience and resourcefulness of the transgender community in the face of hardship, as well as experiences of acceptance and affirmation. "Discrimination" was removed from the title to clarify that the survey was designed to capture all such experiences. Additionally, removing the word

reduced potential bias in respondents' answers or resulting from primarily attracting respondents who felt they had experienced discrimination.

II. USTS Respondents

The study population included individuals who identified as transgender, trans, genderqueer, non-binary, and other identities on the transgender identity spectrum, in order to encompass a wide range of transgender identities, regardless of terminology used by the respondent. Although "transgender" was defined broadly for the purposes of this study as being inclusive of a wide range of identities—such as genderqueer, non-binary, and crossdresser—the research team recognized that many individuals for whom the study was intended may have used different terminology or definitions and might have assumed that the term "transgender" did not include them. To address this, promotional materials affirmed that the survey was inclusive of all transgender, trans, genderqueer, and non-binary people. Additionally, materials specified that the survey was for adults at any stage of their lives, journey, or transition to encourage participation among individuals with diverse experiences regarding their transgender identity. An in-depth description of survey respondents is available in the *Portrait of USTS Respondents* chapter.

The study included individuals aged 18 and older at the time of survey completion, as did the NTDS. The study was not offered to individuals under the age of 18 due to limitations created by specific risk factors and recommendations associated with research involving minors. These considerations, including requirements for parental/guardian consent, would have impacted the survey's scope and content and also reduced the literacy level at which the survey could be offered.[9] Furthermore, the current experiences and needs of transgender youth often differ from those of adults in a number of key areas, including experiences related to education, employment, accessing health care, and updating identity documents, and many of these experiences or needs could not be adequately captured in a survey that was not specifically tailored to transgender people under the age of 18.

The sample was limited to individuals currently residing in a U.S. state or territory, or on a U.S. military base overseas, since the study focused on the experiences of people who were subject to U.S. laws and policies at the time they completed the survey. Individuals residing outside of the U.S. may have vastly different experiences across a number of outcome measures based on each respective country's laws, policies, and culture, particularly in the areas of education, employment, housing, and health care. Additionally, many survey questions were taken from U.S. federal government surveys that also limit their sample population to individuals in the U.S., and the research team sought to examine a similar population with regard to geographical location to allow for comparisons to the U.S. general population.

III. Developing the Survey Instrument

The USTS survey instrument was developed over the course of a year by a core team of researchers and advocates in collaboration with dozens of individuals with lived experience, advocacy and research experience, and subject-matter expertise. When developing the survey instrument, the research team focused on creating a questionnaire that could provide data to address both current and emerging needs of transgender people while gathering information about disparities

that often exist between transgender people and non-transgender people throughout the U.S. To achieve this, questions were included that would allow comparisons between the USTS sample and known benchmarks for the U.S. population as a whole or populations within the U.S. Consequently, questions were selected to best match those previously asked in federal government or other national surveys on a number of measures, such as measures related to income and health.[10] Changes were made to the language of comparable questions whenever it was required to more appropriately reflect issues pertaining to transgender people and language in common use in the transgender community while maintaining comparability to the best extent possible. However, in many cases, language was preserved to ensure that responses to a USTS question would maintain maximum comparability with surveys such as the U.S. Census Bureau's American Community Survey and Current Population Survey.

Several questions were also included in an attempt to provide comparability between the NTDS, where possible, to determine how certain outcomes may have changed since the NTDS data was collected in 2008–09. While the USTS provides crucial updated data, it is important to note that many of the questions asked in the NTDS were either not included in the USTS, or they were asked in a manner that reduced comparability with the NTDS. For example, many USTS questions asked about whether certain experiences occurred within the past year instead of asking whether those experiences occurred at any point during an individual's lifetime. These questions were included for both comparability with federal government or other national surveys and also to yield improved data regarding changing experiences in future iterations of the USTS. In such instances, the NTDS continues to provide the best available data regarding experiences that occurred over respondents' lifetime. The authors suggest referring to both the USTS and the NTDS to gain a full picture of issues impacting transgender people.

The survey instrument was reviewed by researchers, members of the transgender community, and transgender advocates at multiple intervals throughout the development process. This included thorough reviews of sections that addressed specific subject matter and the entire questionnaire. The questionnaire was revised based on feedback from dozens of reviewers.

a. Pilot Study

Prior to finalizing the survey instrument and launching the survey in field, a pilot study was conducted to evaluate the questionnaire. The pilot study was conducted among a small group of individuals with characteristics that were representative of the sample the study was intended to survey. The pilot study was administered through an online test site using the same platform and format in which the final survey later appeared. The purpose of the pilot study was to provide both a substantive and technical evaluation of the survey. Approximately 100 individuals were invited to complete and evaluate the survey online during a specified period of time. In order to receive access to the pilot study test site, invitees were required to confirm their participation by indicating that they met the following pilot study criteria: they were (1) 18 years or older, (2) transgender, (3) willing to provide feedback that would be used to make improvements to the survey, (4) available to take the survey online during specified dates, and (5) agreeing to not share the questions in the pilot study with anyone so as to not compromise the study. Forty (40) individuals confirmed their participation and received access to the pilot study test site. Thirty-two (32) people completed the study and submitted feedback on the questionnaire, including participants in fifteen states ranging in age from 19 to 78. Participants

reported identifying with a range of gender identities[11] and racial and ethnic identities, including 34% who identified as people of color.[12]

In addition to providing general feedback on individual questions and the entire questionnaire, pilot study participants were asked to address specific questions as part of their evaluation, including: (1) how long it took to complete the survey, (2) what they thought about the length of the survey, (3) whether any existing questions were confusing or difficult to answer, (4) whether they found any questions offensive or thought they should be removed or fixed, (5) whether they experienced technical or computer issues while taking the survey, and (6) what they thought about the statement explaining why the term "trans" was used throughout the survey.[13] All participant feedback was compiled, discussed, and used to further develop the questionnaire, such as through the revision of language and the addition of questions to more thoroughly examine an issue.

b. Length

The final survey questionnaire contained a total of 324 possible questions in thirty-two discrete sections addressing a variety of subjects, such as experiences related to health and health care access, employment, education, housing, interactions with law enforcement, and places of public accommodation. The online survey platform allowed respondents to move seamlessly through the questionnaire and ensured they only received questions that were appropriate based on previous answers. This was accomplished using skip logic, which created unique pathways through the questionnaire, with each next step in a pathway being dependent on an individual respondent's answer choices. For example, respondents who reported that they had served in the U.S. Armed Forces, Reserves, or National Guard received a series of questions about their military service, but those who had not served did not receive those questions. Due to the customized nature of the survey, the length varied greatly between respondents, and no respondent received all possible questions. Prior to the pilot study, estimates indicated a survey-completion time of 30–45 minutes. The completion-time estimate was extended to 60 minutes based on feedback from pilot study participants, and it was consistent with many reports during the fielding period.[14]

Despite observations about survey length discussed in the NTDS,[15] evolving data needs relating to issues affecting transgender people required an in-depth treatment of multiple issue areas. This often required multiple questions to thoroughly assess an issue—including in areas where the NTDS asked only one question—and resulted in a lengthier survey. Survey instrument length was assessed throughout its development to ensure it would be manageable for as many participants as possible. Furthermore, through multiple reviews and evaluations of the survey instrument—including the pilot study—survey takers reported that the length was appropriate for a survey addressing such a wide range of issues and the need for data outweighed concerns about the overall length of the survey.

IV. Survey Distribution and Sample Limitations

The survey was produced and distributed in an online-only format after a determination that it would not be feasible to offer it in paper format due to the length and the complexity of the skip logic required to move through the questionnaire. With so many unique possibilities for a customized survey experience for each respondent, the intricate level of navigation through the survey

would have created an undue burden and confusion for many respondents. This could have led to questions being answered unnecessarily or being skipped completely, which could have increased the potential for missing data in the final dataset.[16] This made online programming the best option for ensuring that respondents received all of the questions that were appropriate based on their prior answers, decreasing the probability of missing data. However, the potential impact of internet survey bias on obtaining a diverse sample has been well documented in survey research,[17] with findings that online and paper surveys may reach transgender respondents with "vastly different health and life experiences."[18] With those considerations in mind, outreach efforts were focused on addressing potential demographic disparities in our final sample that could result from online bias and other issues relating to limited access. Although the intention was to recruit a sample that was as representative as possible of transgender people in the U.S., it is important to note that respondents in this study were not randomly sampled and the actual population characteristics of transgender people in the U.S. are not known. Therefore, it is not appropriate to generalize the findings in this study to all transgender people.

V. Outreach

The main outreach objective was to provide opportunities to access the survey for as many transgender individuals as possible in different communities across the U.S. and its territories. Additionally, outreach efforts focused on reaching people who may have had limited access to the online platform and who were at increased risk of being underrepresented in such survey research. This included, but was not limited to, people of color, seniors, people residing in rural areas, and low-income individuals. The outreach strategy was a multi-pronged approach to reach transgender people through various connections and points-of-access, including transgender- or LGBTQ-specific organizations, support groups, health centers, and online communities.

Outreach efforts began approximately six months prior to the launch of the data-collection period with a variety of tactics designed to raise awareness of the survey, inform people when it would be available, and generate opportunities for community engagement, participation, and support. A full-time Outreach Coordinator worked for a period of six months to develop and implement the outreach strategy along with a team of paid and volunteer interns and fellows.[19]

An initial phase of outreach involved developing lists of active transgender, LGBTQ, and allied organizations who served transgender people and would eventually support the survey by spreading the word through multiple communication platforms and in some cases providing direct access to the survey at their offices or facilities. Establishing this network of "supporting organizations" was an essential component of reaching a wide, diverse sample of transgender people.

Over 800 organizations were contacted by email, phone, and social media, and they were asked if they would support the survey by sharing information about it with their members and contacts. Specifically, supporting organizations were asked to share information through email blasts and social media channels, and the research team provided language and graphics for organizations to use in an effort to recruit appropriate respondents into the study. Of the organizations contacted, approximately half responded to requests for support, resulting in direct recruitment correspondence with nearly 400 organizations at regular intervals during the pre-data-collection period and while the survey was in the field.[20,21] These organizations

performed outreach that contributed to the far reach of the survey and unprecedented number of respondents.[22] The organizations were also featured on the survey website so potential respondents could determine whether organizations they knew and trusted had pledged support for the survey.

Nearly 400 organizations responded to outreach and confirmed their support for the survey. The remaining organizations did not respond directly to invitations to learn more about the survey and become supporters. Consequently, these organizations did not receive correspondence aimed at directly recruiting respondents prior to the survey launch or during the data-collection period. It is possible, however, that survey respondents were still made aware of the survey through those organizations. Since there is no information regarding whether these organizations shared information about the survey through their channels, it is difficult to assess the full scope of the outreach efforts.

a. Advisory Committee

A significant element of outreach involved convening a USTS Advisory Committee (UAC). The UAC was created to increase community engagement in the survey project and raise awareness by connecting with transgender people in communities across the country through a variety of networks. The UAC was comprised of eleven individuals with advocacy, research, and lived experience from a wide range of geographical locations.[23] Members were invited to join the committee as advisors on survey outreach to facilitate the collection of survey data that would best reflect the range of narratives and experiences of transgender people in the U.S. Each member brought unique skills and expertise to contribute to the committee's objectives. UAC members participated in five monthly calls with members of the USTS outreach team from May to September 2015. UAC monthly calls focused on providing project updates and identifying pathways by which outreach could be conducted to increase the survey's reach and promote participation from a diverse sample. Members suggested organizations, individuals, and other avenues through which to conduct outreach, shared ideas and strategies for improving outreach to specific populations of transgender people, and spread the word about the survey through their professional and personal networks.

b. Survey-Taking Events

In an effort to increase accessibility of the survey, the outreach team worked with organizations across the country to organize events or venues where people could complete the survey. *Survey-Taking Events*,[24] or "survey events," were spaces in which organizations offered resources to provide access to the survey, such as computers or other web-enabled devices. These organizations provided a location in which to take the survey at one particular time or over an extended period of time, such as during specified hours over the course of several days.[25] The events were created with the intention of providing access to individuals with limited or no computer or internet access, those who may have needed assistance when completing the survey, or those who needed a safe place to take the survey. Additionally, the population that had previously been identified as being more likely to take a paper survey than an online survey were considered,[26] and the events were developed to target those individuals.

Given the potential variety of these survey events—including the types of available resources and times at which they were conducted—guidelines were needed to maintain consistency across the events and preserve the integrity of the data-collection process. A protocol was developed outlining the rules for hosting a survey event to advise hosts on best practices for ensuring

a successful data-collection process, including guidelines to prevent the introduction of bias into survey responses. The protocols described the steps for becoming a survey-event host and tips for how to conduct outreach about the event. The protocol also specified that hosts should inform NCTE of their event prior to hosting and report on how many people attended the event and how many people completed and submitted the survey. This was helpful information for evaluating the relative success and benefits of these events. All confirmed supporting organizations were invited to become survey event hosts, and those who accepted the invitation were sent the protocol. Seventy-one (71) organizations accepted the invitation and confirmed the date(s) and time(s) of their events.[27]

Survey events were promoted on the survey website and given a specific designation on the supporting organization map (described further in the "Survey Website" section), including information about where and when people could attend. Hosts were encouraged to promote their event through multiple channels and consider outreach methods beyond online avenues, such as direct mail or flyers, to better reach transgender people with limited or no internet access. Additionally, hosts were provided with flyer templates so they could promote the events in their facilities or through communications with their members or constituents. Of the organizations who confirmed their survey events, 46 reported information about attendance at the event. The hosts reported that 341 people attended their events, including transgender and non-transgender friends, family, and volunteers. Approximately 199 respondents completed the survey at these events.[28] However, survey responses indicate that additional unreported survey events or similar gatherings may have been held where participants had an opportunity to complete the survey.[29] Event-related information submitted by organizations following the fielding period was not comprehensive enough to make a thorough determination as to whether the events had achieved their previously stated objectives.[30]

c. Incentives

As an incentive for completing the survey, participants were offered a cash-prize drawing. Incentives, such as cash prizes are widely accepted as a means by which to encourage and increase participation in survey research.[31] Studies have shown that such incentives may have a positive effect on survey response rate, which is the proportion of individuals in the population of interest that participates in the survey.[32] Research has also found that lottery-style cash drawings may be beneficial in online surveys,[33] since they offer a practical method for providing incentives in surveys with a large number of respondents by eliminating the potential high cost of both the cash incentive and prize distribution.[34]

USTS respondents were offered the opportunity to enter into a drawing for one of three cash prizes upon completion of the survey, including one $500 cash prize and two $250 cash prizes.[35] After completing and submitting their anonymous survey responses, USTS respondents were re-directed away from the survey hosting site[36] to a web page on the NCTE-hosted USTS website. In addition to being thanked for their participation on this page, respondents received a message confirming that their survey had been submitted and any further information they gave would not be connected to their survey responses. Only individuals who completed and submitted the survey were eligible for one of the cash prizes. To enter into the prize drawing, respondents were required to check a box giving their consent to be entered.[37] Respondents were also asked to provide their contact information in order to be notified if selected in the drawing. The final drawing contained 17,683 entrants. Each entrant was assigned a number, and six numbers were randomly chosen by a non-NCTE party: three

numbers for the prize winners and three for alternates if necessary. The three prize winners were contacted and awarded their prizes upon acceptance.

VI. Communications

Communications for the survey required a multifaceted approach and a coordinated effort with the outreach strategy to most effectively reach a wide range of transgender people and ensure a robust sample size. The goals of survey communications were to: (1) inform people that NCTE would be conducting a survey to further the understanding of the experiences of transgender people in the U.S initially gleaned through the NTDS, (2) communicate when the survey would be available to complete and how it could be accessed, and (3) find creative ways of reaching diverse populations of potential respondents. This involved raising awareness of the survey through several communication methods, including email, social media, and print media, as well as through additional unique campaigns. Many survey promotional materials were produced in English and Spanish to increase the accessibility of the survey.[38]

a. Survey Website

A website was created and designed specifically for the promotion and distribution of the survey.[39] This website served as a platform for providing information about the survey starting several months prior to its release in the field, such as a description of the survey, information about the team working on the survey, frequently asked questions, and sample language and graphics for individuals and organizations to use for email and social media communications, including sample Facebook and Twitter postings. The website also featured an interactive map, which included information about organizations that had pledged to support the survey. Additionally, the map distinctly indicated information about organizations that were hosting survey-taking events, including the date, time, and location of such events. The website later served as the only platform through which the survey could be accessed and provided English and Spanish links to enter the survey, since there was no direct link available to the off-site hosting platform.

b. Survey Pledge

The survey pledge campaign was developed to raise awareness about the survey and generate investment in the project. The campaign engaged potential participants and allies by inviting them to pledge to take the survey and/or spread the word about the survey. The survey pledge was a critical method of both informing people that the survey would be launching and sustaining engagement with potential respondents in the months leading up to the fielding period. Pledges received reminders about the survey launch date and availability through email communications. Beginning in January 2015, pledge palm cards were distributed at a variety of events across the country, including conferences and speaking engagements. The cards contained information about the upcoming survey and asked people to sign up to help by committing to: (1) spread the word about the survey; and/or (2) take the survey. Transgender and non-transgender individuals were asked to complete the pledge information, either through a palm card or directly online through the survey website. Individuals who completed pledge information received email communications throughout the pre-data-collection phase. Pledge information was collected continuously for several months, and by the time of the survey launch, over 14,000 people had pledged to take the survey. Additionally, more than 500 people pledged to promote the survey among their transgender friends and family.[40] The pledge proved to be

an effective method of assessing how many people had learned about the survey and were interested in completing it, where potential survey respondents were distributed geographically, and how more potential respondents could be effectively engaged.

c. Photo Booth Campaign

In January 2015, a photo booth campaign was launched as another method for engaging people and raising awareness about the survey. Individuals and groups were asked to take photos holding one of two signs with messages expressing support for the survey.[41] USTS photo booths were conducted at several conferences and events across the country. More than 300 photos were collected and shared directly through NCTE's Facebook page. Photos were also sent to most participants so they could conduct their own promotion using their photos.

d. Social Media

With the increased use of social media in the years since the previous survey (the NTDS), it was important to engage via these outlets to further the reach of the survey. Facebook and Twitter[42] became the primary social media outlets used throughout the survey project, and their use significantly amplified awareness, increasing the number of people who were exposed to the survey. A series of postings provided the ability to rapidly and succinctly communicate with individuals and groups who had an interest in contributing to the survey's success by completing the survey and spreading the word about it. Although social media reach fluctuated during the months leading up to the survey launch, over 96,000 Facebook users were estimated to have received NCTE's post announcing that the survey was live and available for completion on August 19, 2015.

e. USTS Awareness Week

Prior to launching the survey in the field, communication was maintained with thousands of individuals and organizations who fell into three categories: (1) people who had signed up to take or spread the word about the survey ("pledge list"), (2) organizations that had committed to support the survey through outreach efforts ("supporting organization list"), and (3) people who had signed up to be in communication with NCTE about the organization's work and projects ("NCTE list").

Communication with the individuals and groups on these lists through targeted messages occurred at various intervals; however, one of the most important methods for promoting the survey was through USTS Awareness Week. This campaign was designed to share a significant amount of information about the survey over a concentrated period of time in close proximity to the launch of the survey. Awareness Week occurred during the week of July 27, 2015 and highlighted different aspects of the survey focusing on a different medium each day, including social media, email, and blogs. Awareness Week was introduced to the communication lists on July 15, and recipients were invited to access and download a planning kit for the campaign, which was available on the survey website. The planning kit included language and graphics for email and social media communications. Communications were sent on each of the days devoted to social media,[43] email,[44] and blogs[45] with appeals for organizations to share the information with their membership and individuals to share the information through their personal networks. Awareness Week proved to be one of the most effective methods for increasing the number of individuals who pledged to take the survey and likely increased the number of eventual respondents.[46]

f. Additional Communications Methods

The overall approach to survey communications was diverse and captured many media forms. In addition to the previously stated campaigns and projects, communications involved working with a variety of individuals such as bloggers, artists, advocates, and others to create print blogs and videos promoting the survey. Op-eds were another medium that contributed to survey promotion, and media consultants and traditional media sources aided in expanding the survey's reach even further. Approximately 50 articles, blogs, and op-eds focused on the survey were produced and distributed by organizations, including NCTE, and individuals prior to the launch of the survey and during the data-collection period. The wide variety of approaches contributed to the number of individuals who were reached through all communications and likely impacted the final number of respondents in the sample.

VII. Language and Translation

Throughout the survey questionnaire, the use of accessible language was balanced with preserving the meaning of each question to the greatest extent possible. This was of particular importance in maintaining comparability with questions from existing surveys that allowed conclusions to be drawn about how the experiences of the USTS sample compares to the U.S. population. In order to make assessments about USTS survey respondents in relation to the U.S. population, it was important that USTS respondents had similar interpretations of questions taken from other surveys as non-transgender survey takers had to those questions in federal surveys. In many places, language was revised to use terminology that would most appropriately speak to individuals in the many communities for which the survey was intended. However, several areas required difficult choices about keeping language that may have caused discomfort for some respondents. Throughout the questionnaire, language was avoided that could be interpreted as stigmatizing or characterized as a value judgment wherever possible while maintaining objectivity in crafting sound research questions. For example, at times survey questions referred to work or activities that were "currently considered illegal." Such deliberate language was used in an attempt to separate the issue of criminalization from the activity in question while maintaining comparability with other surveys. This was a difficult balance to achieve throughout the survey. Eliminating technical language was also necessary, unless it was widely used and accepted in transgender communities, such as some medical terminology. Short descriptions or parenthetical explanations were provided whenever technical language was required for those who may not have been familiar with the language. Additionally, hyperlinked explanations of specific terms were included when those terms could be interpreted in several ways or if similar explanations were provided in the federal surveys from which the questions were taken. For example, explanations were provided for the terms "active duty" when asking about military service and "household" when asking about income.

The research team remained conscious of individual and collective identities throughout the survey instrument drafting process, and attempted to use language that acknowledged the breadth and significance of individual identities while also making the questions accessible to the widest range of transgender people possible across the U.S. and in the territories. The questionnaire was reviewed and revised for consistent readability at an eighth-grade literacy level where possible,[47] although several

terms used in the survey were at a considerably higher literacy level. This included places where language was preserved for comparability with other surveys and when language describing transgender-specific experiences or procedures was used. Additionally, community members and researchers reviewed the survey and suggested revised language throughout the development process. This collaborative process was beneficial in providing collective insight on the best language to use in each particular instance based on lived experience and research expertise. The research team acknowledges, however, a continuing need to work towards identifying suitably inclusive terminology within an evolving language and community for future iterations of the survey.

The questionnaire was translated into Spanish by a translation service, and several native-Spanish-speaking community members and NCTE staff and interns reviewed and revised the language to use terminology that was most prevalent in Spanish-speaking transgender communities in the U.S. In many instances, it was difficult to find language that accurately captured the meaning of a question or specific terms, but in each case language was selected to convey interpretations as close to the English-language question interpretations as possible.

VIII. Institutional Review

The study was vetted through an Institutional Review Board (IRB) process, which is meant to ensure confidentiality and protect the rights and welfare of individuals participating in a research study. The USTS underwent a full board review by the University of California Los Angeles (UCLA) IRB. As a requirement of approval, the questionnaire began with a study information sheet describing aspects of the study and rights of individuals as participants in the study.[48] To be included in the study, participants were required to indicate their consent at the end of the information sheet. This process established that participants were fully informed about the risks and benefits of participating in the study and that their participation was voluntary. IRB review also required the submission of all recruitment materials leading up to the launch of the survey and throughout the time the survey was in the field.[49] This required the production of a large volume of messaging for the many different types of media through which people were invited to participate in the survey in both English and Spanish. It also required anticipating how messaging might need to change while the survey was in the field and submitting this language for pre-approval for later use as needed.

IX. Survey Hosting

The survey was hosted online by Rankin & Associates Consulting, under the supervision of USTS research team member, Dr. Susan Rankin. Access to the survey was provided exclusively through the USTS website. All programming of the questionnaire and online administration of the survey was handled through Rankin & Associates Consulting, which managed the process of collecting the survey data throughout the 34-day fielding period.

The survey was anonymous, and maintaining privacy and confidentiality in the collection and maintenance of survey data was an important component of preserving participants' anonymity. Furthermore, as a condition of IRB approval, the research team was required to ensure that confidentiality protections were in place for the study and demonstrate sufficiency of data security protocols. Accordingly, data from online

participants was submitted through seven secure firewalled servers with forced 256-bit SSL (Secure Sockets Layer) security and Security-Enhanced Linux (SELinux) security extensions to encrypt and protect the survey data. Given the volume of traffic on the seven servers during the initial launch of the survey, an eighth server was added. The survey was stored in a SQL database that could only be accessed locally. The servers themselves were only accessible using encrypted SSH (Secure Shell) connections originating from the local network. The servers were also in RAID (Redundant Array of Inexpensive Disks), which is a data storage virtualization technology that combines multiple physical disk drive components into a single logical unit for the purposes of data redundancy, performance improvement, or both, to reduce the chance of any data loss due to hardware failure. The servers performed nightly security audits from data acquired via the system logs and notified the system administrators.

Despite a successful data-collection period evidenced by the large final sample size, it is important to note issues that occurred in the initial days of the survey data-collection period, given the potential impact on the data collection and the final sample. Prior to the survey launch, the online platform had been assessed and capacity was predicted for the seven dedicated servers based on reasonable estimated response rates. However, in the first days of the data-collection period, exceptionally high levels of traffic to the survey far exceeded the predicted response rates and overwhelmed the capacity of the servers, causing significant delays in accessing and completing the survey. The resulting server delays occurred within hours of the survey launch on August 19, 2015, producing unusually long page-loading times and may have served as a barrier to completing the survey.[50] The survey team notified potential respondents of the delays through email and social media communication and updated the first page of the online survey questionnaire with a note about the issues and information about the continued availability of the survey.[51] The hosting team added a server to process the high level of traffic and returned the survey to normal loading speeds within a couple days of the initial reports. Although high numbers of survey submissions were received throughout these days, it is likely that the server delays affected the completion and submission of some surveys or may have discouraged individuals from attempting to take the survey.

X. Cleaning the Data

The dataset was cleaned following collection to remove survey responses that did not belong in the final sample.[52] Data cleaning is the process of detecting and removing some survey responses (e.g., duplicate responses, incomplete responses, illogical responses) in order to improve the quality of the sample. This data set was "cleaned" using commonly accepted procedures.[53] The first step was to remove survey responses from individuals who did not consent to take the survey and those who did not meet the eligibility criteria, such as not being at least 18 years of age and not residing in the U.S. These survey respondents had been automatically sent to a disqualification page,[54] but their responses were included in the initial dataset. Incomplete responses were then removed from the sample based on a requirement that respondents minimally complete specific questions in Section 2 of the questionnaire to be included in the final dataset.[55] Duplicate survey responses were removed next, as were those with illogical responses, such as those with contradictory responses to related questions. Missing-data analyses were then conducted to determine the percentage of missing data.[56]

The next step of the process was recoding data, including re-categorization of answer choices

in several questions for improved analysis or to match existing categories for comparison to other surveys. Answers were evaluated for those questions that allowed a write-in response when the selected option was "not listed above." In some cases, these answers were recoded into existing answer choices where appropriate, and in other cases, new answer categories were created for write-in responses that were frequently repeated. The recoding process included two coding teams. The first coding team conducted initial data recoding, and the second team reviewed the recoding and flagged areas of disagreement. A simple percent agreement score was calculated to determine inter-rater reliability.[57]

Several survey weights were developed for presentation of results in the report.[58] A race and ethnicity weight was developed based on the Census Bureau's 2014 American Community Survey (ACS).[59] Additionally, given the disproportionally large number of respondents who reported an age of 18 years old, a weight was created to balance the representation in the sample of those respondents in relation to the rest of the sample.[60] The race and ethnicity weight and the 18-year-old weight were both included in a "standard weight" applied to the dataset. All results presented in this report are weighted based on the standard weight unless otherwise noted. Additional survey weights were created for the purposes of comparability with federal government and national data sources, including weights for age and educational attainment.[61] These weights were applied in addition to the standard weight when comparing the USTS sample to the U.S. population for items that are sensitive to age and educational attainment, such as individual and household income, and are noted accordingly as the "supplemental weight."

XI. Data Analysis and Presentation of Findings

The data was first analyzed to tabulate individual responses to each of the questions in the survey. The respondents included in each tabulation differed throughout the survey due to certain questions only being asked of a particular set of respondents and/or due to some respondents choosing not to answer a question. Analyses were performed to explore how survey responses differed based on demographic characteristics—such as race, gender, and income—and non-demographic factors—such as experience with sex work, HIV status, and experiences of family support or rejection.

All findings in the report are presented as weighted percentages of the entire sample or of the subgroups being examined. For example, educational attainment is presented as a percentage of the whole sample, while much of the data related to HIV care represent percentages of those respondents who are living with HIV. In limited instances, unweighted frequencies are included where the additional information could be informative and to provide context for the weighted percentages reported.

Percentages are rounded to whole numbers, except in cases where a more exact comparison to national data sources was desired or where more precision was needed due to the reported percentages being small. When rounding to whole numbers, the following convention was generally followed: findings containing decimals of 0.50 and above were rounded up, and findings with 0.49 and below were rounded down (e.g., 1.50% was rounded to 2% and 1.49% was rounded to 1%). Additionally, a finding of 0.49% and below was generally labeled "less than 1%" or "<1%." Throughout the report, results are presented in

various figures and tables. The percentages in these figures and tables do not always add up to 100% due to respondents being able to select more than one answer to a question ("mark all that apply") or due to rounding.

Throughout the report, U.S. population findings are provided for comparison to USTS findings or to provide context for USTS findings, where available and/or applicable. Where USTS data is compared to data from existing research, the data source is specified. When providing U.S. population comparisons, the research team made efforts to limit the comparisons to adults (18 years and older) to most appropriately match the USTS sample. Whenever that was not possible, notes as to age ranges or other limitations are provided. Additionally, calculations made by the research team when necessary to present U.S. population findings are noted. Data in this report is generally presented without information regarding statistical testing.[62]

ENDNOTES | CHAPTER 2: METHODOLOGY

1 The survey included questions related to the following topics (in alphabetical order): accessing restrooms; airport security; civic participation; counseling; education; employment; family and peer support; health and health insurance; HIV; housing and homelessness; identity documents; immigration; income; intimate partner violence; military service; police and incarceration; policy priorities; public accommodations; faith; sex work; sexual assault; substance use; suicidal thoughts and behaviors; unequal treatment, harassment, and physical attack; and voting.

2 Detailed information about survey methodology is available in *Appendix C (Detailed Methodology)*.

3 www.USTransSurvey.org

4 The survey was in the field between August 19 and September 21, 2015.

5 Grant, J. M., Mottet, L. A., Tanis, J., Harrison, J., Herman, J. L., & Keisling, M. (2011). *Injustice at Every Turn: A Report of the National Transgender Discrimination Survey*. (p. 11). DC: National Center for Transgender Equality and National Gay and Lesbian Task Force.

6 Grant et al., p. 182.

7 Grant et al.

8 See Haas, A. P., Rodgers, P. L., & Herman, J. L. (2014). *Suicide Attempts Among Transgender and Gender Non-Conforming Adults*. New York, NY & Los Angeles, CA: American Foundation for Suicide Prevention & Williams Institute.

9 See e.g., The GenIUSS Group. (2014). In J. L. Herman (Ed.), *Best Practices for Asking Questions to Identify Transgender and Other Gender Minority Respondents on Population-Based Surveys* (p. vii). Los Angeles, CA: Williams Institute. ("Adolescents may have particular difficulties with complex vocabulary and sentences. Therefore, questions designed for adolescents should take extra care to use plain language and simple sentences. Terms used in measures of sex and gender should be defined since adolescents, and cisgender (non-transgender) adolescents in particular, conflate the terms sex and gender, and have varying understanding of the term *transgender*, *masculine*, and *feminine*."). Given the need to collect data about the unique experiences of transgender youth, it is important to design and conduct future studies focusing on the issue areas and needs most applicable to transgender youth.

10 Information about the source of survey questions used for comparison to the U.S. population can be found in *Appendix C (Detailed Methodology)*.

11 Forty-four (44%) of pilot participants identified as a woman or trans woman (MTF), 41% as a man or trans man (FTM), and 16% as non-binary or genderqueer.

12 These pilot participants identified as American Indian, Asian, multiracial, Black, Latino/a, and a racial/ethnic identity not listed above, in addition to 66% who identified as white.

13 The following statement was provided to explain why the word "trans" was used throughout the survey: We know that not everyone is comfortable with the word "transgender," but for this survey, we must use one word to refer to all trans and non-binary identities. Because of this we will use the word "trans" in this survey to refer to all trans and non-binary identities."

14 A notable exception to the 30–60 minute estimate for completing the survey occurred during the first days of the survey's availability, when a high volume of survey takers overwhelmed multiple servers, causing lengthy delays when completing the survey. This is discussed further in the "Survey Hosting" section.

15 Grant et al., p. 13.

16 Post-NTDS analysis of respondents who had completed that survey online or in paper format found that surveys completed online were less likely to have missing data, providing further support for the decision to only offer the survey online. See Reisner, et al. (2014). Comparing in-person and online survey respondents in the U.S. National Transgender Discrimination Survey: Implications for transgender health research. *LGBT Health, 1*(2), 98–106.

17 See Dillman, D. A., Smyth, J. D., & Christian, L. M. (2014). *Internet, Phone, Mail, and Mixed-Mode Surveys: The Tailored Design Method* (4th ed.). Hoboken, NJ: John Wiley & Sons.

18 Reisner et al., p. 98. See note 16. This analysis also found that "[a] higher proportion of in-person respondents were young, male-to-female, people of color, publicly insured, with lower incomes and lower educational attainment than online respondents (all $p<0.05$). In-person respondents also were more likely than online respondents to be current daily smokers, to endorse substance use to cope with mistreatment, and to self-report as HIV-positive (all $p<0.05$)."

19 Although outreach efforts were instrumental in obtaining the largest sample of transgender respondents ever collected, a longer outreach period may have resulted in reaching more individuals in communities that are often underrepresented in online surveys.

20 A total of 827 organizations received at least one outreach email, and organizations received additional outreach emails and/or phone calls if no response was received. Out of those organizations, 392 confirmed their support, and 435 did not respond to any communications.

21 Correspondence included almost one dozen emails with asks to spread the word about the survey and with various information about the availability of the survey.

22 The research team attempted to ascertain the level of outreach engagement of supporting organizations; however, the limited amount of information received about the outreach did not allow a calculation of a response rate. Of the 392 organizations that pledged their support, 58 (15%) reported information on their outreach activities and estimated reaching over 20,000 transgender people through their channels. In the future, researchers are encouraged to collect consistent outreach activity data from supporting organizations that will help to better assess the effectiveness of outreach and response rate estimates.

23 Information about UAC members can be found in the *Acknowledgements* section of the report.

24 These events were promoted as "Survey-Taking Events" on recruitment materials and described accordingly (see note 25). However, it is possible that the name did not appropriately capture the nature of these vastly differing events. A lack of clarity may have decreased the number of people who attempted to access the survey through organizations who offered space or computers to complete the survey online.

25 Survey-Taking Events were described as "a function in which an organization or group opens its doors and provides access to its facilities (such as community centers and office buildings) to allow trans survey participants use of its resources (including computers, tablets, and internet access) to complete the USTS. This will occur during specified periods of time or throughout the time the survey is available on a drop-in basis. For example, a community center might participate by setting aside one Saturday from 9am–6pm where some or all of its computers are available for survey takers to use, or it might host people on Monday–Friday from 5pm–9pm each evening for a week, or longer."

26 A total of 435 NTDS respondents completed the survey in paper format (7% of the sample) and were found to differ from online survey takers in sociodemographic characteristics, health outcomes, and life experiences. Reisner et al., p. 98, 103. See note 16.

27 Although only 71 organizations confirmed their events, based on information reported at various intervals throughout the data-collection period, it appeared that more organizations hosted survey events or similar gatherings to complete the survey without reporting them to the survey outreach team. Additionally, it is also possible that individuals and organizations held informal parties where groups of friends could gather to complete the survey at the same time. Data regarding this sort of activity was not collected or received.

28 This completion rate is a conservative estimate based on reports that some individuals started the survey at the event and then left to complete it on their own at a later time.

29 Four hundred and seventeen (417) respondents answered "yes" in response to the following survey question: "Are you taking this survey at a survey event or meeting, such as one hosted by an LGBTQ or Trans organization or meeting?"

30 In future iterations of the USTS and other research studies, the research team suggests a more robust approach towards organizing, conducting, and monitoring survey events to increase the reach and availability of such events in providing access to the survey. Researchers are also encouraged to conduct follow-up analyses to

determine the demographic characteristics of individuals who completed the survey at events and whether these events were successful in capturing a similar demographic to those who had completed paper surveys in the previous survey. See Reisner, et al. (discussing the demographics of online and paper respondents in the NTDS).

31 See e.g., Göritz, A. S. (2006). Incentives in web studies: Methodological issues and a review. *International Journal of Internet Science, 1*(1), 58–70. (finding that "material incentives increase the odds of a person responding by 19% over the odds without incentives").

32 Pedersen, M. J. & Nielsen, C. V. (2016). Improving survey response rates in online panels: Effects of low-cost incentives and cost-free text appeal interventions. *Social Science Computer Review, 34*(2), 229–243.

33 Pedersen et al., pp. 237–238.

34 Singer, E. & Ye, C. (2013). The use and effects of incentives in surveys. *The ANNALS of the American Academy of Political and Social Science, 645*(1), 123–124.

35 Participants were informed of the cash prize incentives in several ways. The study information sheet placed at the beginning of the survey prior to obtaining each respondent's consent to enter the survey contained the following information in response to the question of whether respondents would be paid for their participation: "You will receive no payment for your participation. You will have the option to voluntarily enter a drawing to win one of three cash prizes: one prize of $500 and two prizes of $250." The frequently asked questions section of the survey website also offered the following statement: "When you complete the survey, you will have the option to enter a drawing to win one of three cash prizes: one prize of $500 and two prizes of $250. Because thousands of trans people across the country will complete the survey, we cannot offer payment to each participant." Additionally, some recruitment materials mentioned the cash-prize drawing, including email blasts.

36 The survey was hosted by Rankin & Associates Consulting. Further details are described in the "Survey Hosting" section.

37 The check box stated: "Enter me in the drawing for one of three cash prizes: one prize of $500 and two prizes of $250!"

38 Due to limited funding, it was not possible to translate all survey materials, such as email communications. Translation of all promotional materials may positively impact the response rate amongst respondents with limited English proficiency in future iterations of the study.

39 www.USTransSurvey.org

40 Final pledge numbers were 14,005 and 561 for survey takers and promoters, respectively.

41 Photo booth participants could choose from one of two signs indicating that the survey was coming in the summer of 2015 and stating the following: (1) "My Voice Counts: I'm Taking the #USTransSurvey" or (2) "Every Voice Counts: Spread the Word About the #USTransSurvey."

42 The Twitter hashtag used to promote the survey was #USTransSurvey.

43 For social media day, recipients received one of the following requests, based on whether they were organizations or individuals: (1) "Use the hashtag #USTransSurvey on social media asking your social networks to join us" or (2) "Please join Social Media day. We have sample copy and a variety of photos and graphics."

44 For email day, recipients received one of the following requests, based on whether they were organizations or individuals: (1) "Email a friend explaining why this is so important to you" or (2) "Download the sample email and send it to your membership list today."

45 For blog day, recipients were invited to share a blog written by Outreach Coordinator, Ignacio Rivera, cross post the blog on an organization's blog site, or draft a blog about the importance of the survey.

46 The number of individuals who pledged to take the survey on the pledge list increased from approximately 7,700 when the initial Awareness Week email was sent on July 15 to over 14,000 at the time of the survey launched in the field. The 82% increase in the numbers of survey pledges is likely due to the increased exposure generated by Awareness Week communications.

47 The initial literacy level review and revision was conducted by a certified copy editor proficient in reading levels, and the questionnaire was determined to be at an eighth grade reading level.

48 Due to IRB requirements, the language in the study information sheet was generally at a higher literacy level than the rest of the questionnaire.

49 This included all materials aimed at "recruiting" or getting people to participate in a research study, such as website pages, flyers, emails, and social media messages.

50 The research team received reports that it took some individuals up to several hours to complete the survey on the first day, and others reported that they were not able to complete or submit their survey at all due to the technical issues.

51 The following note was added to the first page of the survey (in English and Spanish) to notify respondents of the delay: "Our servers have been overwhelmed by the number of enthusiastic participants and some are experiencing unusual delays. We apologize for the inconvenience as we work to address this issue. You can complete the survey now but may experience delays. However, the survey will be available to complete through at least September 21st. If you experience delays, we encourage you to return to this site in the coming days. If the survey is slow to respond, you can leave the page open and return later. If the survey times out, you can hit the 'back' button. However, if you close your browser, you may have to restart the survey."

52 A detailed description of the cleaning process is included in *Appendix C (Detailed Methodology)*.

53 Rahm, E. & Do, H. H. (2000). Data cleaning: Problems and current approaches. *IEEE Data Engineering Bulletin, 23*(4), 3–13.

54 Ineligible respondents were sent to one of two disqualification pages notifying them of their ineligibility and providing either an opportunity to visit the survey website for more information or giving information about their gender identity or expression and experiences related to gender identity or expression.

55 See *Appendix C (Detailed Methodology)* for more information on the Section 2 questions that were required to remain in the sample.

56 Missing-data analyses determined that there was less than 5% missing data on all but two questions. Therefore, the research team did not impute the missing data. See *Appendix C (Detailed Methodology)* for more information.

57 A modified version of an inter-rater reliability metric was used by the two teams that conducted the review. Each team included a principal researcher and an outside researcher. One researcher on each team conducted the initial coding and the other researcher reviewed the coding for approval or revisions. See *Appendix C (Detailed Methodology)* for more information.

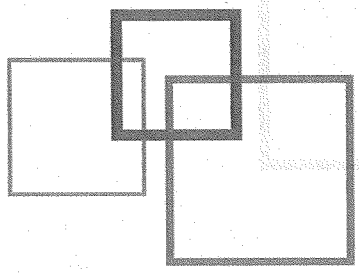
58 "Weighting" is a common statistical technique used to adjust data with disproportionate sample sizes to be more representative of the population from which the sample was drawn. For example, the proportion of respondents aged 18–24 and 25–44 in a survey sample taken in the U.S. may differ from the proportion of those age groups in the total U.S. population. Therefore, weights are applied to survey data in order to make comparisons between the collected survey data and the total population. See *Appendix C (Detailed Methodology)* for more detailed information about weights applied to the survey data.

59 Studies using representative samples of transgender adults have found that transgender adults differ from the general population in regard to race and ethnicity, with transgender people more likely to be people of color. See e.g., Flores, A. R., Brown, T. N. T., & Herman, J. L. (2016). *Race and Ethnicity of Adults who Identify as Transgender in the United States*. Los Angeles, CA: Williams Institute; Conron, K. J., Scott, G., Stowell, G. S., & Landers, S. J. (2012). Transgender health in Massachusetts: Results from a household probability sample of adults. *American Journal of Public Health, 102*(1), 118–122. However, the USTS sample has a higher percentage of white respondents than the U.S. general population. To help correct for this sampling bias, the research team applied U.S. population weights for race and ethnicity. While this may still over-represent white respondents, this weighting procedure brings the sample closer to what is estimated to be the true population distribution for race and ethnicity for transgender people.

60 The weight for 18-year-old respondents was created with propensity scores developed using a regression discontinuity model. For more information on this process and other weighting procedures, see *Appendix C (Detailed Methodology)*.

61 The age, race, and educational attainment weights were created based on the Census Bureau's 2014 American Community Survey (ACS).

62 Due to the large sample size, bivariate statistical tests largely result in statistically significant differences among the groups being compared. Small group differences often will be found to be statistically significant, even when the differences are small and, therefore, not particularly meaningful. In writing the findings to this report, the research team considered other measures when pointing out meaningful differences among groups, such as a particular cell's contribution to an overall chi-square test statistic and effect sizes. These tests are on file with the research team. Future researchers are encouraged to use additional bivariate and multivariate modeling to provide more nuanced understanding of group differences.



CHAPTER 3

Guide to Report and Terminology

Throughout the report, the authors use a variety of terminology to refer to respondents in the sample or experiences that respondents reported. The authors also applied several conventions in the reporting of results. While explanations are often included in chapters to provide context and clarity, several terms and conventions that are used widely throughout the report are outlined in this chapter to make the report more accessible to a broad range of audiences.

I. Use of the Term "Transgender" in this Report

The term "transgender" is often used to describe people whose gender identity or expression differs from what is associated with the gender they were thought to be at birth. Although this term has often been described as an "umbrella term" that encompasses the spectrum of identities and captures the diversity of transgender people, the authors recognize that one term cannot reflect each individual's unique identity and some people prefer to use other terms to describe their gender identity. However, in order to make the report's findings clear and accessible, it was important to select a single term for consistent use throughout this report that could best represent the range of identities expressed in the USTS survey sample.

In promotional materials, the survey was described as being inclusive of all "transgender, trans, genderqueer, and non-binary" people, so that those who might have assumed that "transgender" did not include them would know their voice was welcomed. The survey also acknowledged the limitation of current language and used "trans"—a shorthand term that is widely accepted amongst transgender people—consistently throughout the questions. While respondents in this study identified with a wide range of terms—including more than 500 unique terms that were reported in response to survey questions—88% of respondents thought of themselves as transgender, and 86% expressed that they were "very comfortable," "somewhat comfortable," or "neutral" when asked how comfortable they were with the word "transgender" being used to describe them. This included 82% percent of non-binary respondents. This provides evidence of the term's continued broad usage and general acceptance. Based on this information, the term *transgender* is used for the purposes of this report to represent the diverse identities of the individuals who made their voices heard by completing the survey.

II. Other Transgender-Specific Terminology

Non-binary:

This term is used by some to describe people whose gender is not exclusively male or female, including those who identify as no gender, as a gender other than male or female, or as more than one gender. In this report, "non-binary respondents" refers to respondents who said that the term "non-binary/genderqueer" best describes their current gender identity in response to Q. 2.3.

Crossdresser:

While definitions of "crossdresser" vary, many use this term to describe a person who dresses in a way that is typically associated with a gender different from the one they were thought to be at birth, but who may not identify with that gender or intend to live full time as that gender. In this report, the term "crossdressers" refers to respondents who said that the term "cross-dresser" best described their current gender identity in response to Q. 2.3.

Gender transition:

This is a process in which a person begins to live according to their gender identity, rather than the gender they were thought to be at birth. Not all transgender people have transitioned or intend to do so, but many do. Gender transition looks different for every person. Possible steps in a gender transition may or may not include changing one's clothing, appearance, name

and identity documents (for example, a driver's license), or undergoing medical procedures such as hormone therapy to change one's physical characteristics. This report refers to gender transition in several places when discussing steps that may be included in one's gender transition, such as updating the name and gender on identity documents. Additionally, the report includes a variety of terms to refer to therapy/counseling, hormone therapy, surgical treatments, and other health services transgender people may undergo as part of their transition, including "health care related to gender transition" or "transition-related care." In this report, the term "respondents who have transitioned" refers to respondents who reported that they are living full time in response to Q. 1.12 (see below).

Living full time:

Respondents in the sample who were described in the report as "living full time" are those who reported that they lived full time in a gender different than the gender they were thought to be at birth in response to Q. 1.12. For many people, living full time may include changing one's name, clothing, and/or appearance, or taking other actions related to their gender transition.

Gender identity or expression:

Several questions throughout the report asked whether respondents thought that an experience had occurred due to their "transgender status/gender identity" and/or "gender expression/appearance." Both answer choices were included so that respondents could select what they felt best represented their experience. Since there was a substantial overlap of respondents who selected both reasons, and because these terms are commonly used interchangeably or with very similar meanings, responses of those who selected one or both of these reasons were collapsed for reporting in one "gender identity/expression" category. Additionally, several phrases are used interchangeably to describe experiences that respondents had as a result of biases due to being known or perceived to be transgender. These include, for example: "because they were transgender," "because of their transgender status," or "because of their gender identity or expression."

III. Additional Terms and Conventions Used in the Report

Sexual assault:

In this report, the term "sexual assault" refers to a variety of experiences of unwanted sexual contact. These may include, but are not limited to, oral, genital, or anal contact or penetration, forced fondling, and rape. Respondents were asked about their experiences with unwanted sexual contact or sexual assault in a number of different contexts. Definitions of these terms varied in some questions based on the context or, in some cases, on the national survey from which a question was adapted. Where applicable, the definition provided for "sexual assault" or "unwanted sexual contact" in each question is included in the report.

Underground economy:

This terminology refers to fields of work that, in general, are currently criminalized in the United States. In this report, this term includes income-based sex work (including forms of work in the sex trade that are not criminalized, such as pornography), drug sales, and other income-based work that is currently criminalized. See *Sex Work and Other Underground Economy Income* chapter.

Time period of reported experiences:

In the survey, respondents answered questions about experiences that occurred within a period of time prior to having taken the survey, such as in the past year or the past 30 days. The report refers to the time when these experiences occurred in comparison to the time when the respondent completed the survey. For example, respondents who had certain experiences within the 12 months prior to completing the survey were reported as having those experiences "in the past 12 months" or "in the past year." If a respondent had an experience that occurred within the 30 days prior to completing the survey, the experience was referred to as occurring "in the past month," "in the past 30 days," or "currently."

Write-in responses:

At several places in the survey, respondents were given an opportunity to write in a response to a question. These write-in responses were reviewed for recoded to categorize the responses into existing answer choice categories or new categories when feasible. When it was possible to recode write-in answers into a new category, those answers were often listed in the report and labeled as a "write-in response." In many cases, it was not possible to recode the answers into existing or new categories, and these write-in-responses were included in categories such as "a reason not listed above." For more information about how write-in answers were recoded, refer to *Appendix C: Detailed Methodology.*

U.S. population comparisons and other resources:

References to experiences of the U.S. population are included in the report for comparison and to provide context for findings where feasible. References to other research are also provided as resources in several places throughout the report. However, the list of references is not exhaustive, and should be not be treated as a comprehensive list of sources on any particular subject presented in this report.

Stories included in the report:

Throughout the report, excerpts of stories are included in sections titled "In Our Own Voices." These stories, which were submitted by respondents after they completed the survey, are provided to support the findings of the report and offer important anecdotal evidence and context for respondents' reported experiences. These stories have been edited for length and clarity.

CHAPTER 4

Portrait of USTS Respondents

With 27,715 respondents, the U.S. Transgender Survey (USTS) is the largest survey ever conducted of transgender people in the United States, providing a rich understanding of numerous aspects of their lives and experiences. In this chapter, an overview of respondents' diverse gender identities and experiences with transitioning is presented. Additional characteristics of USTS respondents, such as race and ethnicity, age, educational attainment, and geographic location, are also presented. This information is discussed in the following sections:

I. Gender Identity and Expression
II. Experiences with Transitioning
III. Being Perceived as a Transgender Person by Others
IV. Outness
V. Race and Ethnicity
VI. Age
VII. Location
VIII. Primary Language Spoken in Home
IX. Religious or Spiritual Identity
X. Income and Employment Status
XI. Educational Attainment
XII. Disability
XIII. Citizenship and Immigration Status
XIV. Sexual Orientation
XV. Relationship Status

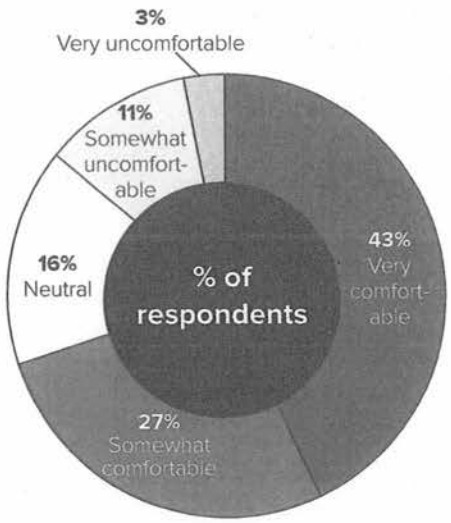
I. Gender Identity and Expression

a. Identity

The word *transgender* is often used as an "umbrella term" intended to encompass the spectrum of identities and capture the diversity of people whose gender differs from the one they were thought to be at birth. However, language describing identity continues to evolve, and it is difficult to describe all of those identities using just one term. Acknowledging this wide range of identities, the survey asked respondents if they thought of themselves as "transgender." Eighty-eight percent (88%) of respondents reported that they thought of themselves as transgender, while the remaining 12% used other terms to describe their gender and related experiences.[1]

Respondents were also asked how comfortable they were with the word "transgender" being used to describe them on a five-point scale from "very comfortable" to "very uncomfortable." Eighty-six percent (86%) expressed that they were comfortable or neutral using this term, including 82% percent of non-binary respondents. Forty-three percent (43%) were "very comfortable," and only 14% expressed discomfort with being described as transgender[2] (Figure 4.1).

Figure 4.1: Respondent's level of comfort with the word "transgender" being used to describe them



Respondents were also offered a list of identity terms from which they could check all terms that described their gender identity, and they were also given an opportunity write in a gender that was not listed (Table 4.1). In addition to the listed terms, respondents wrote in more than 500 unique gender terms with which they identified.

Table 4.1: Gender identity terms

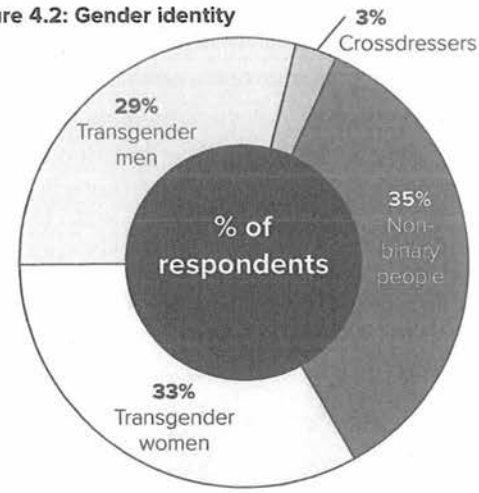
Gender identity terms	% of respondents
Transgender	65%
Trans	56%
Trans woman (MTF, male to female)	32%
Trans man (FTM, female to male)	31%
Non-binary	31%
Genderqueer	29%
Gender non-conforming or gender variant	27%
Gender fluid/fluid	20%
Androgynous	18%
Transsexual	18%
Agender	14%
Two-spirit	7%
Bi-gender	6%
Butch	5%
Crossdresser	5%
Multi-gender	4%
Third gender	4%
Intersex	3%
Drag performer (king/queen)	2%
A.G. or aggressive	1%
Stud	1%
Travesti	1%
Bulldagger	<1%
Fa'afafine	<1%
Mahu	<1%
A gender not listed above	12%

b. Gender Identity Categories Used for Analysis

Respondents were also asked to choose only one term that best described their current gender identity out of six possible terms (*woman, man, trans woman (MTF), trans man (FTM), non-binary/genderqueer,* or *crossdresser*) to determine the gender identity categories used for primary analysis.[3] Respondents

were grouped into four gender identity categories based on their responses. These four categories are used throughout this report to discuss the experiences of those who completed the survey: *transgender women*, *transgender men*, *non-binary people*, and *crossdressers*.[4] Those who said that *woman* or *transgender woman* best described their gender identity were included in the transgender women analytical category (33%), and those who said that *man* or *transgender man* best described their gender identity were included in the transgender men analytical category (29%). Overall, 62% of respondents were included in the transgender men and women categories. Three percent (3%) said that *crossdresser* best described their gender identity. More than one-third (35%) of respondents indicated that their gender identity was best described as *non-binary* or *genderqueer*, a term often used to describe people whose gender is not exclusively male or female, including those who identify with a gender other than male or female, as more than one gender, or as no gender[5] (Figure 4.2). Throughout the report, these respondents are referred to as "non-binary."

Figure 4.2: Gender identity



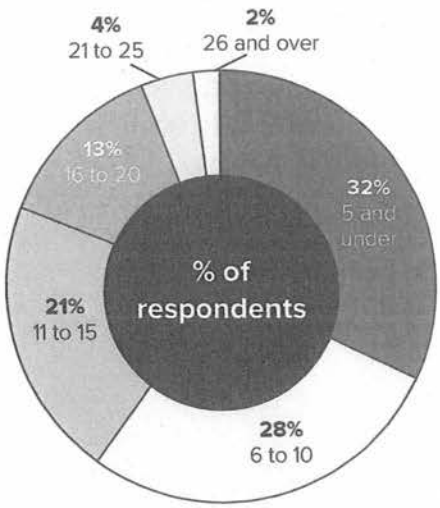
c. Gender Assignment at Birth

Respondents were asked about the sex they were "assigned at birth, on [their] original birth certificate."[6] In this report, the term "respondents with male on their original birth certificate" is used to describe respondents who were thought to be male when they were born (such as transgender women), and "respondents with female on their original birth certificate" is used to describe respondents who were thought to be female when they were born (such as transgender men). More than half (57%) of respondents had female on their original birth certificate, and 43% had male on their original birth certificate. Of those who were non-binary, 80% had female on their original birth certificate, and 20% had male on their original birth certificate.

d. Development of Transgender Identity and Interactions with Other Transgender People

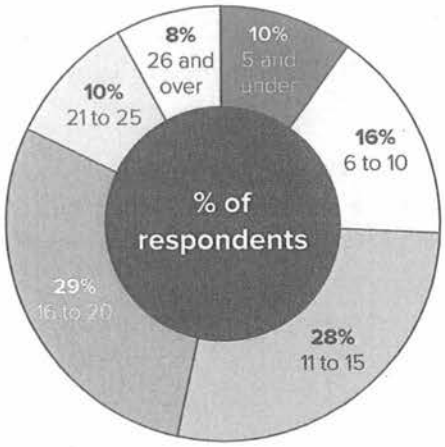
Respondents received questions related to the development of their transgender identity throughout their lives. A majority of respondents (60%) reported that they began to feel "different" from the sex on their original birth certificate at age 10 or younger, including 32% who began to feel different at age 5 or younger, and 28% who began to feel different between the ages of 6 and 10. Six percent (6%) reported that they began to feel different at age 21 or older (Figure 4.3).

Figure 4.3: Age they began to feel gender was different from the one on their original birth certificate



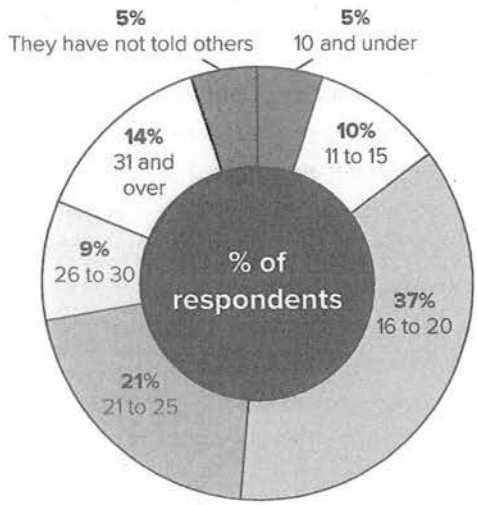
Respondents were also asked how old they were when they started to think of themselves as transgender, even if they did not know that word. One in ten (10%) reported that they began thinking of themselves as transgender at age 5 or younger. Sixteen percent (16%) began to think of themselves as transgender between the ages of 6 and 10, and 28% between the ages of 11 and 15. Eight percent (8%) reported beginning to think of themselves as transgender at age 26 or older (Figure 4.4).

Figure 4.4: Age they started to think they were transgender



Respondents were also asked at what age they began to tell others that they were transgender. One in ten (10%) respondents reported that they began to tell others that they were transgender between the ages of 11 and 15, and more than one-third (37%) did so between the ages of 16 and 20. Another 30% began telling people that they were transgender between the ages of 21 and 30, and 14% began telling people that they were transgender at age 31 or older. Additionally, 5% reported that they had not told anyone else that they were transgender (Figure 4.5).

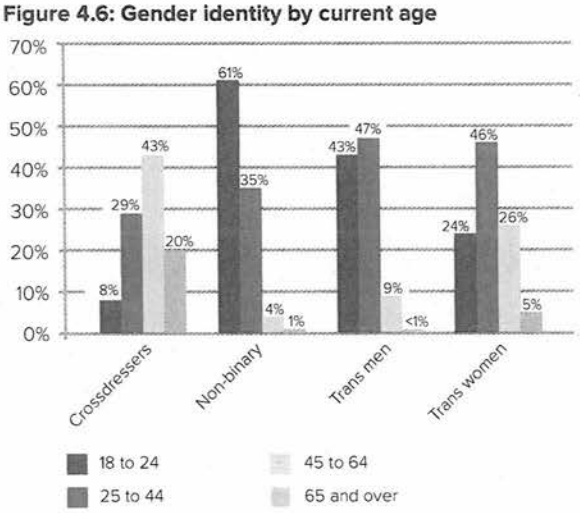
Figure 4.5: Age they started to tell others that they were transgender



e. Gender Identity and Current Age

The age profile of respondents[7] differed widely by gender identity categories, with nearly half (47%) of transgender men and women being aged 25–44, compared to 35% of non-binary respondents, and 29% of crossdressers. Non-binary respondents were more likely to be younger, with nearly two-thirds (61%) being aged 18–24, in contrast to transgender men (43%), transgender women (24%), and crossdressers (8%). One in five (20%) crossdressers were aged 65 or older, compared to only 5% of transgender women, 1% of non-binary respondents, and less than 1% of transgender men (Figure 4.6).

Figure 4.6: Gender identity by current age



II. Experiences with Transitioning

Transitioning is a process by which a person begins to live in a gender that is different than the one on their original birth certificate. Not all transgender people have transitioned or intend to do so, but many do. Gender transition can involve many different aspects, including changing one's clothing, appearance, name, and identity documents (such as driver's licenses or passports) and asking people to use different pronouns (such as he, she, or they) than the ones associated with the gender on one's original birth certificate. Transitioning may also include undergoing medical procedures, such as hormone therapy or surgeries, to change one's physical characteristics. Some people make many of these changes while others do not, depending on their needs and resources. Additionally, some transgender people may desire and make some of these changes even if they do not intend to live full time in a gender that is different than the one on their original birth certificate. However, many people who want to take these steps are not able to do so because of financial constraints, safety concerns, fear of discrimination and rejection, and other barriers.

a. Full-Time Status and Transition

Nearly two-thirds (62%) of respondents were currently living full time in a gender that was different from the one on their original birth certificate. Throughout the report, the process of living full time in a gender that is different than that on one's original birth certificate is described as "transitioning." Twenty-two percent (22%) of respondents reported that they wanted to transition someday, 13% were unsure, and 3% did not want to transition (Figure 4.7). Three-quarters (75%) of transgender men and women had transitioned, and 43% of non-binary respondents had transitioned (Figure 4.8).[8]

Figure 4.7: Transition status of respondents

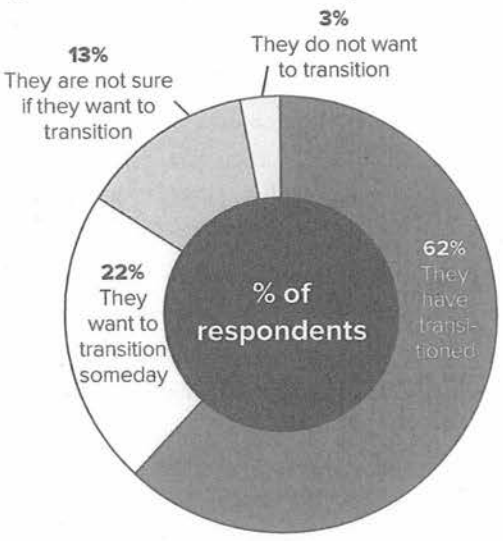
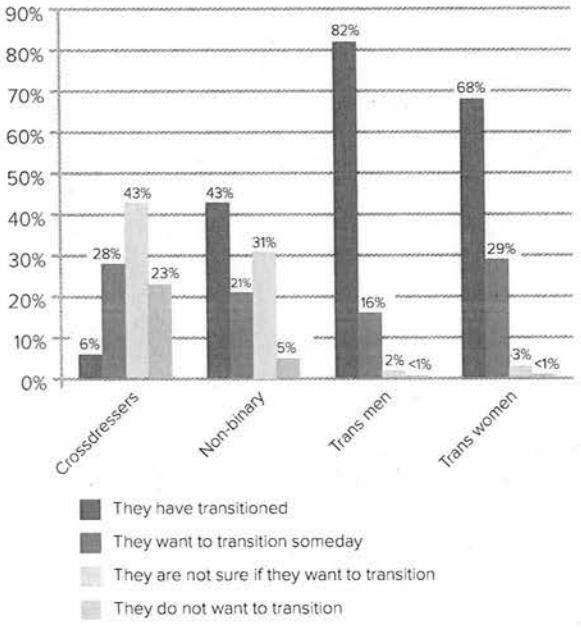


Figure 4.8: Transition status of respondents
GENDER IDENTITY (%)

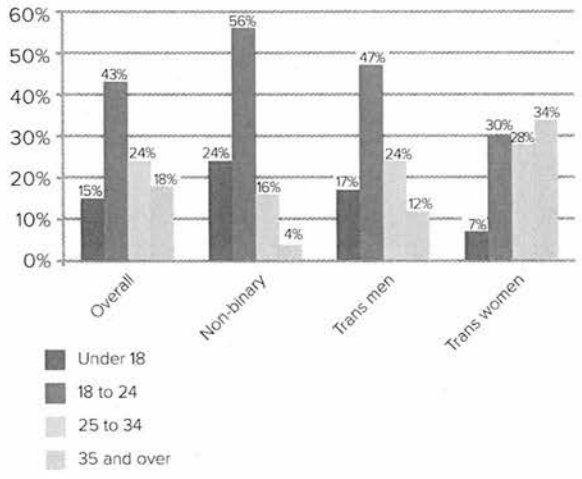


Respondents were also asked what gender they were living in on a day-to-day basis. Thirty-five percent (35%) of respondents reported that they currently lived as a man on a daily basis, 30% lived as a woman, 21% lived as neither a man nor a woman, and 15% lived part time in one gender and part time in another.

b. Age of Transition

Those who have transitioned reported the age at which they began transitioning, or living full-time in a gender other than that on their original birth certificate. Nearly half (43%) reported that they began transitioning between the ages of 18 and 24, and nearly one-quarter (24%) transitioned between ages 25 and 34. Fifteen percent (15%) transitioned under the age of 18, and 18% transitioned at age 35 or older. Non-binary respondents and transgender men were more likely to have transitioned at a younger age, with 24% of non-binary respondents and 17% of transgender men transitioning under the age of 18, compared to 7% of transgender women (Figure 4.9).[9]

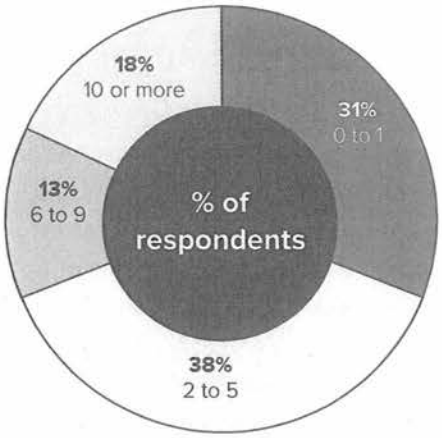
Figure 4.9: Age began transitioning
GENDER IDENTITY (%)



c. Number of Years Since Transitioning

The number of years since a respondent had transitioned was determined in order to provide valuable information and context for some of the respondents' experiences.[10] Nearly one-third (31%) of those who had transitioned had done so within one year of taking the survey, 38% had transitioned 2 to 5 years prior, 13% transitioned 6 to 9 years prior, and 18% had transitioned 10 or more years prior (Figure 4.10).

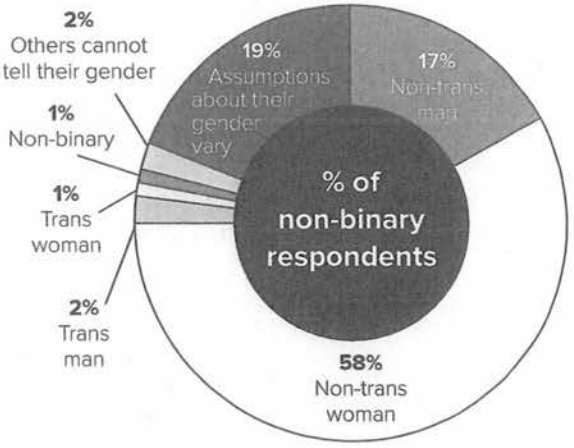
Figure 4.10: Number of years since transitioning



d. Additional Questions for Non-Binary Respondents

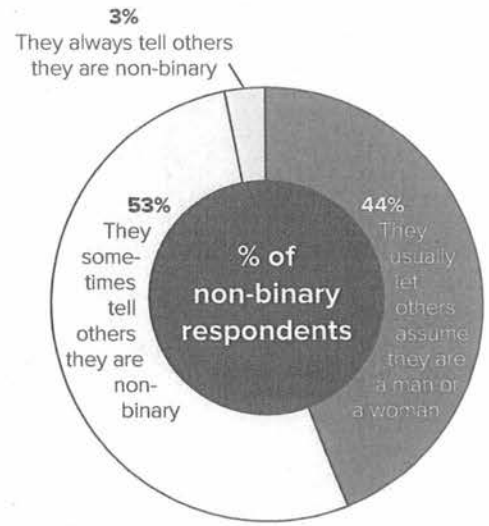
Non-binary respondents received questions about what they tell other people about their gender identity. They were asked about what gender they were perceived to be by people who did not know they were non-binary. A majority reported that people usually assumed they were non-transgender women (58%), including 72% of non-binary respondents with female on their original birth certificate, and 2% of non-binary respondents with male on their birth certificate. Seventeen percent (17%) reported that other people assumed they were non-transgender men, including 77% of non-binary respondents with male on their original birth certificate, and 3% of non-binary respondents with female on their birth certificate. Nearly one in five (19%) reported that assumptions about their gender varied (Figure 4.11).

Figure 4.11: Gender that people who do not know they are non-binary usually assume they are



Non-binary respondents were asked how they responded when people in their life assumed their gender was something other than non-binary. Almost half (44%) reported that they usually let others assume they were a man or woman, and 53% sometimes corrected others and told them about their non-binary identity. Only 3% always told others that they were non-binary (Figure 4.12).

Figure 4.12: Response when people assume that their gender is something other than non-binary



Non-binary respondents who reported that they usually let others assume they are a man or woman or only sometimes tell people they are non-binary were asked for the main reasons they do not tell others about their non-binary identity. Respondents could select multiple reasons for choosing not to tell people about their non-binary identity. A majority of non-binary respondents reported that people do not understand so they do not try to explain it (86%) or that it is easier not to say anything (82%). Approximately two-thirds reported that their non-binary identity is often dismissed as not being a real identity or just a phase (63%), and others feared they might face violence (43%) (Table 4.2).

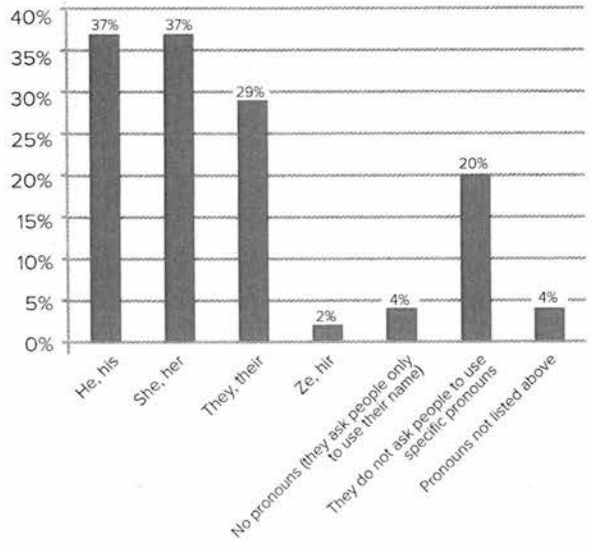
Table 4.2: Main reasons for not telling people they are non-binary

Main reasons for not telling others about non-binary identity	% of non-binary respondents
Most people do not understand so they do not try to explain it	86%
It is easier not to say anything	82%
Most people dismiss it as not being a real identity or a "phase"	63%
They might face violence	43%
They are not ready to tell people they identify as non-binary	35%
They might lose their job or not be able to get a job	35%
They might not get the medical care they need	24%
They might be hurt financially	23%
They might face mistreatment at school	18%
Their friends might reject them	18%
They might become homeless	12%
Their church or faith community might reject them	6%
A reason not listed above	18%

e. Pronouns

Eighty-four percent (84%) of respondents reported that the pronouns they used were different from those associated with the sex on their original birth certificate. Respondents reported a wide range of pronouns that they asked people to use when referring to them and could select more than one pronoun. The most widely used pronouns were "he/his" (37%), "she/her" (37%), and "they/their" (29%). One in five (20%) reported that they did not ask people to use specific pronouns when referring to them, and another 4% indicated that they used pronouns other than those provided in the answer choices. This included more than a dozen additional pronouns provided through write-in responses (Figure 4.13).

Figure 4.13: Pronouns respondents ask people to use



III. Being Perceived as a Transgender Person by Others

Some transgender people find that others can routinely tell that they are transgender without being told, while others are generally perceived as the gender they identify with, and still others are perceived as the gender they were thought to be at birth. Many interactions and experiences of transgender people may be influenced by others' perceptions of them as being a transgender person. Transgender people who are visually or otherwise perceived by others as transgender or gender non-conforming may be more vulnerable to negative interactions in public or other settings.

To assess whether respondents were perceived as transgender, they were asked whether others could tell that they were transgender even without being told on a five-point scale from "always" to "never." Nearly one in ten (9%) reported that others could tell they were transgender without being told "most of the time," 32% said others could "sometimes" tell, and 24% said that others could never tell (Figure 4.14).[11] Respondents' experiences with others' perception of their transgender status varied by gender identity (Figure 4.15).

Figure 4.14: How often people could tell they were transgender without being told

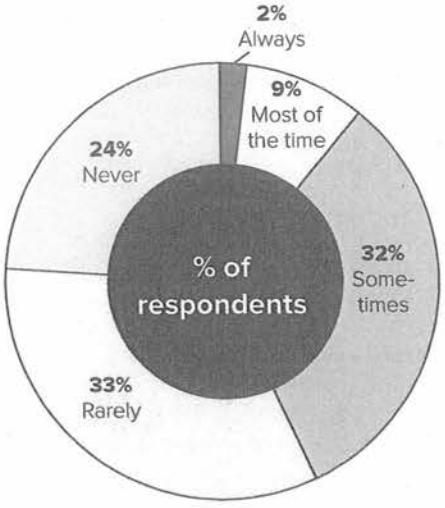
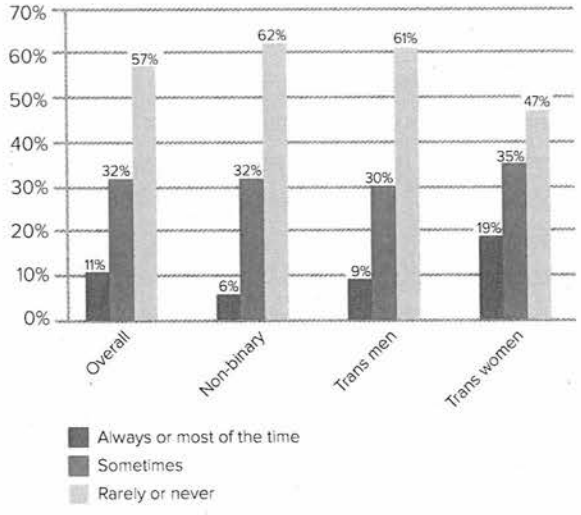


Figure 4.15: How often people could tell they were transgender without being told
GENDER IDENTITY (%)



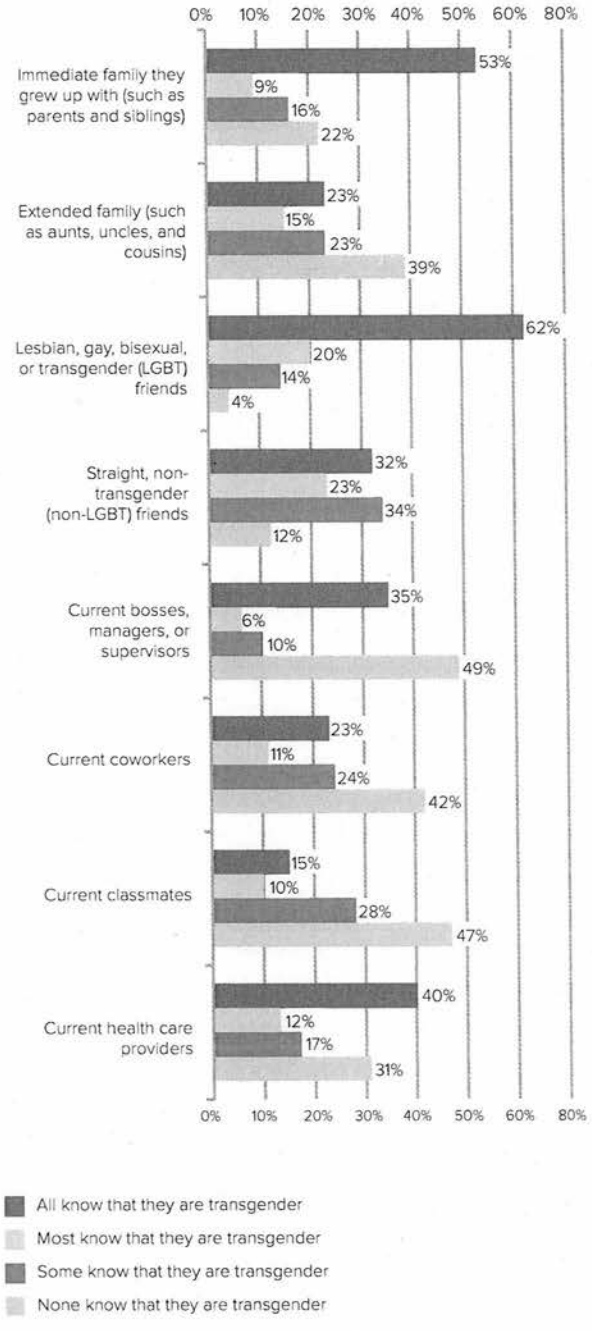
IV. Outness

Respondents were asked whether they thought different groups of people in their lives knew that they were transgender to determine if they were "out"[12] about their transgender identity to family members, friends, supervisors and colleagues at work, classmates, and health care providers. Respondents were asked whether all, most, some, or none of the people in their lives knew they were transgender in each of the groups of people in their lives. Results reflect only those respondents who had people from each group in their lives. Overall, 8% reported that they were out to all of the people in their lives, across all groups of people, 48% were out to most, 43% were out to some, and only 2% were out to none of the people in their lives.

Nearly two-thirds (62%) were out to all or most of the immediate family that they grew up with, and 38% were out to all or most of their extended family.[13] Regarding workplace environments, nearly one-half reported that none of their current supervisors (49%) or coworkers (42%) knew that they were transgender.[14] In terms of health care providers, although 40% reported that all of their health care providers knew that they were transgender, almost one-third (31%) indicated that none of their health care providers knew that they were transgender (Figure 4.16).

Of all groups of people the survey asked about, respondents were most likely to be out to all of their LGBT friends (62%). Respondents were also asked about the methods by which they socialize with other transgender people. Sixty-four percent (64%) reported that they socialized with other transgender people in person, and 79% socialized online. Nearly one-third (32%) said they interacted with transgender people in political activism, and 10% reported that they did not socialize with other transgender people.

Figure 4.16: Outness to people in respondents' lives



V. Race and Ethnicity

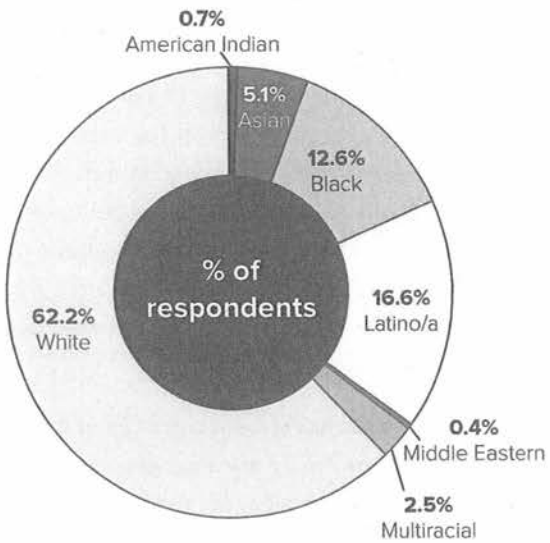
Respondents received a question on race and ethnicity and were asked to select only one of the following categories that most accurately described their racial or ethnic identity:

- Alaska Native (received a write-in option)[15]
- American Indian (received a write-in option)[16]
- Asian or Asian American
- Biracial or multiracial (received a follow-up question)[17]
- Black or African American
- Latino/a or Hispanic
- Middle Eastern or North African
- Native Hawaiian or Pacific Islander
- White or European American
- A racial or ethnic identity not listed above (received a follow-up question)[18]

Throughout the report, respondents who identified as biracial, multiracial, or more than one racial or ethnic category are included in the multiracial group. Additionally, due to small sample sizes and for purposes of analysis, certain racial and ethnic groups were combined into single categories. American Indian and Alaska Native respondents are combined in one category and reported as "American Indian." Similarly, the Asian/Asian American and Native Hawaiian/Pacific Islander groups are also combined in one category and reported as "Asian."[19]

The USTS sample had a percentage of white respondents that is notably higher than the U.S. general population, which is common among internet-based surveys.[20] Therefore, a race and ethnicity weight was developed to more closely represent what is estimated to be the actual racial and ethnic distribution for the transgender population in the U.S., based on the Census Bureau's 2014 American Community Survey (ACS).[21] Racial and ethnic categories were weighted to reflect the ACS distribution for race and ethnicity as part of the standard survey weight that was applied to all results presented in the report (Figure 4.17).[22]

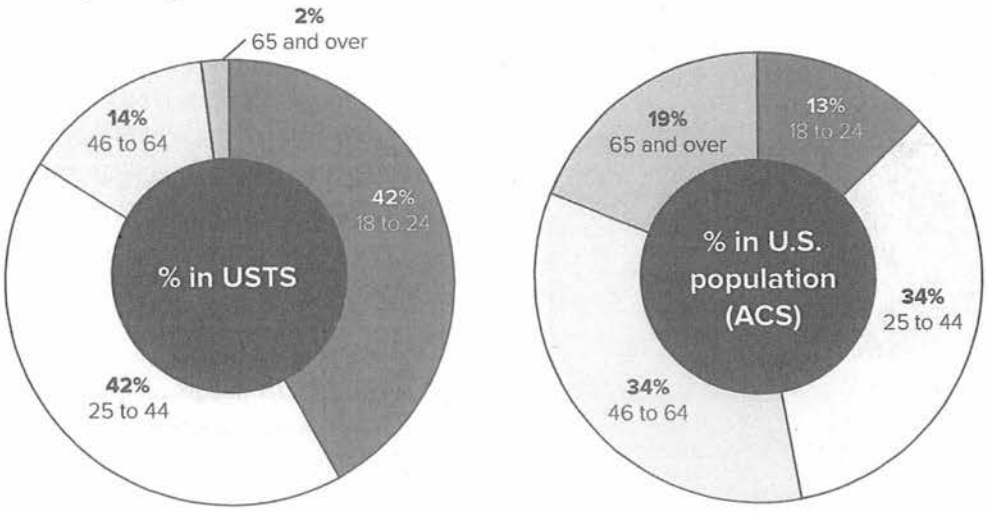
Figure 4.17: Race and ethnicity of respondents



VI. Age

The age of respondents in the sample ranged from 18 to 87. The overall age of respondents in the sample was generally younger than that in the U.S population. In addition to having a younger age distribution, a disproportionally large number of respondents reported an age of 18 years old. Therefore a weight was created to balance the representation in the sample of those 18-year-old respondents in relation to the rest of the sample. This weight was part of the standard survey weight that was applied to all results presented in this report (Figure 4.18). Additionally, for certain findings in this report, a "supplemental weight" was applied to adjust the USTS sample to reflect the age distribution for the U.S. population based on the ACS.[23]

Figure 4.18: Age of respondents

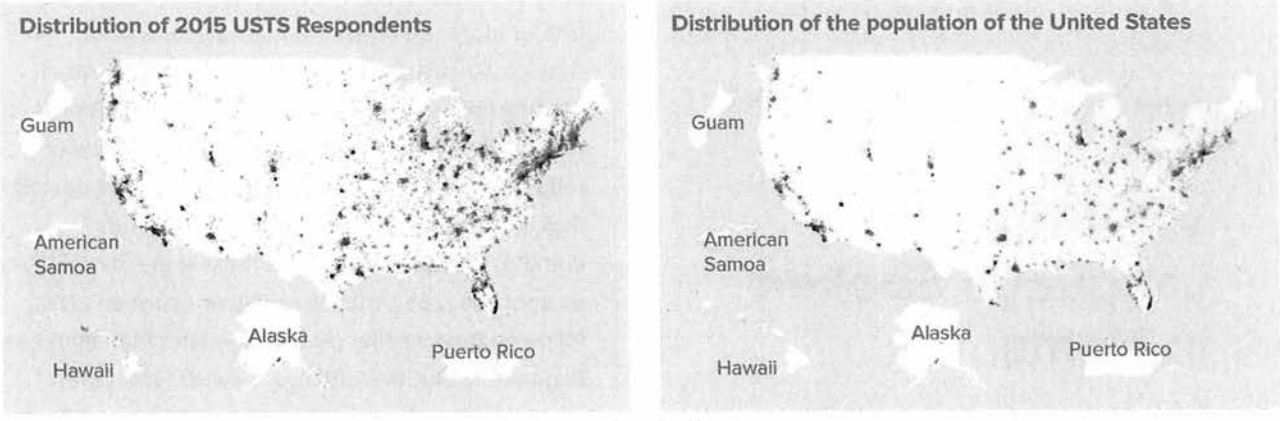


VII. Location

The sample included respondents from all 50 states, the District of Columbia, American Samoa, Guam, Puerto Rico, and several U.S. military bases overseas. The geographic distribution of the sample generally mirrors that of the U.S. general population (Figure 4.19).

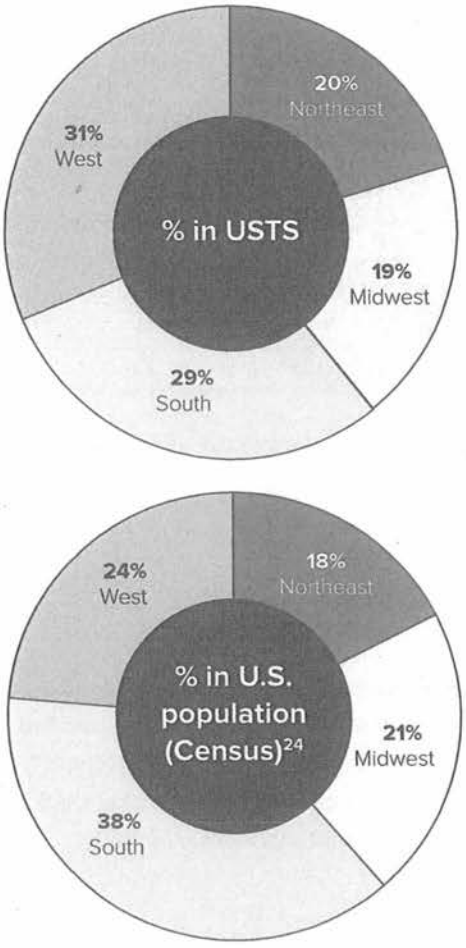
The sample was divided into regions based on the Census Bureau regions, which included the Northeast, Midwest, South, and West (Figure 4.20). These regional categories did not include U.S. territories or U.S. military bases overseas.

Figure 4.19



Each dot on the maps represents the number of people in a zip code. Every dot corresponds to at least one person, and the size of each dot increases in accordance with the number of people in each zip code.

Figure 4.20: Respondents' location by region



VIII. Primary Language Spoken in Home

Respondents were asked about the primary language spoken in their home. Eighty-four percent (84%) reported that English was the only language spoken in their home, compared to 79% in the U.S. general population, as reported in the American Community Survey (ACS).[25] Fourteen percent (14%) reported that English and another language were mainly spoken in their home, and 2% reported that a language other than English was the primary language spoken in their home. In addition to spoken languages, 0.4% of respondents also reported that American Sign Language was either the main language or one of the main languages used in their home.

Spanish (including Spanish Creole) was reported as the most common language spoken in their home other than English, with 10% of respondents reporting Spanish was the main language spoken in their home, exclusively or along with English. This was slightly lower than the percentage of those who spoke Spanish in the home in the U.S. general population (13%).[26] Each of the other identified languages were spoken by less than 1% of respondents.

IX. Religious or Spiritual Identity

Respondents were asked about their current religious or spiritual identity and could select one or more identities from a provided list, or they could select a religious affiliation or spiritual identity not listed.[27,28] Sixty-three percent (63%) of respondents reported that they had a spiritual or religious identity, and 37% of respondents reported that they did not have a spiritual or religious identity.[29] Respondents were most likely to identify as agnostic (23%), atheist (22%), or Christian (21%), followed by a smaller percentage who identified as Pagan (9%), Buddhist (6%), or Jewish (4%). One-quarter (25%) of respondents identified as spiritual, but with no religious affiliation. Thirteen percent (13%) had no religious or spiritual affiliation, and 7% identified a religious affiliation or spiritual identity that was not listed (Table 4.3).

Table 4.3: Current religious or spiritual identity

Current religious or spiritual identity	% of respondents
Spiritual, but no religious affiliation	25%
Agnostic	23%
Atheist	22%
Christian	21%
Pagan	9%
Buddhist	6%
Jewish	4%
Secular Humanist	4%
Wiccan	4%
Druid	1%
Hindu	1%
Muslim	1%
Native American Traditional Practitioner or Ceremonial	1%
Polytheist (write-in response)	1%
Taoist	1%
Baha'i	<1%
Confucian	<1%
Jain	<1%
Jehovah's Witness	<1%
Rastafarian	<1%
Scientologist	<1%
Shinto	<1%
Sikh	<1%
Tenrikyo	<1%
A religious affiliation or spiritual identity not listed above	7%
No affiliation	13%

X. Income and Employment Status

Respondents were asked about various aspects of their income using a series of questions based on the Current Population Survey (CPS).[30] Results for income and employment status are presented briefly in this section and discussed in greater detail in the *Income and Employment Status* chapter. In order to compare USTS respondents' income and employment data with data from the CPS and other national data sources, income and employment results are presented with the "supplement weight" applied.[31]

a. Sources of Income

Nearly half (45%) of respondents received income from multiple sources, such as employment, Social Security income, or a pension. Thirty-six percent (36%) received income solely from their own employment or a partner or spouse's employment (not including underground economy work, such as sex work, drug sales, or other work that is currently criminalized). Nearly one in ten (9%) received income from Social Security, including disability, and 3% received income solely from a pension. Three percent (3%) reported that they were currently working in the underground economy, including 1% whose income came solely from underground economy work (Table 4.4).

Table 4.4: Current sources of income by single and multiple sources

Sources of income	% of respondents (supplemental weight)
Employment only (from their own employer, partner/spouse's employer, or self-employment)	36%
Social Security income/disability only	9%
Pension/retirement only	3%
Other sources of income only	3%
No income	2%
Sex work and other underground economy work only	1%
Unemployment benefits/cash assistance only	1%
Multiple sources	45%

b. Individual and Household Income

Individual and household incomes for the USTS sample and the U.S. population were reported from 2014, the last full year prior to the survey for which annual income figures were available. Respondents reported lower incomes than the U.S. population (Figure 4.21 & Figure 4.22).[32]

Figure 4.21: Individual income in 2014

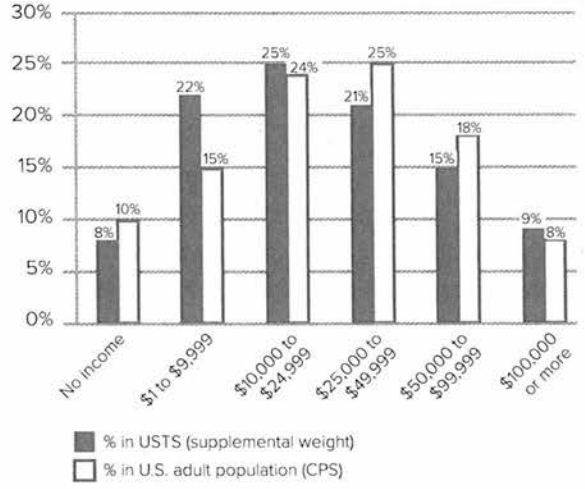
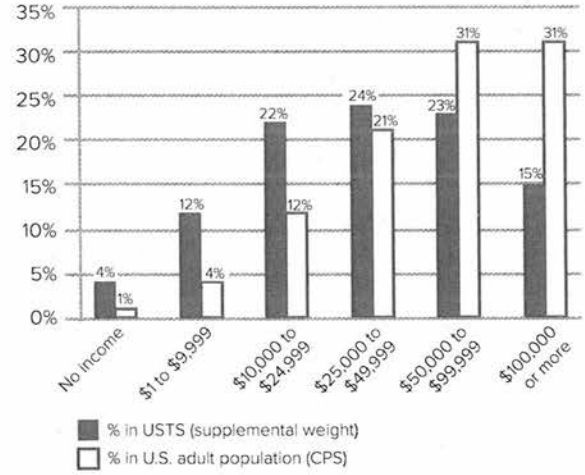


Figure 4.22: Household income in 2014



c. Poverty

Nearly one-third (29%) of respondents were living in poverty,[33] nearly twice the poverty rate among the general U.S. adult population (14%).[34]

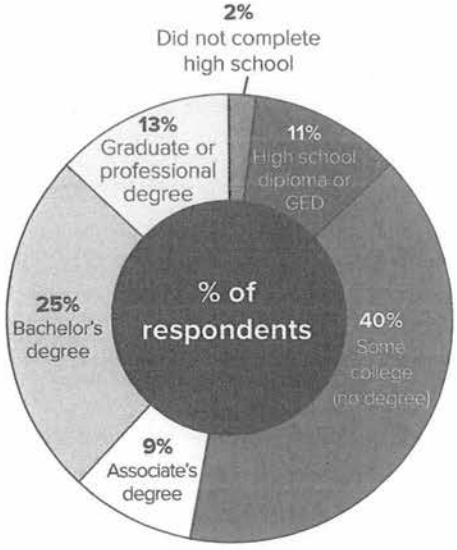
d. Employment Status

When asked about their current employment status, 35% of respondents reported that they currently had at least one full-time job, 15% had at least one part-time job, 15% were self-employed, and 11% were students. The unemployment rate for USTS respondents was 15%, three times the U.S. unemployment rate at the time of the survey (5%).[35]

XI. Educational Attainment

Respondents were asked about the highest level of education or degree that they had completed. Thirteen percent (13%) of respondents had a high school diploma or GED, or did not complete high school. Forty percent (40%) had completed some college but had not obtained a degree, 9% had an associate's degree, and 38% had received a bachelor's degree or higher (Figure 4.23).

Figure 4.23: Educational attainment (categories used in report)



Throughout the report, educational attainment is reported according to the categories reflected in Figure 4.23. However, alternative categories are