

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

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Editor - Madeline B. Deutsch, MD, MPH



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

Director of Clinical Services

Center of Excellence for Transgender Health

Associate Professor of Clinical Family and Community Medicine

Department of Family and Community Medicine

University of California, San Francisco

Madeline.Deutsch@ucsf.edu

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Contributors

- **Madeline B. Deutsch, MD, MPH**
University of California, San Francisco, Department of Family and Community Medicine
Center of Excellence for Transgender Health
- **Paula Amato, MD**
Oregon Health and Science University
- **Mark Courey, MD**
University of California San Francisco, Voice and Swallowing Center
- **Curtis Crane, MD**
Brownstein & Crane Surgical Services
- **Iore m. dickey, PhD**
Northern Arizona University
- **Jamison Green, PhD**
Jamison Green & Associates, Transgender Policy Consultants and Educators
- **Jennifer Hastings, MD**
University of California San Francisco, Department of Family & Community Medicine
Planned Parenthood Mar Monte, Transgender Healthcare Program
- **Katherine T. Hsiao, MD, FACOG**
Sutter Health, California Pacific Medical Center, Department of Obstetrics and Gynecology
- **Dan H. Karasic, MD**
University of California San Francisco School of Medicine, Department of Psychiatry
- **Esther A. Kim, MD**
University of California San Francisco, Department of Surgery, Division of Plastic and
Reconstructive Surgery
University of California San Francisco, Department of Surgery at San Francisco General
Hospital
- **Toby R. Meltzer, MD**
Toby R. Meltzer MD, PC Plastic and Reconstructive Surgery
- **Juno Obedin-Maliver, MD, MPH**
University of California San Francisco Medical Center
Stanford University School of Medicine - Lesbian, Gay, Bisexual, and Transgender Medical
Education Research Group
- **Johanna Olson-Kennedy, MD**
Children's Hospital Los Angeles, Department of Adolescent and Young Adult Medicine

- **Tonia Poteat, PhD, MPH, PA-C**
Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Center for Public Health and Human Rights, Center for AIDS Research
- **Asa Radix, MD, MPH**
Callen Lorde Community Health Center, Research and Education
- **Cecily Reeves, PhD, FNP-C/PA-C**
Samuel Merritt University, School of Nursing
- **Stephen M. Rosenthal, MD**
University of California San Francisco, Pediatric Endocrinology Clinics, Child and Adolescent Gender Center
- **Sarah Schneider, MS, SLP-CC**
University of California San Francisco, Department of Otolaryngology Head and Neck Surgery
University of California San Francisco, Voice and Swallowing Center
- **Nathaniel G. Sharon, MD**
University of New Mexico, Division of Child and Adolescent Psychiatry
- **Eric D. Wang, MD**
University of California San Francisco, Department of Surgery, Division of Plastic and Reconstructive Surgery
- **Linda Wesp, MSN, NP-C**
University of Wisconsin-Milwaukee, College of Nursing
- **Andre A. Wilson, MS**
Jamison Green & Associates, Transgender Policy Consultants and Educators
- **Jeannine Wilson Stark, LE, CPE**
Transgender SF Electrolysis
- **Barry Zevin, MD**
San Francisco Department of Public Health, Tom Waddell Health Center

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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 criteria 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 spectræ.

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 onboarding 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. Transgender 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 occurrence 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 cartilage shave)
- [Voice surgery](#)

Surgeries not specific to transgender populations:

- [Augmentation mammoplasty](#)
- [Hysterectomy / oophorectomy](#)
- 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

Primary author: Madeline B. Deutsch, MD, MPH

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

Primary author: Madeline B. Deutsch, MD, MPH

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 adherence, 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 chorionogonadotropin (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, 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 norethandrone 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
Spirolactone	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 suprapsychoic 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 dihydroepiandrosterone 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 consulting 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

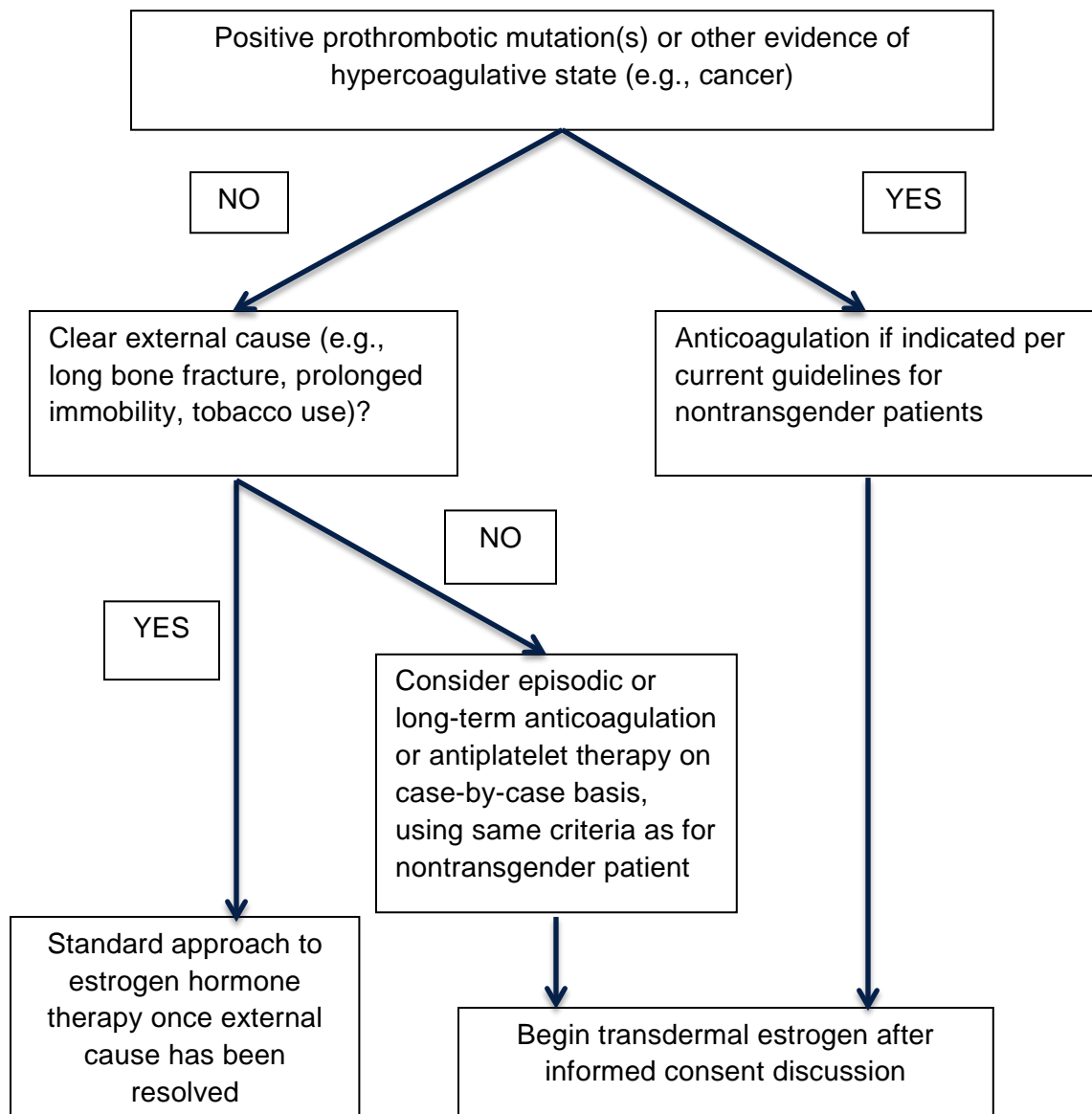


Figure 7-2. Approach to management of estrogen in patients with a family history of VTE but no personal history of VTE

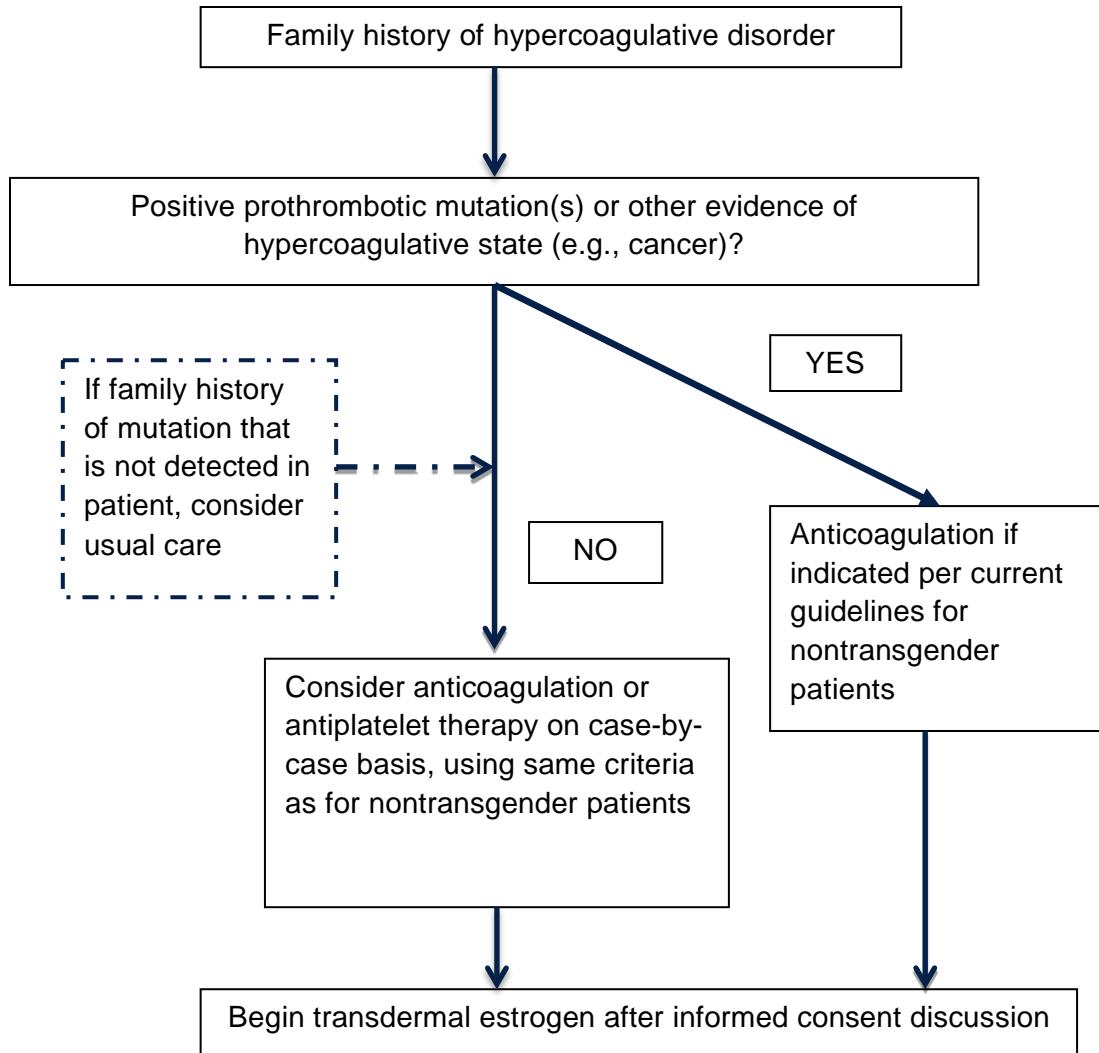


Figure 7-3. Approach to patient using oral or injected estrogen at time of first diagnosis of VTE

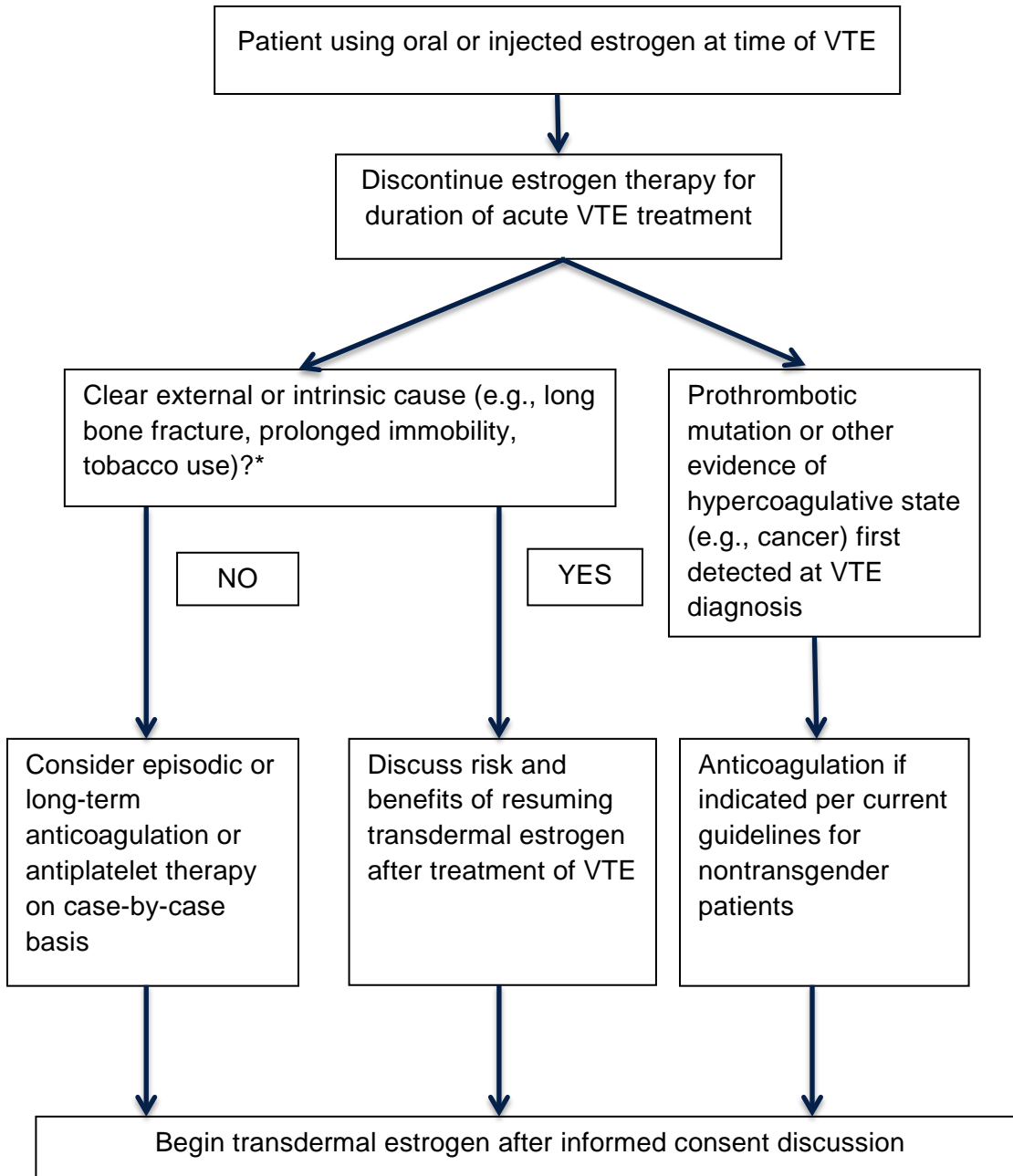


Figure 7-4. Approach to patient using transdermal estradiol at time of first diagnosis of VTE

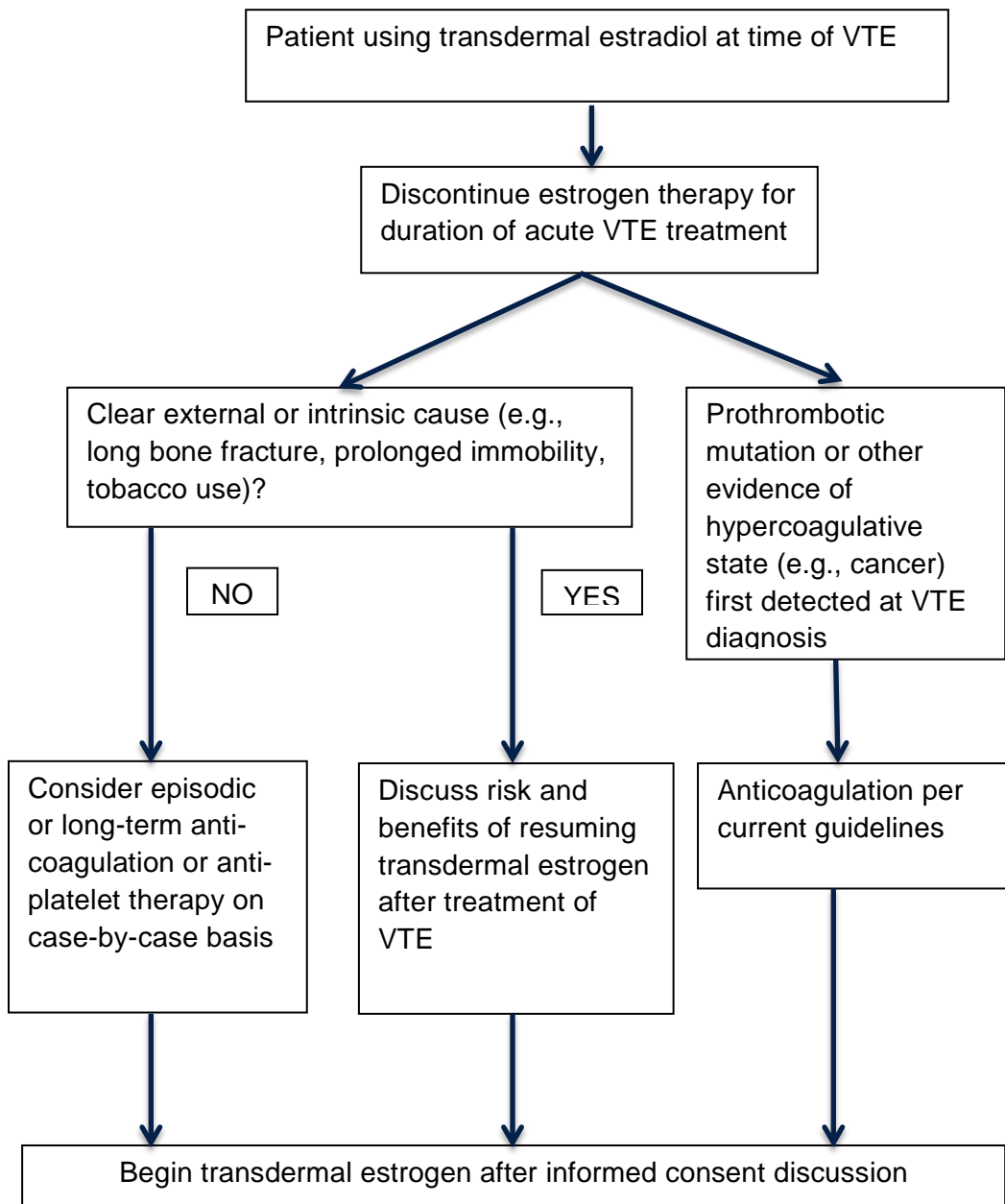
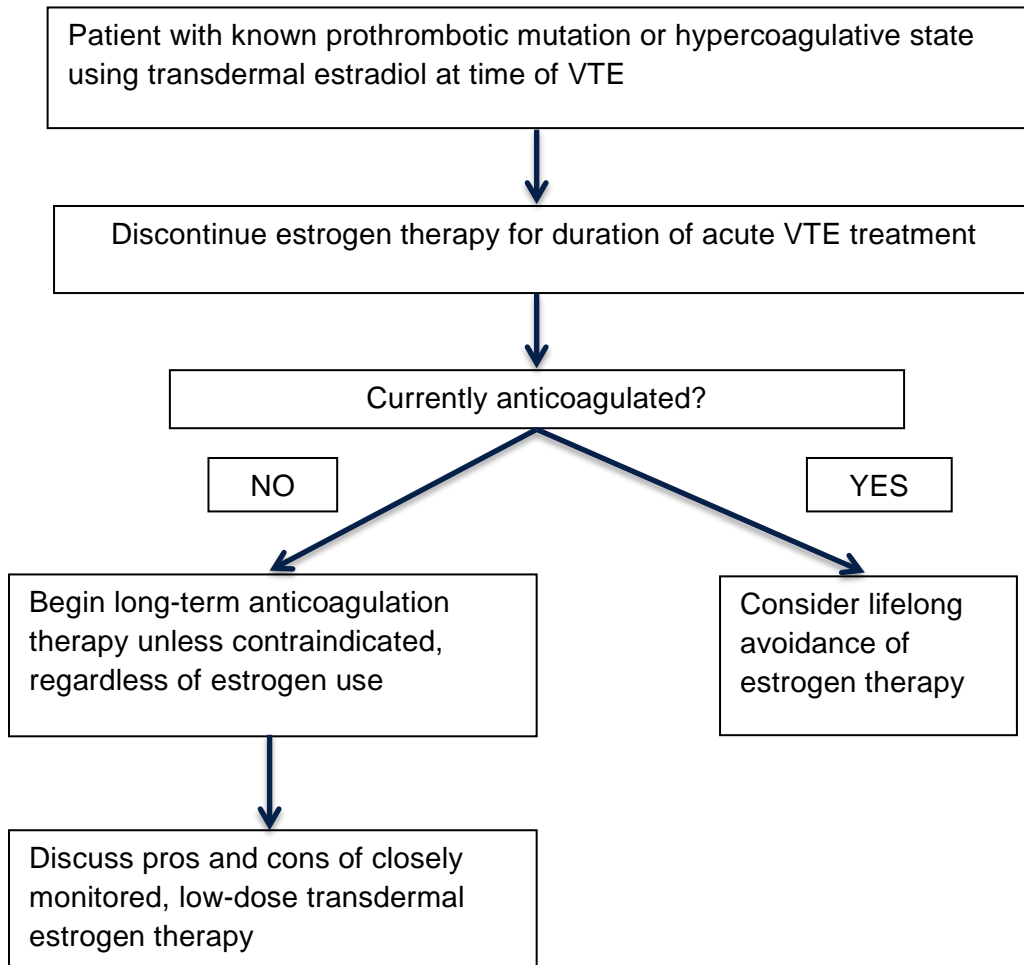


Figure 7-5. Approach to patients with known hypercoagulative state who use transdermal estradiol and present with acute VTE



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

Primary author: Madeline B. Deutsch, MD, MPH

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 Enanthate^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 menorrhagic*	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 hormone therapy at or around age 50, the age at which non-transgender women undergo menopause. Regardless of the presence of gonads at this age, withdrawal 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), there 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 injection dosing intervals may help minimize acne.

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9. Pelvic pain and persistent menses in transgender men

Primary author: Juno Obedin-Maliver, MD, MPH

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 hypoestrogenic state which promotes atrophy, increases vaginal pH and thus 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, menses 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 ruled 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 minimal 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 levonorgestrel 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, oophorectomy 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 anastrozole or letrozole 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): <http://www.pelvicpain.org>

- [American Physical Therapy Association](http://moveforwardpt.com/Default.aspx): <http://moveforwardpt.com/Default.aspx>

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

Primary author: Jennifer Hastings, MD

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

Primary authors: Asa Radix, MD, MPH and Madeline B. Deutsch, MD, MPH

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

Primary author: Linda Wesp, MSN, NP-C

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

Primary authors: Asa Radix, MD, MPH and Madeline B. Deutsch, MD, MPH

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/) (<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

Primary author: Tonia Poteat, PhD, MPH, PA-C

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 prophylaxis (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

Primary author: Tonia Poteat, PhD, MPH, PA-C

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 undecanoate 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	Boceprevir	Daclatasvir	Ledipasvir/Sofosbuvir	OBV/PTV/r	OBV/PTV/r + DSV	Simeprevir	Sofosbuvir	Telaprevir
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) (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)

Primary author: Tonia Poteat, PhD MPH PA-C

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 metoidioplasty 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 fibroblastic 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 to 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

Primary author: Paula Amato, MD

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

Primary author: Madeline B. Deutsch, MD, MPH

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

Primary author: Madeline B. Deutsch, MD, MPH

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

Primary author: Linda Wesp, MSN, NP-C

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

Primary author: Madeline B. Deutsch, MD, MPH

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

Primary author: Katherine T. Hsiao, MD, FACOG

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

Primary author: Linda Wesp, MSN, NP-C

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 amenorrhea 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 oophorectomy may be performed in transgender men as part of the management of gender dysphoria or for a pathologic process, routine oophorectomy 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

Primary authors: lore m. dickey, PhD; Dan H. Karasic, MD; Nathaniel G. Sharon, MD

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.

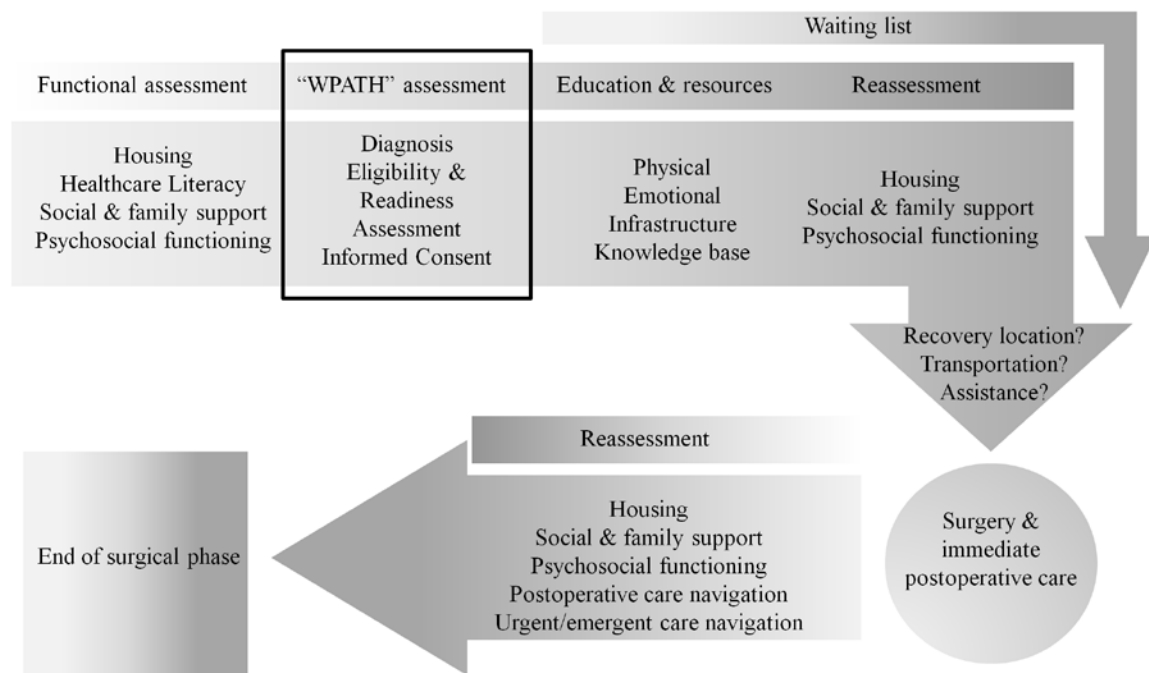
The preoperative assessment process has historically been focused on making a diagnosis of gender dysphoria, determining capacity to provide informed consent, and assessing for certain specific criteria (i.e. length of time taking hormone therapy). However, recovery from gender-affirming surgeries can 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

Primary authors: Eric D. Wang, MD; Esther A. Kim, MD

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 paresthesias 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 mammoplasty

Primary authors: Eric D. Wang, MD; Esther A. Kim, MD

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 of adequate 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 (4th or 5th 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 asymptomatic 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

Primary author: Toby Meltzer, MD

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 comparison, 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 electrolysis 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 be 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 clitoral and other genital tissues.

Complications associated with metoidioplasty are very similar to free flap phalloplasty, 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

Primary author: Juno Obedin-Maliver, MD, MPH

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

Primary author: Madeline B. Deutsch, MD, MPH

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

Primary authors: Cecily Reeves, PhD, FNP-C/PA-C; Madeline B. Deutsch, MD, MPH; Jeannine Wilson Stark, LE, CPE

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 phalloplasty.[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 erythematosus [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 isotretinoin, 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

Primary authors: Sarah Schneider, MS, SLP-CC; Mark Courey, MD

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 cricothyroid 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 not 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 glottoplasty, 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

Primary authors: Andre A. Wilson, MS; Jamison Green, PhD

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
	<p>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.</p>
<p>Employer Plans, Self-Insured (non-ERISA)</p>	<p>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.</p>
<p>Health Maintenance Organizations (HMO)</p>	<p>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.</p>
<p>Medicaid</p>	<p>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.</p>
<p>Medicare</p>	<p>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.</p>
<p>Railroad Medicare</p>	<p>Under this program, people who worked for railroads for at least 10</p>

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 Services (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

Primary author: Dan Karasic, MD

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

Primary author: Barry Zevin, MD

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

Primary authors: Johanna Olson-Kennedy, MD; Stephen M. Rosenthal, MD; Jennifer Hastings, MD; Linda Wesp, MSN, NP-C

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 μ g [achieved by cutting a 25- μ g patch] with gradual increase to full adult dose of 400 μ g);
- 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 17 β -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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