Clinical Care of the Transgender Patient

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

Sandra Mesics, CNM, MSN, RN, is a native of Bethlehem, Pennsylvania. She attended Penn State University where she graduated with a BS in Psychology. In 1983, she moved to Miami, Florida, where she earned a BS degree in Nursing at Barry University, graduating magna cum laude. Ms. Mesics worked as an RN in Labor & Delivery, postpartum, and newborn nursery at Mount Sinai Medical Center, Miami Beach, FL, and started work on her Master's degree in 1994. She became a certified nurse-midwife in 1997, and was the first nurse-midwife granted privileges at Mount Sinai Hospital of Greater Miami. In 2001, Ms. Mesics returned to Bethlehem, PA, to accept a faculty position teaching maternity nursing at St. Luke's School of Nursing. She also maintains privileges at St. Luke's Hospital, providing nurse-midwifery care in the women's health clinic. In 2004, Ms. Mesics became director of the School of Nursing. She is a member of Sigma Theta Tau Nursing Honor Society, the American College of Nurse-Midwives, and the National League for Nursing. She served on the advisory committee for fetal fibronectin.

Faculty Disclosure

Contributing faculty, Sandra Mesics, CNM, MSN, RN, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for all members of the interdisciplinary healthcare team, including physicians, physician assistants, and nurses, involved in the care of transgender patients.

Accreditations & Approvals

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INTERPROFESSIONAL CONTINUING EDUCATION

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NetCE designates this continuing education activity for 10 ANCC contact hours.

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Disclosure Statement

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Course Objective

The purpose of this course is to provide members of the interdisciplinary healthcare team with the knowledge and resources necessary to improve the care provided to transgender patients, a population historically underserved.

Learning Objectives

Upon completion of this course, you should be able to:

1. Define terms used to describe the spectrum of gender expression.
2. Review the historical perspective of the treatment of gender dysphoria.
3. Assess current theories and quality of evidence that pertains to the etiology of gender dysphoria.
4. Discuss efforts to determine the prevalence of transgender individuals in the population.
5. Describe the unique healthcare needs of the transgender population.
6. Summarize the unique barriers to care in this population.
7. Facilitate the management of psychologic issues experienced by transgender individuals.
8. Discuss the potential benefits, limitations, and risks of hormonal and nonsurgical procedures and associated care involved in the treatment of transgender individuals.
9. Describe the care transgender patients require in undergoing various surgical procedures.
10. Develop a strategy of collaborative practice that addresses lifelong healthcare needs unique to transgender patients.
11. Discuss the unique needs of transgender children and adolescents.
12. Summarize the state of the education of healthcare professionals in the care of transgender patients.

E B
EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

It is likely that most healthcare providers will encounter transgender individuals in the course of their professional careers, and all healthcare agencies and providers should be prepared to provide competent and compassionate care for gender-variant individuals. A professional level of knowledge combined with sensitive and empathetic care can help reduce needless stress for these patients. By becoming familiar with current research and striving to understand transgendered patients, healthcare providers can become effective advocates for individuals for whom accessing health care creates considerable anxiety.

One of the objectives of Healthy People 2030 is to "improve the health, safety, and well-being of lesbian, gay, bisexual, and transgender people" [1]. Public Health Infrastructure objective LGBT-01 aims to "increase the number of national surveys that collect data on lesbian, gay, and bisexual populations" [1].

DEFINITIONS

There are a variety of terms used in the transgender community that may not be widely recognized by healthcare providers. In some cases, the words used may be inadvertently offensive or exclusionary, and it is incumbent on all healthcare professionals to have a basic knowledge of the terminology involved in the care of transgender patients. The following definitions are meant to provide an introduction to the preferred terms and possible missteps that may occur when discussing gender and/or sex with patients.

Asexual: An individual who does not experience sexual attraction. There is considerable diversity in individuals' desire (or lack thereof) for romantic or other relationships.

Bottom surgery: Popular terminology for genital surgery, particularly among female-to-male transpersons. Also called "lower surgery."

Cisgender: People whose gender identity and gender expression align with their biological sex. This is a newer term used within the transgender community to refer to those who are not transgender.

Coming out: The process of accepting and telling others about one's heretofore hidden gender identity or sexual orientation.

Crossdresser: A person who wears the clothing, jewelry, and/or makeup not traditionally associated with their anatomical sex. Crossdressers have no desire to change their anatomical sex. This is a preferred term to "transvestite," which is considered pejorative in the transgender community.

Female-to-male (FTM): A person assigned as female at birth but who identifies and lives as or hopes to live as a man. Synonymous with "transgender man" or "transman."

Gender: Social categories that are differentiated by psychosocial characteristics and role expectations. In our society, gender is initially assigned based on biological sex.

Gender dysphoria: The distress and suffering experienced when gender identity and biologic sex are not completely congruent. This term is used in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) and is considered less stigmatizing than "gender identity disorder."

Gender expression: The external manifestation of a person's gender identity, which may or may not conform to the socially defined behaviors and external characteristics that are commonly referred to as either masculine or feminine. This is generally expressed through carriage, dress, grooming, hairstyles, jewelry, mannerisms, physical characteristics, social interactions, and speech patterns.

Gender fluid: A wider and ever-changing form of gender expression in which the experienced or expressed gender varies from day to day.

Gender identity: An individual's internal sense of gender, or sense of being a man, woman, both, or neither. Gender identity may not be binary, and some now consider it to be a spectrum. A person's gender identity may or may not match their biological sex.

Gender identity disorder (GID): A DSM-IV-TR diagnosis given when strong and persistent cross-gender identification, combined with a persistent discomfort with one's sex or sense of inappropriateness in the gender role of that sex, causes clinically significant distress. This term has been replaced in the DSM-5 with "gender dysphoria."

Gender non-conforming ("genderqueer"): Individuals whose gender expression is different from society expectations and/or stereotypes related to gender.

Intersex: Anomalies of the sex chromosomes, gonads, reproductive ducts, and/or genitalia. Generally, this includes individuals born with both male and female genitalia or genitalia that are not clearly male or female. This condition is sometimes not identified until puberty.

LGBTQIA: An acronym used to refer to the lesbian, gay, bisexual, transgender/transsexual, queer/questioning, intersex/intergender, asexual/ally community. In some cases, the acronym may be shortened for ease of use or lengthened for inclusivity. Members of this group may also be referred to as gender and sexual minorities and allies (GSMA).

Male-to-female (MTF): A person assigned as male at birth but who identifies and lives as or hopes to live as a woman. Synonymous with "transgender woman" or "transwoman."

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

Sexual orientation: A person's relative responsiveness to sexual stimuli, particularly the sex of the person to whom one is attracted sexually.

Stealth: When a transgender person who has transitioned into a different sex or gender does not divulge the fact of transition.

Transgender: Generally, an umbrella term for those whose gender identity or expression is different than that typically associated with their assigned sex at birth, including transsexual individuals, androgynous people, crossdressers, genderqueers, and other gender non-conforming people who identify as transgender. Some, but not all, of these individuals desire to transition; some, but not all, desire medical changes to their bodies as part of this process. Sometimes abbreviated as trans or trans*.

Transgender man (transman): A transgender individual who, assigned female at birth, currently identifies as a man. In this course, the terms transgender man, female-to-male transgender person, and FTM are used interchangeably. It is important to note that these patients are men and do not require additional description unless medically necessary.

Transgender woman (transwoman): A transgender individual who, assigned male at birth, currently identifies as a woman. In this course, the terms transgender woman, male-to-female transgender person, and MTF are used interchangeably. It is important to note that these patients are women and do not require additional description unless medically necessary.

Transition: The period of time during which transgender persons change their physical, social, and legal characteristics to the gender opposite that of their biologic sex. Transition may also be regarded as an ongoing process of physical change and psychologic adaptation. This may involve changing one's identity on legal documents and coming out to family, friends, coworkers, and others.

Transphobia: Dislike of or discomfort with people whose gender identity and/or gender expression do not conform to traditional or stereotypic gender roles.

Transsexual person: Individual whose gender identity is different from their assigned sex at birth and who live in a gender different from their birth sex, or desire to do so. Often, but not always, transsexual people alter or wish to alter their bodies through hormones or surgery in order to align themselves physically with their gender identity. This term first appeared in the DSM-III in 1980 [2].

Transvestite: One who dresses in the clothing of the opposite sex. This is the older clinical name for crossdresser and is considered pejorative and outdated; the preferred term is crossdresser. This term was first included in the DSM-II [2].

HISTORICAL PERSPECTIVE

While gender variance has been recorded since ancient history, the first scientist to examine gender nonconformity was an Austro-German psychiatrist, Richard von Krafft-Ebing, in the late 1800s [3]. His principle work was *Psychopathia Sexualis*, published in 1886. In the early twentieth century, Magnus Hirschfeld, a German physician and sexologist, started to explore medical transitions for transgender individuals. He had worked with Lili Elbe, widely regarded as the first person to undergo gender-affirming surgery in 1931 [3]. Unfortunately, most of Hirschfeld's research was destroyed by the Nazis in 1933.

The clinical support of medically transitioning people began in the United States with Harry Benjamin, who used the term "transsexual" to describe people who physically change their body to be congruent with their gender identity [4]. In 1948, he prescribed estrogens in order to bring about physical changes in his first patient, a woman whom he ultimately helped to travel to Germany for gender-confirmation surgery (GCS). He wrote about the provision of care for transsexual individuals in his book *The Transsexual Phenomenon*, documenting some of what he learned in his long practice treating transsexual men and women in New York City [4; 5].

In the 1950s, some GCS was done discretely in the United States, but there were legal objections to castrating otherwise "healthy" men, under the "mayhem" laws. Dr. Elmer Belt, a California urologist, is widely recognized as the first American surgeon to do GCS on a regular basis, and he circumvented the law by moving the testicles into the abdomen rather than removing them [3]. In 1952, Christine Jorgenson made headlines when she became the first American to publicly acknowledge traveling to Denmark for GCS. The news of her conversion brought about a flood of transgender individuals seeking care. While GCS had been performed as early as the 1930s, Dr. Georges Burou (1910–1987) is considered the pioneer of modern techniques. Burou first performed his one-stage GCS technique in 1956 in Casablanca, and by 1973, he had performed more than 3,000 MTF operations. While some FTM surgeries had been performed in Germany in the 1930s and 1940s, the details are lost, and Michael Dillon, an Englishman, is considered to be the first modern FTM individual to undergo surgery. He transitioned in England in the early 1940s and underwent surgery by the pioneering English plastic surgeon, Sir Harold Gillies [3].

In the United States during the 1960s and 1970s, gender identity centers were established at academic medical centers, notably Johns Hopkins, Stanford University, and the University of Minnesota. Although many in the public considered this controversial, the involvement of these prestigious medical institutions helped to "legitimize" the care and diagnosis of transgender individuals. This care was largely covered by health insurance policies and incorporated psychologic counseling, endocrine care, and GCS. Despite good outcomes, in 1975 Paul McHugh, chairman of the Department of Psychiatry at Johns Hopkins, advocated against providing care to transgender patients. He asked Johns Hopkins psychiatrist Jon Meyer for follow-up data on patients who received GCS in order to determine how much the surgery had helped them.

Meyer found that most of the patients were content with what they had done and only a few regretted it. Despite this, McHugh stated, "But in every other respect, they were little changed in their psychologic condition. They had much the same problems with relationships, work, and emotions as before. With these facts in hand I concluded that Hopkins was fundamentally cooperating with a mental illness. We psychiatrists, I thought, would do better to concentrate on trying to fix their minds and not their genitalia" [6]. Shortly thereafter, Johns Hopkins closed their clinic. Other clinic closings followed, with the exception of the University of Minnesota [5]. In the 1970s, the psychologic literature on transgender issues was limited and generally pathologized transsexual persons [7].

While academic center-based gender identity clinics were closing, private physicians began providing these services. Dr. Stanley Biber in Trinidad, Colorado, performed his first GCS surgery in 1969. By the time of his retirement in 2003, he had performed more than 5,000 procedures and had made Trinidad the "sex change capital of the world" [8]. During this time, physicians providing GCS could be found in most major cities in the United States. The Erickson Educational Foundation served as a clearinghouse of information and referrals for those seeking treatment.

In 1979, the first standards of care for transgender patients were published by the Harry Benjamin International Gender Dysphoria Association, now known as the World Professional Association of Transgender Health (WPATH). Its aim was to exclude other pathologic states in the differential diagnosis and to confirm the diagnosis. In 1980, transsexualism was included in the third edition of the DSM (DSM-III). While this diagnosis is now under contention in the transgender community because of the stigma of mental disorder, at the time it legitimized the diagnosis [5].

According to the World Health Organization's International Classification of Diseases (ICD-11), the relevant diagnoses fall under Chapter 17, Conditions Related to Sexual Health. Gender Incongruence includes the subcategories of gender incongruence in adolescence/adulthood or childhood. This represents a significant departure from the ICD-10, which categorized "gender identity disorders" under the general category of Mental and Behavioral Disorders [9].

The DSM-IV abandoned the term "transsexualism" and instead used the term "gender identity disorder" [10]. The DSM-5 now uses the term "gender dysphoria." This is defined as "the distress that may accompany the incongruence between one's experienced or expressed gender and one's assigned gender" [11]. The critical element of this diagnosis is the presence of clinically significant distress associated with the condition, as the American Psychiatric Association (APA) points out that gender nonconformity is not a mental disorder. The intent of this change was to better characterize the experiences of affected children, adolescents, and adults and to avoid stigma and ensure clinical care for individuals who see and feel themselves to be a different gender than their assigned gender [11].

Beginning in the mid-1980s, a paradigm shift occurred in looking at gender identity as nonbinary. The term "transgender" began being used in the LGBT community as an umbrella term that encompassed crossdressers, transsexual persons, and those individuals who live in the opposite gender role without GCS. Gradually, more and more transgender individuals began to define their gender identity "outside of the boundaries of male versus female, man versus woman, and masculine versus feminine" [12]. According to Fraser, a cultural shift is occurring regarding transgender people, from a pathologic view to an acknowledgement of gender diversity and fluidity [7].

In the 1990s and 2000s, many transgender individuals became experts in medicine, health care, law, and social change. The human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) epidemic generated public health research that revealed the impact of the disease on the transgender community. There has been growth in the online transgender community, which can offer relief from the loneliness and isolation many transgender people face [7].

Because GCS can cost in the range of $30,000 in the United States and is not generally covered by health insurance, many transgender individuals have gone abroad for surgery. Thailand has now replaced Trinidad, Colorado, as the "sex change capital of the world," and the same procedure offered by experienced surgeons in Thailand will cost in the range of $7,000 [13]. The affordable cost paired with Thailand's prominent transgender community led many transgender individuals to consider medical tourism. This trend may be reversed as a result of the Affordable Care Act (ACA) and its regulations, which remove discrimination against transgender status as a pre-existing condition [14].

The critical point for transgender individuals is that there is incongruence between their gender identity and their birth sex. The intensity of this incongruence can vary, and transgender individuals may choose varying degrees of transition. Transgender individuals often attempt to conform to the social gender expectations of their birth sex. For instance, some MTF individuals marry, raise families, and generally lead lives of conformity to the expectations of the male role. FTM persons may conceal their gender identity by leading their lives as lesbians, making gender variance among FTMs "relatively invisible" in society [15].

Transgender individuals experience significant challenges whether or not they choose to disclose their transgender identity. Individuals who "come out" as transgender risk becoming victims of violence, losing relationships, or losing employment. Other challenges include anxiety and depression related to transition issues. These individuals must make decisions regarding how to transition in the workplace and how to assimilate socially appropriate behavior in the new gender. Once disclosure occurs, transgender individuals may face feelings of guilt associated with the disruption of current personal relationships and other relational challenges. Despite these potential negative consequences, the potential positive effects of living authentically in their chosen gender motivate many transgender persons to disclose and begin transition. On the other hand, given these same possibilities, some transgender persons remain closeted and at risk for psychosocial consequences, including depression, anger, anxiety, and suicidal ideation. In fact, caring for patients who present with conditions such as sexual disorders, depression, anxiety, substance abuse, and personality disorders on occasion uncovers transgenderism [16].

ETIOLOGY OF GENDER DYSPHORIA

At present, scientific investigation has neither established the true incidence nor clarified the etiology of non-conforming gender identity formation [17]. Genetic, physiologic, and psychologic causes have been investigated, and available evidence seems to support physiologic causes. Gender dysphoria cannot be explained by variations in chromosomal patterns or identifiable hormonal abnormalities, nor is there convincing evidence that psychologic factors (e.g., being exposed to certain family dynamics or being raised as a member of the opposite sex) cause this condition [18].

Research has focused on the brain and how exposure to sex hormones in utero may influence the development of gender dysphoria. In the human brain, there are known sex differences in the central region of the bed nucleus of the stria terminalis. This structure is androgen-dependent and is larger in males than in females. However, the size of the structure in MTF individuals has been found to be within the range of that observed in biological females [19]. This variance is not attributable to chronic estrogen use, as non-transgender men who have received long-term estrogen therapy to control prostate cancer do not show this change [20]. Unfortunately, analysis of the stria terminalis has only been done on postmortem examination, as the structure is too small to visualize with presently available imaging techniques [21].

In a postmortem study of the brains of six MTF individuals, matched with 36 controls from non-MTF individuals, the brains of cisgender men had significantly more somatostatin neurons in the bed nucleus of the stria terminalis than the brains of cisgender women, and the number of these neurons in the brains of MTF participants was statistically similar to that of cisgender women [22]. The sample also included one brain of an FTM individual, for whom the number of somatostatin neurons was in the male range. The researchers hypothesize that this is the result of androgen exposure in early brain development in utero. Presumably, a lack of exposure to androgens in a male fetus at this critical time of development would cause MTF transsexualism, and conversely, exposure to androgens in a female fetus would result in FTM status.

Nawata et al. used computerized tomography to examine cerebral blood flow in 11 FTM individuals and nine non-transsexual female control subjects [23]. They found that in FTM individuals, there was a significant decrease in regional cerebral blood flow in the left anterior cingulate cortex and a significant increase in regional cerebral blood flow in the right insula compared with the control group. The authors hypothesize that regional cerebral blood flow changes in the anterior cingulated cortex and the insula affect neuron networks active in human sexual behavior and consciousness and may contribute to a biological basis of gender dysphoria.

In utero, the formation of both digits and genitals are controlled by the same genes: homeobox or HOX genes. Because testosterone (or the lack thereof) influences the development of genitalia, it has been proposed that this might also hold true for the fingers. In humans, the second digit to fourth digit (2D:4D) ratio differs between the sexes; in girls and women, the two fingers are approximately the same length, but in boys and men, the fourth digit is usually longer than the second [24]. Some have hypothesized that differences in prenatal testosterone levels may cause gender dysphoria, which could be reflected in a difference in finger length ratios. Specifically, lower prenatal testosterone levels would result in MTF individuals, reflected in a female-type 2D:4D ratio. Conversely, higher prenatal testosterone levels would result in FTM individuals, reflected by a male-type 2D:4D ratio. A study by Wallien et al. showed that among FTM individuals, the 2D:4D ratio was similar to males, adding support to the assumption that in utero testosterone exposure in female fetuses may lead to gender dysphoria in females [24].

However, Kraemer et al. found contradictory results for FTM individuals, whose ratios were significantly more feminized than the female controls [25]. These researchers also found that MTF individuals had ratios that were significantly different from the male control subjects. These findings may indicate that lowered prenatal testosterone levels play a role in gender dysphoria in both sexes. Similar findings by Schneider et al. for MTF individuals support this hypothesis, but these researchers did not find a difference between FTM individuals and female controls [26]. This research indicates a possible biological basis for gender dysphoria, particularly to the role of antenatal androgen exposure, but the exact mechanism is still not understood. A meta-analysis of 2D:4D associations involving 690 individuals found that finger length associations with transgender identity are limited and fluctuate based on sampling variables [27]. Evidence is insufficient to decide whether ratios are sexually asymmetric.

Another theory of etiology proposes that in some mothers, maternal immunization against the Y-linked minor histocompatibility antigens (H-Y antigens) occurs and increases with each successive male fetus, affecting sexual orientation and gender identity. However, sibling studies have not supported this hypothesis [17].

In summary, the etiology of gender dysphoria is poorly understood. Research has focused on intrauterine hormone exposure, childhood psychologic factors, anatomic differences in brain structure and activation, and subtle genetic variations. It is likely that the origin is multifactorial [28; 29].

PREVALENCE OF TRANSGENDERISM

Because of variability in terminology and definitions, differing modes of presentation, and reluctance to disclose for fear of social stigmatization, it is difficult to obtain accurate data about the prevalence of transgender individuals in the general public [30]. However, as society becomes more accepting and familiar with transgender individuals, more transgender individuals are willing to "come out." The result is that this condition is more prevalent than previously thought.

In the United States in the 1960s, it was estimated that 1 in 100,000 males and 1 in 400,000 females were transgender. By the 1990s, this estimate had increased to 1 in 20,000 males and 1 in 50,000 females [31]. Based on data from 2008, the prevalence of MTF transsexualism was estimated to be 1 in 12,700–45,000 and FTM transsexualism 1 in 30,400–200,000 [32]. Another study cites the incidence of transsexualism at 1 in 20,000 males and 1 in 50,000 females [31]. Approximately 0.6% of adults in the United States, or 1.4 million individuals, identify as transgender [33]. By age, transgender identity is expressed by 0.7% of adults 18 to 24 years of age, 0.6% of adults 25 to 69 years of age, and 0.5% of adults 65 years of age or older. This is supported by findings of the 2014–2016 Behavioral Risk Factor Surveillance System (BRFSS), which estimated that 1.5 million Americans identify as transgender—770,000 as MTF and 458,000 as FTM [34]. This translates to an incidence in the general population of 0.35% to 0.53%.

In Sweden, there appears to be no difference between the biological sexes, and prevalence rates are estimated to reach 0.14 per 100,000 inhabitants older than 15 years of age [35]. In 1990 in the Czech Republic, the prevalence of transsexualism was estimated to be 1 in 10,000 inhabitants [31].

Perhaps the most accurate estimate of the prevalence of transsexualism comes from New Zealand, where since 1995, passport holders have been able to have the sex omitted on their passport. In these cases, sex is shown as "X" on the passport. These persons must provide a statutory declaration stating that they live as a member of the opposite sex. Analysis of passports yields an estimate of MTF transsexualism at 1 in 3,639 and FTM transsexualism at 1 in 22,714. This frequency matches data from Singapore, which puts the MTF prevalence at 1 in 2,900 and FTM at 1 in 8,300 [32].

All of these published studies indicate a greater incidence of MTF than FTM transsexualism, with a ratio of anywhere between 2.5:1 and 6:1 [32]. A ratio of 3:1 is common throughout the Western world, but not necessarily elsewhere (e.g., Japan, Serbia). Before puberty, there is a preponderance of MTF individuals, but gender dysphoria in children often resolves, and in adolescents the ratio is closer to 1:1 [29]. The subsequent increase in the MTF to FTM ratio is explained by the higher frequency of men with late-onset gender dysphoria [18].

At present, a precise measure of the incidence and prevalence of transgender individuals remains elusive. There seems to be a slightly higher prevalence of MTF than FTM individuals, although the ratio of MTF to FTM appears to be decreasing. Estimates of prevalence have been increasing over time, which likely reflects increased access to care [28; 36].

UNIQUE HEALTHCARE ISSUES

Caring for transgender individuals is complex and requires some preparation and forethought, taking into account knowledge of anatomical reassignments, the effects of therapy, and cultural sensitivity. This requires an interprofessional collaborative practice that includes an accurate diagnosis, then moving on to psychotherapy or counseling, hormone therapy, the "real-life experience" (i.e., the period of time spent living in the chosen gender prior to GCS), cosmetic interventions (e.g., hair removal), in some cases voice therapy, and surgical interventions [17].

The Institute of Medicine (IOM) has noted that there is a paucity of research on the unique healthcare needs of transgender individuals, and most existing research consists of small nonprobability samples [36]. The IOM calls for an evidence base for providing transgender-specific health care to address gender dysphoria and a more rigorous research program to understand the health implications of hormone use and other transgender-specific issues.

If a primary care provider has little knowledge or training on transgender issues, it is best to disclose this to the patient and seek experts as needed. Jenner points out that competence in taking care of transgender people "…seems to include a healthy portion of unconditional acceptance and an understanding empathy from the healthcare community" [37].

There are often comorbidities among the transgender population. Although research is sparse, it appears that HIV infection rates among MTF transgender individuals are over four times the national average, with even higher rates among transgender people of color [38]. Approximately 28% of MTF transgender persons in the United States are HIV positive [38]. Transgender individuals are also at high risk for other sexually transmitted infections, such as syphilis, gonorrhea, chlamydia, herpes, and human papillomavirus (HPV) [1]. In addition, smoking, drug and alcohol use, depression, and suicide attempts are higher in the transgender population than the general population [39].

Transgender individuals are at risk for HIV as a result of engaging in unprotected sex and from sharing needles used for hormone injections [40; 41]. A significant percentage of transgender individuals engage in sex work; 11% of transgender respondents in a large national survey reported engaging in sex work for income, compared with 1% of women in the United States [39]. This survey has been the largest to date of the transgender population, involving 6,450 transgender and gender non-conforming individuals across all 50 states, as well as the District of Columbia, Puerto Rico, Guam, and the U.S. Virgin Islands. The study was conducted on behalf of the National Gay and Lesbian Task Force and the National Center for Transgender Equality.

A staggering 41% of respondents to the survey reported attempting suicide, compared with 1.6% of the general population [39]. The highest rates of suicide attempts in transgender individuals are among those 18 to 44 years of age. Rates are lower among older individuals, with 16% of those older than 65 years of age reporting a suicide attempt, which is inverse to the rates in the general population.

Twenty-six percent of transgender and gender non-conforming individuals have been physically assaulted and 10% have been sexually assaulted [39]. In a study of MTF individuals, 78.1% experienced gender-related psychologic abuse and 50% experienced gender-related physical abuse [42]. The Transgender Day of Remembrance is held in November of each year to memorialize those who were killed due to anti-transgender hatred or prejudice. In total, 2,411 murders have been documented between 1970 and 2019 [43]. The 2019 update revealed a total of 331 murders in 2018–2019, which is slightly less than the 369 reported in 2018 [43]. The National Center for Transgender Equality recommends that ending violence against transgender people should be a public health priority, because

of the direct and indirect negative effect violence has on both victims and on the healthcare system that treats them.

As noted, transgender individuals have a significantly higher rate of substance abuse than the general population, and there is a correlation between having experienced a transphobic event and substance abuse [44]. Tobacco use is higher in the transgender population, with 30% of transgender or gender non-conforming individuals reporting smoking daily or occasionally, compared with 20.6% in the general population [39].

Reasons for substance abuse in this population include all the reasons others abuse drugs, as well as reasons unique to the transgender community: to suppress the experience of gender dysphoria, to allow desired gender expression, to cope with experiences of transphobia (including internalized transphobia, negative self-image, and trauma), and to cope with involvement in the street economy [45]. Moreover, "safe spaces" where transgender individuals can socialize often include bars, clubs, and restaurants, where smoking and drinking are popular. Tobacco and alcohol companies have also exploited gay and transgender social networks, including gay and transgender magazines, events, and organizations, to aggressively market their products [46]. These kinds of targeted marketing campaigns account, in part, for the higher rates of substance use in the LGBT population.

Barriers to obtaining education because of gender identity issues or harassment lead to higher rates of unemployment, which places transgender people in financial difficulty and makes access to housing and medical care difficult [47]. Schools are not safe places for transgender individuals; 61% report experiencing significant abuse in educational settings [39]. In another study, 90% of transgender youth in schools reported feeling unsafe, compared with 46% of gay or bisexual male students and 41% of lesbian and bisexual female students [48].

Transgender individuals may experience or fear reprisal at work related to their gender identity. Employment was noted as one of the top three immediate perceived needs in the Transgender Needs Assessment Survey [49]. Finding employment is challenging for transgender individuals, especially those who are preoperative and do not have proof of identity in the chosen gender. Transgender people have double the national unemployment rate, and 26% report having lost a job because of their transgender status [50]. A large majority (97%) reports having experienced mistreatment, harassment, or discrimination on the job. In an incidental finding of a study of 376 FTM individuals in the United States, although 48% had a Bachelor's degree or higher, the majority earned less than the U.S. national average [50].

Data from the BRFSS indicate that, compared with cisgender respondents, transgender respondents were younger, more racially/ethnically diverse, had lower educational attainment, tended to have lower income levels, and were more likely to be unemployed, never married, and uninsured [34]. FTM individuals were the most socioeconomically disadvantaged and the least likely to have a college degree, be homeowners, an annual income greater than $50,000, or health insurance. Overall, transgender people experienced a higher burden of mental health problems than cisgender people, likely due to minority stress. There is also a higher likelihood of disability among transgender people, particularly FTM individuals, who have a greater risk for multiple chronic conditions [34].

A 2012 Equal Employment Opportunity Commission ruling included transgender employment discrimination as gender discrimination and consequently protected under Title VII of the Civil Rights Act (Pub. L. 88-352). Some employers now have nondiscrimination policies inclusive of transgender persons, and there has been an improvement in nondiscrimination policies among large corporations.

According to the 2021 Human Rights Campaign (HRC) Corporate Equality index, 94% of Fortune 500 companies and 99% of businesses surveyed offer explicit gender identity non-discrimination protections (significant increases compared to 2015 data) [51]. Additionally, a majority of surveyed businesses (92%) offer education and training programs that specifically include definitions and/or scenarios on gender identity in the workplace. Hundreds of major businesses have adopted gender transition guidelines for employees and their teams to establish best practices in transgender inclusion.

However, there has also been a seeming backlash against the transgender community in the United States. In 2016, North Carolina passed a law that invalidated municipal sexual orientation and gender identity nondiscrimination statutes and pre-emptively banned future nondiscrimination legislation [52]. On a national level, in 2017, the CDC was ordered to avoid use of the term "transgender" and six other words (including "diversity" and "evidence-based") in all budget documents [52].

Strides are also being made in transgender-inclusive healthcare benefits, though these have not kept pace with nondiscrimination protections. Ninety-one percent of the businesses surveyed by the HRC offer transgender-inclusive healthcare coverage, up from just 8% in 2009 [51].

As of 2021, Medicaid provides some transition-related care in 22 states plus the District of Columbia, and in May 2014, Medicare overturned its 30-year ban on coverage for GCS. However, implementation of the policy is proceeding piecemeal by region [53; 54].

ACCESS AND BARRIERS TO CARE

Transgender people face barriers to health care whether seeking preventive medicine, routine and emergency care, or transgender-related services. Transgender people may be poor, uninsured, homeless, or lack access to regular medical care, including providers who are trans-friendly [51]. One survey reported that only 30% to 40% of transgender individuals utilize any regular medical care, due to economic limitations, lack of insurance, comorbidities such as substance abuse, and stigmatization [55]. In addition, some providers will not treat transgender patients because of moral objections [37]. In fact, in 2016, Mississippi and Tennessee passed laws allowing health providers to refuse to provide services if doing so would violate their religious beliefs [52]. The Mississippi bill explicitly identifies same-sex couples and LGBT individuals as being potentially incongruent with some providers' beliefs.

One study showed that 20% of transgender individuals in the United States lack health insurance, and insurance coverage is even worse for racial/ethnic minority transgender individuals [39; 56]. Even for those who have insurance, most health insurance plans do not cover the cost of mental health services, cross-sex hormone therapy, or GCS, often because these interventions are deemed cosmetic and non-essential [50]. This barrier exists despite evidence that such treatments are safe and effective and that cross-gender behavior and gender identity issues are not an issue of choice for the individual and cannot be reversed with psychiatric treatment [57].

Before 2014, the Centers for Medicare and Medicaid Services (CMS) did not cover the cost of GCS based on a 1981 evaluation that described the surgery as experimental and cited "the lack of well-controlled, long-term studies of the safety and effectiveness" and "a high rate of serious complications" [58].

However, long-term studies done in Europe have found that GCS is effective, with low complication rates [1]. This policy banning GCS was overturned in May 2014, but because policy guidelines are issued from Medicare contractors by region, widespread implementation has been slow [53]. While the Veterans Administration (VA) has policies in place to provide comprehensive care to transgender veterans, including ongoing hormone therapy, mental health care, and long-term care following GCS, the VA specifically does not cover GCS, on the basis of a VA regulation excluding gender alterations from the medical benefits package [59; 60].

Sufficient time has not yet elapsed for the ACA requirement of coverage for transition-related care to apply to grandfathered policies. The ACA bans coverage denial based on being transgender as a pre-existing condition [61]. Although the ACA prohibits discrimination on the basis of sex, including gender identity, in any hospital or health program that receives federal funds and The Joint Commission requires that discrimination on the basis of gender identity is prohibited to maintain accreditation, this information is not widely known and many transgender patients still experience discrimination. The American Medical Association, the APA, the American Congress of Obstetricians and Gynecologists (ACOG), the American Academy of Family Physicians, and the National Association of Social Workers have called for public and private health insurance coverage for this condition [61; 62].

Although every major U.S. medical association recognizes that gender-affirming healthcare is medically necessary, several state legislatures introduced bills seeking to limit gender-affirming care for adolescents in 2020–2021 [174]. Though only one state (Arkansas) has passed a bill as of August 2021, nine additional states are still considering bills. As a result, healthcare professions may have confusion regarding the legal care and insurance coverage of these patients.

Lack of health insurance, when combined with provider ignorance about the healthcare needs of transgender people, deters some transgender individuals from seeking and receiving high-quality health care and makes them more likely to obtain hormones illicitly and participate in risky behaviors such as needle sharing and smoking [39; 56]. Many transgender individuals have been victims of hostility or discrimination at the hands of healthcare providers [63]. In a large survey of transgender individuals, 19% reported being refused medical care due to their transgender or gender non-conforming status, with even higher numbers among people of color [39]. Even more alarming is the fact that 28% of respondents in this same study reported verbal harassment in medical settings and 2% were physically attacked in medical offices [39]. In 1995, Tyra Hunter, a young, African American, preoperative transgender woman, was injured as a passenger in a car accident. Emergency medical technicians at the scene of the accident uttered derogatory epithets and withdrew medical care after discovering she had male genitalia. After transfer to the emergency department, Hunter received dilatory and inadequate care, resulting in her death. A jury subsequently awarded Hunter's mother $1.75 million in a wrongful death suit [64].

Many transgender individuals fear contact with health professionals. When sick or injured, transgender individuals may postpone medical care due to discrimination or inability to afford it [39]. The difficulty in finding knowledgeable, sympathetic providers has resulted in higher costs, a market for illicit hormone suppliers, and networking systems to identify willing and unwilling providers [37].

The National Center for Transgender Equality recommends that transgender-sensitive care be integrated into the medical profession's standards of care, as part of a commitment to cultural competency. Providers who harass, assault, or discriminate against transgender and gender non-conforming patients should be disciplined.

Transgender individuals in some European countries such as Holland, Sweden, and Belgium are recruited into specialized clinics, given state-funded, evidence-based care, and are followed over time by a consistent team of healthcare professionals. By contrast, most transgender individuals in the United States receive health care in a fragmented, unsystematic fashion and are fortunate if they receive sensitive, non-discriminatory primary care [50]. Because of this fragmented healthcare system, it is difficult to obtain well-controlled studies of transgender care in the United States. Federal agencies, such as the VA, will provide ongoing therapy but will not initiate gender reassignment [37].

Improving access to care can be facilitated, in part, by providing a welcoming environment for transgender patients. The ACOG recommends the adoption and posting of a nondiscrimination policy that signals to both healthcare providers and patients that all persons will be treated with dignity and respect [57]. Also, adding a "transgender" option to checklists on patient visit records can help to better capture information about transgender patients and be a sign of acceptance to that person. Simply asking transgender patients what name and gender they prefer works well [65]. Experts also recommend referring to body parts with gender-neutral language whenever possible, such as "chest" and "genitals," as well as phrases like "persons with vaginas" [65]. Providers should admit their lack of experience with transgender patients and seek guidance from patients regarding their expectations of the visit.

Front office staff can avoid using gender-based pronouns, both on the phone and in person. Instead of asking, "How may I help you, sir?" the staff person could simply ask, "How may I help you?" Avoiding gender-based pronouns when talking to other office staff is also advised. It is acceptable to politely ask a person what name he or she prefers to use. For example, a staff member may say "I would like to be respectful—how would you like to be addressed?" or "What name would you like me/us to use?" After a patient has given a preferred name, it is very important for staff to use this name in all interactions. Not using the patient's preferred name can cause embarrassment and confusion.

In office settings that require insurance or the use of third-party payers, transgender patients may have a name and gender on record that do not match their preferred name and gender. In situations in which a patient's name or gender does not match the insurance or medical records, the staff person could politely ask, "Could your chart be under a different name?" or "What is the name on your insurance?" Offices that utilize electronic health records should have a system to track and record the preferred gender, name, and pronoun of all patients. This can be accomplished by standardizing the notes field to document a preferred name and pronoun for all patients [66]. Some persons who identify as non-binary (i.e., neither or both genders) may prefer that plural pronouns (e.g., they) be used.

Questions should be framed in ways that do not make assumptions about gender identity, sexual orientation, or behavior. Language should be inclusive, allowing the patient to decide when and what to disclose. Assurance of confidentiality should be stressed to the patient to allow for a more open discussion, and confidentiality should be ensured if a patient is being referred to a different healthcare provider. Asking open-ended questions can be helpful during a history and physical. Asking "How can I be a part of affirming your gender identity?" may be a better question than "How can I assist you in your transition?"

The FACT acronym may be helpful for healthcare providers. Providers should:

- **F**ocus on those health issues for which the transgender individual seeks care
- **A**void intrusive behavior
- **C**onsider transgender people as individuals
- **T**reat individuals according to their preferred gender

Training office staff to increase their knowledge and sensitivity toward transgender persons will also help facilitate a positive experience for patients. Additional guidelines for creating a welcoming office environment for transgender patients have been developed by the Gay and Lesbian Medical Association and can be found online at http://www.glma.org.

Nurses are in a unique position to provide care for transgender patients because the nursing model is holistic and patient-centered. However, the nursing profession requires more awareness of issues facing LGBT individuals, and nursing organizations have lagged behind other professional organizations representing physicians, psychologists, and social workers in promoting the care of LGBT individuals [67]. While it is necessary to educate nursing students on the unique healthcare needs of the LGBT community, there are no standards in place to assure these topics are taught in nursing school curricula. In 2010, the National Student Nurses Association adopted a resolution to include LGBT content in nursing school curricula to improve cultural competence. The Association adopted additional LGBT-affirming resolutions in 2015, 2016, and 2019; in 2021, it adopted a resolution in support of gender-affirming healthcare practices [68]. Recognizing the importance of addressing LGBT health needs as a matter of justice and equity, this group also adopted a 2012 resolution in support of The Joint Commission's LGBT field guide [69].

Electronic health records are typically not transgender friendly [47]. Products that pre-populate an individual encounter with a sex-specific history, exam, or ordering template will prevent the provider from accurately documenting care [70]. In response to the limitations of currently available electronic health records, the WPATH convened an Electronic Medical Records Working Group to make suggested guidelines for electronic health records developers. This group recommended that the patient's preferred name, gender identity, and pronoun preference be included as demographic variables and that the system effectively notify providers and staff of the preferred name and pronoun. Electronic health records should also provide a way to maintain an inventory of a patient's transition history and current anatomy and to effectively be able to change over time without negatively affecting the rest of the patient history [70].

In addition to concerns about how a patient's demographic information is listed, such as official versus preferred name, gender, and pronouns, providers need a way to accurately chart which organs a patient may or may not have. The electronic health records should not be limited or defined by the patient's assigned sex. The WPATH gives the following example [70]:

> A patient may have been assigned female at birth and have transitioned to male through the use of testosterone and surgical removal of the breasts; they may also have obtained a court-ordered name and sex or gender change and are registered in the electronic health records system under a male name and gender. However, because this patient still has a cervix, ovaries, and uterus, healthcare providers will require the ability to enter pelvic exam findings and gynecologic review of systems and to order a cervical Pap smear within the electronic health records system.

STANDARDS OF CARE

The WPATH is composed of diverse professionals with the mission to promote evidence-based care, education, research advocacy, public policy, and respect in transgender health. Since 1979, the group has published *Standards of Care for the Health of Transsexual, Transgender, and Gender Non-Conforming People*, with seven editions published as of 2021 [71].

The WPATH Standards of Care provide clinical guidelines for the provision of mental health care, hormone therapy, reproductive health, voice and communication therapy, surgery, postoperative care, and lifelong preventive and primary care [71]. The Standards of Care are intended to be flexible to meet individuals' needs, but some critics consider them to be overly restrictive and inflexible [57].

An alternative to the WPATH Standards of Care is the informed consent model. Under this model, after a discussion between the patient and the provider in which the risks, benefits, and alternatives to treatment are discussed, treatment can be provided. The provider determines whether the patient understands the risks and benefits and is competent to consent to treatment. With this model, a letter from a mental health professional is not required for treatment; psychotherapy is an option, not a requirement, for accessing health care. This removes a layer of gatekeeping that may be a barrier to care.

While an increasing number of providers and clinics use the informed consent model for hormone therapy, American surgeons provide GCS based on the WPATH guideline. Insurance providers also generally require adherence to the WPATH Standards of Care in order to consider GCS to be medically necessary.

PSYCHOLOGIC MANAGEMENT

The WPATH Standards of Care recommend that the diagnosis of gender dysphoria be made by a mental health professional with a minimum of a Master's degree, with knowledge about gender variation, competence in using the DSM, and the ability to diagnose co-existing mental health concerns [71]. In the case of children and adolescents, the professional should have training in child and adolescent development and psychopathology. The WPATH guideline does not require a referral from a qualified mental health professional before initiating hormone therapy but strongly encourages this practice. Because of this, it is estimated that 84% of transgender individuals have received counseling related to their gender identity [39]. Generally, counseling results in a diagnosis of gender dysphoria.

While obtaining a referral for hormone therapy is the main reason that transgender individuals seek psychologic therapy, other reasons include understanding the meaning of their feelings; whether to externally express those feelings; coming out to self, work, and family; seeking to network following a negative experience; or following up on information obtained on the Internet. In some cases, an individual may have been "caught" expressing his or her gender variance by a spouse or significant other or when there has been a program on transgender issues in the popular media [72]. Coming out trans is a time of heightened vulnerability [73]. Not everyone transitions. Some learn to live comfortably in their role consistent with their assigned birth sex, and others may transition partially or totally [7].

The first counseling visit with a transgender person is of great importance [72]. It is imperative that the counselor obtain as much information as possible during the initial intake, including a sex history, screening for sexual trauma, suicidal ideation, and history of self-harm. It is important to determine when the patient last saw a medical provider, whether he or she is taking hormones, and if so, who is prescribing them. It is also vital to assess the support system and screen for other mental health issues.

Additionally, the mental health professional should screen for conditions that have similar features to gender dysphoria, such as body dysmorphic disorder [17]. It is estimated that as many as 50% of MTF individuals have a history of what were previously described as other "Axis I disorders," and a significant percentage of MTFs also report a history of substance abuse, body image disturbances, and eating disorders [42].

Common diagnostic presentations in transgender individuals include anxiety, depression, conduct disorder, oppositional defiant disorder, autism spectrum disorder, substance use disorder, and dissociative disorder [72]. The incidence of autism spectrum disorder has been found to be 10 times higher in the population of gender dysphoric individuals than in the general population [74]. In a major study of MTF individuals, more than 50% had suffered from major depression at some point in their life, as opposed to 19.6% in the general population [42]. In a review of the literature on depression in transgender individuals, Rotondi concludes that this is a multifaceted condition, with the common causative factors being: discrimination, disclosure, identity support, hormones and GCS, sociodemographics, socioeconomic factors, substance use, and access to health and social services [75]. Transgender individuals commonly report victimization and post-traumatic stress disorder, systemic stressors, and depression [76]. Interestingly, when a gender identity is truly and authentically affirmed, some of these conditions resolve [72].

The National Institute for Health and Clinical Excellence recommends that local care pathways should be created that promote access to services for all transgender adults with autism.

(https://www.nice.org.uk/guidance/CG142. Last accessed July 13, 2021.)

Level of Evidence: Expert Opinion/Consensus Statement

In a Japanese study of 579 MTF and FTM patients of a national gender clinic, the majority of subjects had no psychiatric comorbidity [77]. Of those who did, the majority were MTF individuals. However, even among the subjects without current psychiatric comorbidity, 71.8% had thought seriously about suicide and 30.6% had performed self-mutilation [77]. In transgender individuals, self-harm may include cutting or injuring the breasts or the genitals [44; 72].

There is some evidence that transgender individuals may have a higher incidence of personality disorders. In one study, 52% of a sample of 50 transgender patients had a personality disorder, regardless of MTF or FTM status [78]. The most prevalent diagnosis was narcissistic personality disorder. In contrast, the incidence of personality disorder in the general population is 15%.

Research on the incidence of suicide in transgender people is scarce, but transgender people are believed to have similar suicide risks as other people who experience major life changes, relationship difficulties, chronic medical conditions, or discrimination on the basis of minority status. The incidence of suicide ideation is as high as 64% and suicide attempts as high as 38% in the adult transgender population [76]. These rates are significantly higher than in the general population [76]. Predictors of suicide among transgender individuals are similar to those of the general population, most notably previous suicide attempts or near attempts, past psychiatric hospitalizations, and past psychiatric treatment. Parental rejection is one of the highest risk factors for suicide among transgender youth [73].

According to the U.S. Preventive Services Task Force, prejudice or discrimination associated with being lesbian, gay, bisexual, or transgender should be considered a risk factor for suicide.

(https://www.acpjournals.org/doi/10.7326/M14-0589. Last accessed July 13, 2021.)

Level of Evidence: Expert Opinion/Consensus Statement

It has been suggested that MTF individuals may be at increased risk for eating disorders due to estrangement from body, biological gender, and expected social role. However, in a study of 40 MTF individuals in the United Kingdom, researchers found no support for this hypothesis [79]. They administered the Eating Disorder Inventory to patients preoperatively and six months postoperatively. While

the MTF group showed higher levels of body dissatisfaction preoperatively than biologic women, this level was significantly lower postoperatively. On the "drive for thinness" subscale, the MTF group scored similarly to biological males and lower than biological females. This did not change postoperatively. Also, scores on bulimia subscales were lower in the MTF group than in gender-conforming men or women [79].

Fraser has worked in counseling using a nonpathologizing, trans-affirming model of transgender identity for 37 years and observes that many transgender people, aside from a mismatch between body and mind, seem quite healthy given the challenges of their condition [7]. Issues that arise in working with transgender individuals are the same as for the general population: issues of self, self in relation, autonomy and connection, identity, and intimacy.

There is little research on the effect of disclosure of transsexualism on relationships. Female partners of FTM persons report experiencing confusion regarding their own sexuality, relationship, patterns of interaction, and future following disclosure. Female partners of MTF individuals often respond to their partners' disclosure with profound shock and confusion, specifically their sexual identity and relationship uncertainty, MTF decision making, and public presentation. Concerns may arise regarding marginalization, finding acceptance as a couple, and being viewed as lesbian. Examples of activities that are supportive include open communication, maintaining a positive mood, social networking, social activism, impression management, and positive self-talk [15].

There is also a paucity of research on children of transgender parents. There is some evidence that the younger a child is when he or she is informed that a parent is transitioning, the better the outcome and the better the parent-child relationship. A healthy parent-child relationship at the time of transition tends to result in a healthier long-term relationship [80].

HORMONAL AND NONSURGICAL MANAGEMENT

The goal of hormone therapy is to reduce the unwanted secondary sex characteristics of the original gender and to induce the development of secondary sex characteristics of the desired gender. Hormone therapy has also been found to enhance the person's sense of self and well-being [81]. Criteria for hormone therapy include persistent, well-documented gender dysphoria, a capacity to give informed consent, age of majority, and control of any significant medical or mental health issues [71]. In accordance with the WPATH guideline, it is recommended, though not required, that the decision to initiate hormone therapy be made in consultation with a qualified mental health professional [71].

There are no randomized clinical trials designed to determine the optimal regimen for cross-sex hormone use. The formulations and dosages employed are derived from experience treating hypogonadism [17]. In the case of MTF individuals, hormone therapy might include an anti-androgen, an estrogen, and in some cases, a progesterone component. In FTM individuals, hormone therapy is primarily testosterone. Gonadotropin-releasing hormone (GnRH) agonists can be used for both MTF and FTM individuals to reduce the amount of innate hormones secreted. GnRH agonists initially stimulate and then depress luteinizing hormone (LH) release from the pituitary gland. In the MTF individual, they reduce the serum concentration of testosterone to the castrate range within one week, and in the FTM individual, they stop the ovaries from making estrogen. Examples of GnRH agonists include leuprorelin, triptorelin, and goserelin [17]. However, these medications are expensive and require subcutaneous injections every 4 to 12 weeks. Prior to initiation of hormone treatment, storage of gametes should be discussed with the patient.

Many transgender patients hope for maximum doses of hormone treatment for transition as fast as possible, while others desire to proceed slowly in order to have more control over the effects or to present in a more androgynous way. Some MTF individuals want to maintain the ability to have erections, while others want to eliminate them [82]. Hormone therapy should be individualized based on the patient's goals, keeping in mind that hormone therapy is recommended in conjunction with some, but not all, surgical treatments for gender dysphoria [71].

Some transgender individuals obtain hormones from non-traditional sources, including the Internet, friends, and street vendors. In an urban environment, the prevalence of unsupervised hormone use in MTF individuals ranges from 29% to 63% [56]. This exposes patients to significant health risks from needle sharing, inappropriate dosing or combinations of hormones, and lack of screening for potential side effects such as thromboembolism [56].

When transgender individuals seek hormones, some providers will require an initial visit to conduct a thorough history, physical, and laboratory tests; provide referrals for mental health if needed; obtain informed consent; and provide appropriate vaccinations and a skin test for tuberculosis. Hormones are then prescribed at the second visit. Follow-up visits should take place every two to three months for the first year, after which patients can be seen every 6 to 12 months [71].

The Tom Waddell Health Center in San Francisco uses the following protocols for the initial visit for a patient seeking hormone therapy [82]:

- Conduct nurse initial screening intake.
- Conduct psychosocial intake.
- Obtain baseline labs:
  - Complete blood count (CBC) with differential
  - Liver panel
  - Renal panel
  - Glucose
  - Hepatitis A antibody
  - Hepatitis B total core antibody
  - Hepatitis B surface antibody and antigen
  - Hepatitis C antibody
  - Venereal disease research laboratory (screening test for syphilis)
  - Lipid profile
  - Prolactin level (for MTF)
  - HIV antibody
  - Tuberculosis blood test
- Review healthcare maintenance needs according to standard criteria.
- Address medical problems as needed.
- Discuss patient's goals and expectations for therapy.
- Review side effects, risks, and benefits of hormone therapy and obtain informed consent.
- Prescribe medications and follow patients per protocols.

In addition to the laboratory studies recommended by the Waddell protocols, initial laboratory studies prior to initiating hormone therapy might include prostate-specific antigen, glucose, electrolytes, thyroid-stimulating hormone, and perhaps testosterone and estradiol levels.

MTF HORMONAL AND NONSURGICAL MANAGEMENT

There are several choices of hormone therapy for the MTF transition and maintenance (***Table 1***). The goals of hormone therapy prescribed for MTF individuals are to induce breast formation and a more female distribution of fat and to reduce male-pattern hair growth while neutralizing the biologic effects of endogenous androgens [18]. Additional effects include decreased muscle mass and strength, softening of skin, decreased libido, decreased sperm production and testicular volume, and less frequent and less firm erections [71]. Commonly, hormonal treatment of MTF individuals will include an antiandrogen along with an estrogen.

MEDICATIONS USED FOR MTF INDIVIDUALS			
Medication	**Dosage/Route**	**Indication**	**Comments**
Spironolactone	100–200 mg/day PO	Anti-androgen	Monitor potassium
GnRH agonist	3.75 mg/month IM	Anti-androgen, used as puberty-blocker	Expensive Used mainly in Europe
Leuprolide	3.75 mg/month IM	Anti-androgen, used as puberty-blocker	Expensive Used mainly in Europe
Histrelin implant	SC implant	Anti-androgen, used as puberty-blocker	Expensive Used mainly in Europe
Finasteride	Low: 1–5 mg/day High: 5–10 mg/day	Low: Male pattern baldness High: Anti-androgen	—
Conjugated estrogen	1.25–10 mg/day PO	Feminization	Derived from pregnant mares
Estradiol	2–8 mg/day PO	Feminization	—
Estrogen patch	0.1–0.4 mg twice weekly	Feminization	Safest in regards to thromboembolism and cardiovascular disease
Estradiol valerate	5–30 mg IM every two weeks	Feminization	—
Progesterone	20–60 mg/day PO	Adjunct to feminization	Monitor bone density and lipids
Source: [82; 83]			*Table 1*

Because the use of anti-androgens and estrogens will reduce sperm production over time, providers should discuss sperm banking prior to beginning hormone therapy. Sperm banking is an easy, non-invasive, fairly inexpensive and viable option for preserving reproductive options and can be done through a medical facility or sperm bank. At the Fenway Health Center in Boston, pre-treatment gamete banking is strongly encouraged for all natal males post-puberty up to 35 years of age prior to initiation of estrogen therapy. However, banking may be done at any post-puberty age and prior to hormone treatment [84; 85].

Hormone Therapy

Anti-Androgens

Anti-androgens reduce endogenous testosterone levels, allowing the full effect of estrogen therapy. The anti-androgen of choice in the United States is usually spironolactone (Aldactone), a potassium-sparing diuretic that directly inhibits testosterone secretion and inhibits androgen binding to the androgen receptor. It is usually given orally at a dose of 50 mg twice daily [82]. Side effects of spironolactone include gastrointestinal upset, hyperkalemia, increased urinary output, and hypotension. It is contraindicated in patients with renal insufficiency or with serum potassium levels greater than 5.5 mEq/L. Spironolactone should not be given with digoxin, angiotensin-converting enzyme inhibitors, other potassium-sparing diuretics, and angiotensin receptor blockers [82]. Patients taking spironolactone should have baseline levels of electrolytes, blood urea nitrogen (BUN), and creatinine, and repeat levels in two months or at every dose change, and then every six months when the dose is established [82].

Another commonly used anti-androgen is finasteride (Propecia or Proscar). This is a 5-alpha reductase inhibitor that blocks the conversion of testosterone to its potent form of dihydrotestosterone (DHT). The Propecia brand is approved to treat male pattern baldness, and the Proscar brand is approved for the treatment of benign prostatic hypertrophy; the use of finasteride to facilitate gender/sex transition is

off label. Typical dosage for male pattern baldness is 1–5 mg per day [82; 83]. Larger dosages are required to facilitate transition and range from 5–10 mg per day [82]. Finasteride for transition is generally only used as second-line therapy for patients intolerant to spironolactone. It does not have any significant food or drug interactions.

As mentioned, another category of anti-androgens is the GnRH agonists. These drugs occupy GnRH receptors in the pituitary, leading to a decrease in LH and follicle-stimulating hormone (FSH) secretion. This leads to a decrease in estradiol and testosterone levels in both sexes. Drugs in this class include nafarelin (Synarel), goserelin (Zoladex), and leuprorelin (Lupron). GnRH agonists are particularly useful in the treatment of adolescents, because their effects are fully reversible should there be a change in the desire to transition. Goserelin has been shown to be effective in reducing testosterone levels with a low incidence of adverse reactions [82]. When GnRH agonists are first given, testosterone levels go up briefly before falling to very low levels; this effect is called flare [82]. It can be avoided by giving other anti-androgen drugs for a few weeks when starting treatment.

Leuprolide is given at a dose of 3.75 mg monthly as intramuscular (IM) injections. Nafarelin is given via nasal spray, and goserelin is given via a monthly implant that delivers 3.6 mg over 28 days [82]. All these methods are relatively expensive and not as commonly used as spironolactone.

There are also progestins with anti-androgen activity. In Europe, a commonly used progestin is cyproterone, but this agent is not approved for use in the United States. When included in hormone therapy for MTF individuals, cyproterone is prescribed for the initial two weeks of GnRH therapy to reduce the effects of the androgen flare [82]. Side effects of cyproterone include fatigue, depression, and rarely, liver dysfunction.

Estrogen

In the MTF individual, estrogen will soften the skin, stimulate breast development, and cause a more feminine redistribution of fat while reducing testosterone levels via negative feedback on the hypothalamus. Estrogen also down-regulates gonadotropins to lower serum testosterone levels. This reduces the frequency of erections and ultimately causes prostate and testicular atrophy and infertility. It is unclear whether estrogen has a permanent effect on spermatogenesis, though it is likely to be related to the duration of therapy. However, there are no data on restoration of spermatogenesis after prolonged estrogen treatment [17].

Breast growth is moderate in MTF individuals taking estrogen. In a large multicenter study of 229 transwomen, breast development predominantly occurred in the first six months of estrogen therapy [86]. Only seven patients (3%) gained a bra size larger than an A cup. While transwomen treated with transdermal estradiol experienced more rapid breast growth, overall breast growth did not differ by route of administration after one year. Serum estradiol level did not predict breast development, possibly because exposure to high testosterone during male puberty induces structural changes in the breasts' adipose and fibrous connective tissue that inhibit development [86]. Breast development is generally maximal after two years of therapy [17].

Prior to initializing treatment with estrogen, baseline tests that should be performed include: liver panel, renal panel, lipid profile, prolactin level, and glucose level. These should be rechecked one to two months after starting, three months after changing dose, and every six months after establishing a stable dose [82]. Testosterone levels may be checked for patients not showing expected feminization after six to 12 months on maximum anti-androgens. While some practitioners recommend monitoring serum estradiol levels to maintain the mean daily level for premenopausal women, other providers feel that serum estrogen levels are not useful [82].

It is generally recommended that estrogen initially be given at lower dosages and increased gradually [82]. Excessive initial estrogen doses may cause early breast duct fusion, leading to small, hard, conical breasts [87]. This can be avoided by starting at a daily dose of 2 mg and progressively increasing the dose every three months until the serum estradiol level is 400–600 pmol/mL—typically 2 mg three times per day [87].

Estrogen can be given orally, transdermally, or parenterally, and each type of delivery has advantages and disadvantages. Estrogen given sublingually, transdermally, and parenterally avoids first-pass metabolism (with less effect on liver enzymes) and is associated with fewer vascular complications in patients older than 40 years of age [17]. Oral forms of estrogen have the additional advantage of being easy to titrate or stop. One study of long-term cross-sex hormone usage revealed that the use of ethinyl estradiol in MTF individuals was associated with an increased risk of death from thrombotic events [88]. This is one reason that the Endocrine Society, the Waddell protocols, and the WPATH Standards of Care no longer recommend ethinyl estradiol as a safe medication for feminizing hormone therapy [17; 71; 82].

One commonly prescribed oral estradiol product is Estrace. Generally, dosing of oral estradiol starts at 0.5–1 mg per day and gradually increases to a typical dose of 4 mg daily [82]. Conjugated estrogens are sometimes used, starting at 1.25–2.5 mg per day and increasing over time to 5 mg per day [82]. Some providers and patients have ethical issues with how this product is obtained (from the urine of pregnant mares) and the theoretical increased risk of thrombotic events [82].

Many providers prefer the injectable form of estrogen, either estradiol valerate (Delestrogen) or estradiol cypionate (Depo-Estradiol). Both of these products are typically started at 20–40 mg IM every two weeks, with an average maintenance dose of 40 mg every two weeks [82].

AGENTS THAT MAY ALTER ESTROGEN LEVELS

Medications and Substances that Decrease Estrogen Levels	Medications and Substances that Increase Estrogen Levels
Benzoflavones	Cimetidine
Carbamazepine	Clarithromycin
Dexamethasone	Diltiazem
Lopinavir	Efavirenz
Nelfinavir	Erythromycin
Nevirapine	Fluconazole
Phenylbutazone	Fluoxetine
Phenytoin	Fluvoxamine
Phenobarbital	Grapefruit
Progesterone	Indinavir
Rifampin	Isoniazid
Ritonavir	Itraconazole
Sulfadimidine	Ketoconazole
Sulfinpyrazone	Miconazole
Tobacco	Nefazodone
	Paroxetine
	Sertraline
	Verapamil

Source: [90] *Table 2*

Estrogen can also be delivered transdermally via patch. Patches are started at 0.1 mg per day and increased as necessary to achieve the desired result. The average dose is 0.2 mg per day.

Common side effects of estrogens include breast tenderness, nausea and vomiting, depression, dry skin, brittle nails, headaches, and in some cases, increased appetite and weight gain [17; 82; 87]. More rarely, patients may experience migraines, gallbladder disease, abnormal liver function tests, mood disorder/depression, melasma, acne, lipid abnormalities, hypertriglyceridemia, increased risk of myocardial infarction, hepatitis, stroke, and increased risk of breast and other cancers [82; 89]. In addition, estrogens may interact with other medications and foods (***Table 2***).

MTF individuals taking estrogen are at a greater risk of forming thrombotic emboli as a result of increased production of coagulation factors and pituitary prolactin production. This complication has been linked specifically to synthetic estrogens, such as ethinyl estradiol [91]. Deep vein thrombosis and pulmonary embolism are particular concerns for individuals who are older than 40 years of age, cigarette smokers, sedentary, or obese [82]. Two systematic reviews and meta-analyses of hormone use and cardiovascular risk found that estrogens increase serum triglycerides in MTF individuals, but data were too weak to draw conclusions about long-term cardiovascular morbidity and mortality [92; 93]. Due to the increased risk of thrombosis and peripheral vascular disease, tobacco use is strongly discouraged [37; 82]. Among oral estrogen users, there is potential for transient liver enzyme abnormalities, increased triglycerides, diabetes, and hypertension [82].

Hyperprolactinemia may occur, and there have been reported cases of prolactinomas in MTF individuals [17]. If present, hyperprolactinemia may respond to GnRH agonist therapy. Liver damage is also possible, particularly with oral therapy; it may be avoided by using parenteral or transdermal delivery. Other potential adverse effects include cholelithiasis, Budd-Chiari syndrome (a condition caused by occlusion of the hepatic veins that drain the liver and characterized by abdominal pain, ascites, and hepatomegaly), hepatic adenoma, and pancreatitis [87]. Estrogens and anti-androgens reduce circulating levels of phenylalanine, tyrosine, and tryptophan, which may lead to depressive and anxiety disorders [94].

Conversely, estrogen therapy reduces prostatic malignancy rates, as the prostate is not removed during GCS [87]. However, a prostate exam and cancer screening should be done as in the general male population.

The risk of breast cancer from estrogen therapy during MTF transition has not been clearly established. It is believed that progesterone used along with estrogen may raise this risk, but very few cases have ever been reported [87; 95]. Nevertheless, if MTF patients are taking high levels of estrogen, they may be at increased risk for breast cancer, and providers should consider monitoring with a mammogram or breast ultrasound according to age and other risk factors (e.g., family history, duration of therapy) [81; 96].

Response to estrogen is highly variable. Younger age and less body hair before initiation of therapy are predictive of a more satisfactory outcome [82]. Although estrogen administration will reduce body hair growth after six to 36 months, electrolysis or laser hair removal is commonly necessary to remove facial hair [17]. Clinicians providing care to MTF individuals who are undergoing electrolysis may consider prescribing topical lidocaine or lidocaine/prilocaine cream to reduce the discomfort associated with electrolysis. Approximately 2–2.5 g of the cream is applied to the area to be treated for one hour under an occlusive dressing.

Estrogens should be used with caution in patients with hyperlipidemia, diabetes, a history of smoking, hepatitis, alcoholic liver disease, renal insufficiency, migraines, seizure disorder, retinopathy, obesity, coronary heart disease, valvular heart disease, congestive heart failure or other cardiac dysfunction, any condition causing tendency to thrombosis, or a strong family history of breast cancer or other estrogen-dependent tumor [82]. Absolute contraindications to estrogen therapy include previous thrombotic events related to an underlying hypercoagulable condition, a history of estrogen-sensitive neoplasm, and end-stage liver disease [71].

Suggested annual laboratory tests for MTF individuals taking estrogens include lipid profile, liver function tests, glucose, and prolactin. BUN, creatinine, and electrolytes should be measured more frequently (i.e., every six months) [82].

Estrogen should be discontinued two weeks before GCS or any major surgery or immobilizing event and may be resumed one week after the surgery/event [82]. Estrogen doses should be reduced to the minimum necessary after GCS or maximum feminization is evident, usually after two years of treatment [82]. There are reports of decreased libido among MTF individuals who have taken estrogen for long periods, possibly due to long-term androgen depletion. Androgens play an important role in female libido and sexual enjoyment, and in MTF individuals, circulating androgen levels are lower than those in cisgender women [97]. To address this side effect, some providers add a small amount of testosterone to the hormonal regimen of MTF individuals.

Progesterones

Progesterones have anti-androgen effects at high doses, but have no proven advantages over spironolactone for MTF patients [82]. They have been included in hormone regimens due to the perceived effects of augmenting estrogen-induced breast development and maintaining libido. However, there is no evidence that progestins improve breast development, and progesterone may cause an increased risk of thrombotic illness when combined with estrogen [98]. Some patients also report depressed mood and increased androgenic effects. Progesterone may cause salt/water retention, leading to elevated blood pressure or venous varicosis [99]. If indicated, medroxyprogesterone may be used as an adjunct for patients on maximum estrogen doses with unsatisfactory effects or in patients intolerant of other drugs. Typical dosing starts at 2.5 mg per day, increasing to a maximum dose of 20 mg per day. It can be given in 10-day cycles per month to reduce the total amount given [82].

The precautions and contraindications for progesterones are the same as those described for estrogens. Adverse effects may include lipid abnormalities, weight gain, edema, mood disorders (primarily depression or irritability), and facial and body hair growth and coarsening.

Voice Therapy

When boys reach puberty, the increase of androgens causes the larynx to grow and the vocal cords to lengthen and thicken, resulting in a deeper pitch. Additionally, the growth of facial bones, sinus cavities, the nose, and the throat creates more vocal resonance in men. Being perceived as a woman in vocal interactions is of importance to MTF individuals. Because the physiologic changes affecting the voice are not reversed with the use of female hormones, many MTF individuals will seek out voice therapy (with a speech therapist or speech-language pathologist) to change the quality of the voice to a more feminine range.

Voice therapy involves the conscious manipulation of the vocal mechanism to produce a more feminine-sounding voice [100]. The goal of therapy is not merely raising the pitch of the voice, but also "feminizing" the resonance, intonation (rhythm of speech), rate of speech, volume, intensity, choice of language, articulation, and social rules of communication [101]. The process includes an assessment of the individual's current voice, resonance, articulation, spoken language, and non-verbal communication. The patient is also assessed for vocal health and current practices that may be damaging to the voice.

Feminine voices have a higher pitch and breathier vocal quality, and they resonate at higher frequencies and have different speech rates, inflections, and intonations. The fundamental frequency (pitch) of the adult male voice is about 100 Hz, with a range of 77–482 Hz; the adult female voice has an average frequency of 195 Hz, with a range of 137–634 Hz. There is considerable overlap between the two ranges, but in order to be perceived as female, the fundamental frequency should be around 172 Hz (165–180 Hz). According to a study by King et al., a mean speaking pitch above 180 Hz and maintaining a speaking pitch range of approximately 140–300 Hz appear to be the most powerful acoustic features or markers in the perception of a female voice in MTF individuals [102]. Raising the fundamental frequency near this range is one of the goals of voice therapy.

MEDICATIONS USED FOR FTM INDIVIDUALS			
Medication	**Dosage/Route**	**Indication**	**Comments**
Testosterone enanthate or cypionate	100–200 mg IM every two weeks or 50–100 mg SC/IM per week	Masculinization	Watch for allergies to sesame or cottonseed oil
Testosterone gel 1.6%	50–100 mg/day	Masculinization	Increased incidence of breakthrough bleeding
Testosterone patch	2.5–7.5 mg/day	Masculinization	Expensive Increased incidence of breakthrough bleeding

Source: [17] *Table 3*

MTF speakers can effectively raise their resonance by learning to speak with the tongue positioned relatively more forward in the oral cavity. Because women tend to use a smaller range of semitones than men when speaking declarative and interrogative sentences, MTF individuals can change intonation by reducing the range of semitones they use and utilizing more upward intonations and downward shifts in conversational speech.

In addition to voice characteristics, MTF individuals also may alter their nonverbal communication to a more feminine manner by maintaining eye contact, using hand gestures, using more varied facial expressions, altering posture, and nodding more. Women tend to move their heads during conversation and often mirror the movements of their conversational partner. They are also generally more expressive with their hands and use arm movements that are closer in proximity to their own body. Feminine gestures tend to be more fluid than those perceived as masculine and tend to move toward and away from the body. Additionally, women may have conversations with more disclaimers and qualifiers and be more emotionally expressive [103]. Another important area of therapy is alerting patients to the difference in lexicon between the genders. The words commonly used by men and women are different, and therapy can include the differences in masculine and feminine language and word usage [104].

Voice therapy may involve individual and/or group sessions. The frequency and duration of treatment will vary according to a patient's needs. During voice therapy, the MTF patient can easily become fatigued, and one goal is to build vocal stamina in order to prevent harming the vocal folds [101]. Exercise is a prerequisite to voice modification, as building strength and flexibility will increase the likelihood of success and reduce the risk of vocal stress and strain [104; 105].

FTM HORMONAL AND NONSURGICAL MANAGEMENT

Androgens

The goal of hormone therapy for FTM individuals is masculinization of the body through the use of testosterone (***Table 3***). Testosterone therapy in FTM individuals results in cessation of menses within three to five months due to suppression of the hypothalamic-pituitary axis. However, ovulation may continue, and pregnancies have been reported in FTM persons even after prolonged testosterone treatment [17; 106]. As such, it is important to discuss contraception with FTM individuals who have sex with men. Other effects of testosterone therapy include increased libido, increased facial and body hair, increased skin oiliness, increased muscle, mild breast atrophy, and redistribution of fat mass, usually within three months of the initiation of testosterone therapy.

Within one year, the voice usually deepens, clitoromegaly occurs, and male pattern hair loss may be apparent [17]. After 13 years of testosterone use, androgenic alopecia occurs in 50% of FTM individuals [99]. On average, the clitoris enlarges to 3–5 cm, and in some cases, testosterone may be applied topically to the clitoris to stimulate growth [106]. These changes in voice range, hair follicles, and clitoral size are permanent. Other effects, such as increased muscle mass, acne, increased libido and energy level, and amenorrhea are reversible if testosterone is discontinued [82]. FTM individuals report a better quality of life after receiving male hormones regardless of the duration of treatment [50].

Contraindications to testosterone include estrogen receptor-sensitive breast cancer; uterine, endometrial, and/or ovarian cancer; pregnancy; and hypersensitivity to sesame or cottonseed oil, if injectable testosterone is used. Testosterone should be used with caution in individuals with uncontrolled coronary heart disease or any unstable heart disease, hyperlipidemia, diabetes, liver disease, cigarette smoking, extreme obesity, hypertension, kidney failure, prolactinoma, or active thyroid disease [106].

There is an increased incidence of polycystic ovarian syndrome (PCOS) in FTM individuals regardless of testosterone use. Because PCOS is associated with insulin resistance, obesity, hypertension, cardiac disease, and endometrial cancer, it is important that candidates for testosterone therapy be evaluated for PCOS prior to the initiation of treatment; testosterone may exacerbate many of these conditions [71].

Baseline levels should be established before initiating testosterone therapy for the lipid profile, comprehensive metabolic profile (CMP), CBC, free and total testosterone, estrogen, and prolactin. Free testosterone, CBC, and CMP should be repeated four to six weeks later, as well as blood pressure and weight. At four to six months and then every six to 12 months, a fasting lipid panel, CMP, CBC, and free testosterone should be assessed. Specimens should be drawn midway between testosterone injections, and clinicians should strive to maintain testosterone levels within the normal male range [71; 106].

Because a common side effect of testosterone therapy is polycythemia, hematocrit levels should be carefully monitored. Polycythemia is exacerbated by excessive testosterone dosages and is more likely in smokers [87]. If necessary, treatment involves reducing the dosage or switching to transdermal delivery.

FTM individuals receiving testosterone may have elevated renin, triglyceride, and cholesterol levels, putting them at a higher risk for heart disease. If they smoke cigarettes, their risk of coronary heart disease is increased even more [81]. In two systematic reviews and meta-analyses, testosterone therapy was associated with increased serum triglycerides and low-density lipoprotein cholesterol, decreased high-density lipoprotein cholesterol, and a small increase in systolic blood pressure in FTM individuals [92; 93]. However, there is a lack of evidence that these changes result in increased morbidity or mortality [106].

Testosterone also increases plasma tryptophan levels, reducing vulnerability to depressive and anxiety disorders [94]. All FTM individuals of reproductive age who wish to preserve reproductive options should be counseled about gamete (unfertilized ova) or fertilized embryo banking by a fertility specialist prior to initiation of testosterone therapy [84; 85]. Although menses and ovulation will resume after testosterone is withdrawn and pregnancies have occurred in FTM individuals even while on testosterone therapy, there are no studies that examine the long-term impact of testosterone on fertility or the health of offspring.

There is little standardization in hormone regimens for FTM individuals, and the choice of product may be limited by a patient's economic situation or geographic location. The Endocrine Society guidelines provide specific guidance regarding the types of hormones and suggested dosages that have proven effective [17]. In the United States, oral testosterone is not available, so it will not be discussed in this course.

In the United States, most regimens involve parenteral or transdermal testosterone in the form of testosterone cypionate or enanthate. These agents avoid the first-pass effect and can achieve testosterone levels in the normal male range of 320–1,000 ng/dL. Intramuscular testosterone is released slowly from the muscle, so injections are spaced every two to four weeks.

It is important to advise patients using transdermal testosterone to avoid contact with others immediately after administration in order to prevent accidental virilization. In the United States, transdermal testosterone is available as the Androderm patch, AndroGel topical gel, or Axiron topical solution [17; 107].

Testosterone is associated with some food/drug and drug/drug interactions, which are similar to those found with estrogens (***Table 4***). It increases the anticoagulant effect of warfarin, increases the clearance of propranolol, and increases the hypoglycemic effects of sulfonylureas [107].

The effect of testosterone on endometrial hyperplasia is unclear. While some studies indicate an increased risk of endometrial cancer, others have found that testosterone causes endometrial atrophy or decreased endometrial thickness [108; 109]. If FTM individuals are receiving large doses of testosterone, it may be converted into estrogen through aromatization. Without progesterone, this estrogen is unopposed, and if the patient has a uterus, unopposed estrogen increases the risk of endometrial hyperplasia and uterine cancer. Therefore, twice-yearly ultrasonic monitoring of endometrial thickness after three years of testosterone therapy is recommended if hysterectomy has not been performed [87]. Paradoxically, patients on smaller doses of testosterone may have better effects because less estradiol circulates [37].

While FTM individuals perceive that receiving gynecologic care is important, many struggle with dealing with healthcare providers [110]. Use of improper pronouns and the male/female boxes on standard forms are considered barriers to care. Breast exams cause considerable anxiety in FTM individuals, and special care should be taken during a pelvic exam to reduce patients' anxiety.

AGENTS THAT MAY ALTER TESTOSTERONE LEVELS

Medications and Substances that Decrease Testosterone Levels	Medications and Substances that Increase Testosterone Levels
Benzoflavones	Cimetidine
Carbamazepine	Clarithromycin
Dexamethasone	Diltiazem
Lopinavir	Efavirenz
Nelfinavir	Erythromycin
Nevirapine	Fluconazole
Phenylbutazone	Fluoxetine
Phenytoin	Fluvoxamine
Phenobarbital	Grapefruit
Progesterone	Indinavir
Rifampin	Isoniazid
Ritonavir	Itraconazole
Sulfinpyrazone	Ketoconazole
	Miconazole
	Nefazodone
	Paroxetine
	Sertraline
	Verapamil

Source: [90; 107] *Table 4*

Ongoing care for FTM individuals includes cervical Pap tests according to guidelines while the patient still has a cervix. With testosterone therapy, the cervix will atrophy, showing an increase of parabasal cells or other atrophic changes on Pap reports. Because of this, patients may require 25 mcg of estrogen intravaginally one to two weeks prior to a pelvic exam to achieve proper cell collection from the squamocolumnar junction. It is important to note on the lab slip that the patient is on testosterone and is amenorrheic [108].

Spontaneous vaginal bleeding may be caused by missed testosterone doses, excessive testosterone, weight increase, or thyroid disorders. Atrophic vaginitis may occur, resulting in bacterial vaginitis or candidiasis. If bacterial vaginitis is suspected, the vagina should be cultured for atypical bacteria [108]. Pelvic cramping has been noted in some people on testosterone for longer than three to six months, in some cases associated with orgasm. The pain typically lasts 10 to 15 minutes and can be alleviated by pre-medicating with nonsteroidal anti-inflammatory drugs [108].

Care of the FTM patient should include a sensitive history of sexual practices and partners. It is important not to assume sexual orientation based on gender identity. Instead, consider asking "What sexual practices do you engage in?" or "What body parts do your sexual partner(s) have, and which of your body parts do you use?" [108]. Screening for HIV and other sexually transmitted infections should be based on history, symptoms, or risk factors. Patients should be counseled regarding the safe use of sex toys and safer sex practices, including the use of condoms, gloves, and dental dams, as appropriate. If the patient is having sex that could lead to pregnancy, contraception should also be discussed. If the patient desires to conceive, counseling would include the use of folic acid, prenatal vitamins, and stopping testosterone.

Some FTM individuals have had successful pregnancies during transition. A survey of 41 FTM individuals who gave birth after transitioning with or without the use of testosterone showed that FTM individuals may desire to have children and be willing and able to conceive, carry a pregnancy, and give birth [111]. Participants who discontinued testosterone to attempt pregnancy reported resumption of menses within six months, with the majority within three months. Some conceived before the return of menses. More than 30% of the pregnancies were unplanned, suggesting an unmet need for better contraception counseling for FTM individuals [111]. Pregnancy outcomes were not significantly different from the general population, except for an increased incidence of postpartum depression. Most FTM individuals who had used testosterone gave birth via cesarean section. Although most transgender men in the study received prenatal care from physicians and delivered in hospitals, participants used non-physician providers and nonhospital birth locations more frequently than the general public. The researchers speculate that the choice of healthcare provider and delivery location may have been responses to actual or anticipated negative experiences [111].

Because serum testosterone levels are lower in individuals using transdermal testosterone, progestin, most commonly medroxyprogesterone, is often needed to assist with menstrual cessation [18]. Drug interactions include potentiation of warfarin and hypoglycemic agents [82].

Voice Therapy

Because hormone therapy will result in voice changes for FTM individuals, voice therapy is often overlooked or considered unnecessary. However, research has indicated that voice change in FTM individuals is not always fully achieved through hormone therapy [112]. In a study of 38 FTM transsexual persons, pitch-lowering difficulties occurred in about 10% of cases and appeared, at least in part, to be associated with diminished androgen sensitivity [113]. Aside from changes in pitch and voice quality, voice therapy may also help inform nonverbal communication and gestures to reinforce a masculine presentation.

SURGICAL INTERVENTIONS

At some point in transition, transgender individuals typically seek surgical interventions to meet their goals to masculinize/feminize the body. Although obtaining a true estimate of the number of individuals undergoing surgical procedures as part of gender transition is difficult, available research indicates that more transgender patients are having surgery [114]. The American Society of Plastic Surgery's 2018 annual report included 2,885 MTF and 6,691 FTM patients undergoing GCS, an increase of 61% and 22%, respectively, compared with 2017 [115]. In addition, many surgeries are performed by other surgical subspecialties (e.g., urologists, obstetricians/gynecologists, maxillofacial surgeons). A large-scale survey found that among FTM individuals, 21% had chest reconstruction, 8% hysterectomy, 1% metoidioplasty, and 1% phalloplasty; among MTF individuals, 10% had vaginoplasty or labiaplasty, 9% orchiectomy, 8% augmentation mammoplasty, and 6% facial surgery [114].

The WPATH guideline suggests separate criteria for non-genital and genital surgery for transgender individuals. The criteria for non-genital surgery include [71]:

- One referral from a mental health professional
- Persistent, well-documented gender dysphoria
- Capacity to provide informed consent
- Age of majority
- Reasonable control of significant medical or mental health concerns, if present

Hormone therapy is not a prerequisite, but 12 months of feminizing hormone therapy is recommended in the case of MTF individuals seeking augmentation mammoplasty, as this will result in better surgical (aesthetic) results.

Criteria for genital surgery (except for metoidioplasty or phalloplasty in FTM individuals and vaginoplasty in MTF individuals) include those outlined for non-genital surgery as well as:

- Two referrals from mental health professionals
- 12 continuous months of hormone therapy as appropriate to the patient's gender goals (unless the patient has a medical contraindication or is otherwise unable or unwilling to take hormones)

The criteria for metoidioplasty or phalloplasty in FTM patients and for vaginoplasty in MTF patients include all of these criteria plus 12 continuous months of living in a gender role that is congruent with his/her gender identity. This criterion is based on expert clinical consensus that "real-life" experience allows the patient to experience and socially adjust to his/her desired gender role before undergoing irreversible surgery [71]. Occasionally, patients may have unrealistic expectations about what it means to be a member of the opposite sex; it is important that these are brought to light before surgery is done. The real-life experience has been shown to reduce gender dysphoria and improve social and sexual functioning [18].

SURGICAL MANAGEMENT FOR MTF TRANSITION

In the MTF individual, some common surgical interventions include breast augmentation, facial feminization surgery, tracheal shave, and genital surgery, including orchiectomy, penectomy, vaginoplasty, clitoroplasty, and labiaplasty. It is important to note that in order to achieve comfort in their gender identity, not all individuals will seek genital surgery. Some individuals may opt for hormone therapy only, others will seek some cosmetic procedures or orchiectomy, and still others will seek many or most of these procedures.

Breast Augmentation

An estimated 60% to 70% of all MTF individuals seek breast augmentation in addition to hormone therapy [86]. Breast augmentation is generally performed as an outpatient procedure under general anesthesia. During the procedure, saline or silicone gel implants are placed, most commonly below the pectoral muscle through a periareolar, inframammary, axillary, or trans-umbilical incision.

The periareolar incision has the advantage of hiding the incision scar along the skin-areola border. However, this is only practical if the areolae are large enough to insert the implants. The inframammary incision provides an easier approach to creating a pocket to place and inflate the implant, but the incision may be more noticeable. The axillary approach moves the incision away from the breast area, but it makes visualization of the surgical area and control of bleeding more difficult. The trans-umbilical approach involves making an incision at the umbilicus and tunneling to the implant site, where a deflated saline implant is placed and then inflated. Various sizes and shapes of implants are available, and patients generally discuss their wishes and expectations with their surgeon so consensus can be reached on what is possible [116].

After the procedure, the dressings will remain in place for about three days, but the strips over the incision are generally left in place until they fall off, usually in seven to 10 days. Showering is permitted, but the wound closure strips should not be soaked and should be patted dry afterwards. A sports bra should be worn for compression and support.

Erythema at the incision site is normal, provided it does not extend beyond 1–2 cm from the incision. Edema is also normal and is only concerning if it is an unusually large, one-sided mass. Suture knots may be visible or felt at the end of the incision and may eventually work their way to the surface of the skin. Shooting pains, burning sensations, and general discomfort during the healing process are common. Mild analgesics are usually prescribed to control these.

Patients often resume normal routines within one to two weeks, with strenuous activity avoided for three to four weeks. Patients are instructed to perform implant displacement massage beginning three to five days post-procedure [116].

The most common complications of breast augmentation surgery include the general surgical complications of bleeding, infection, or hematoma. Complications specific to augmentation mammoplasty are capsular contraction, asymmetry, malpositioned implants, and altered nipple sensation. Infection is rare [87; 117].

Facial Feminization Surgery

Facial feminization surgery is a set of surgical procedures that alter typically male facial features to provide a more feminine appearance. This is achieved by procedures such as brow lift, rhinoplasty, cheek implants, lip augmentation, scalp advancement, frontal cranioplasty, and reduction mandibuloplasty [118]. Through the 1980s and 1990s, facial feminization surgery as part of MTF transition was pioneered in the United States by maxillofacial surgeon Douglas K. Ousterhout. Since then, other surgeons in the United States and abroad have continued to develop and improve approaches to facial feminization.

There are notable differences between the male skull and the female skull (***Table* 5**). The male skull usually has a square or rectangular shape; forehead brow bossing with a steep, flat slope; a larger and thicker mandible; a wider, rectangular chin; and more muscle and less fat. The zygomatic prominence is usually larger and flatter [117].

Facial feminization surgery includes forehead modifications, cheek/zygomatic bone modifications, rhinoplasty, mandibular angle changes, and genioplasty. Modifications to the brow include burring of the brow or removal of the anterior table along with osteotomies and miniplates and repositioning of the periosteum. Very often, this is combined with a brow lift and scalp advancement, as women generally have less distance between the brows and the hairline.

TYPICAL DIFFERENCES BETWEEN THE MALE AND FEMALE SKULL		
Feature	**Male Skull**	**Female Skull**
Overall shape	Square/rectangular	Oval
Forehead	Brow bossing with steep flat slope	Round, convex, smooth
Nose	Acute glabellar angle, larger bones, sharper angle at midline	Delicate
Zygomatic prominence	Larger bone, flatter	Thinner bone, more prominent
Mandible	Large, thick	Softer angles
Chin	Wide, rectangular	Pointed, trapezoidal
Soft tissue	More muscle, less fat	More fat, softer wrinkles
Source: Compiled by Author		*Table 5*

Cheek implants or fillers are used to provide a fuller cheek with more projection. The chin can be rounded with a burr or implants to improve the contour. The mandible may be repositioned downward and posteriorly, and a mandibular angle reduction may be performed [117].

A chondrolaryngoplasty (tracheal shave) may be requested to remove or reduce the laryngeal prominence (Adam's apple). This procedure is not designed to feminize the voice—only to alter the appearance. A small incision is made on the upper crease of the neck or in a wrinkle in the skin. Using a laryngoscope, the vocal cords are visualized and this location is marked externally. The surgeon then exposes the thyroid cartilage and removes all of the prominent cartilage and its borders above the vocal cord marking. The incision is then closed and cleaned and a bandage is placed over the incision. During the first 24 to 48 hours after the surgery, it is common to experience some bruising and swelling as well as a sore throat. Discomfort is typically minor; however, pain medication is often given in order to keep the patient as comfortable as possible [119]. Complications may include a scar, changes in vocal quality, pain, and difficulty swallowing [117].

There is a paucity of data on patient satisfaction following facial feminization surgery. However, one study of 247 MTF individuals revealed that those who had facial feminization surgery scored higher on measures of satisfaction and quality-of-life outcomes in regard to physical, mental, and social functioning compared with those who did not have facial feminization surgery [118].

Occasionally, MTF individuals who are seeking an inexpensive alternative to cosmetic surgery may resort to injectable silicone and body molding substances that are not approved for human use. These injections are often industrial grade silicone and/or substances such as paraffin, oil, and other industrial materials (e.g. caulk, tire sealant). They are illegal, often performed by unlicensed practitioners, and may be injected at so-called "pumping parties." Common areas for injection include the cheeks, breasts, and buttocks.

Immediate dangers of these injections include transmission of HIV, hepatitis B and C, methicillin-resistant *Staphylococcus aureus*, embolism, and foreign substance reaction. Possible long-term effects include migration of the substance to other body areas, disfigurement, nodules, granulomata, and pain. Treatment is palliative, as there is no safe way to remove encapsulated silicone from body tissue [82].

Orchiectomy

Bilateral orchiectomy is commonly performed as part of GCS. However, it may also be done as a separate procedure to reduce total testosterone levels by about 90%, particularly in individuals who are intolerant of anti-androgen therapy. This also reduces the amount of estrogen needed to achieve feminization. In performing this procedure for MTF individuals, the scrotal skin is preserved as much as possible if there is a desire for vaginoplasty/labiaplasty in the future. Disadvantages of orchiectomy are the irreversibility of the procedure and the shrinkage/potential scarring of scrotal tissue, which would be used in subsequent GCS to create the neovagina. For this reason, some surgeons recommend performing the orchiectomy at the same time as the vaginoplasty. Combining procedures also minimizes the risks if general anesthesia is used [116].

Orchiectomy is usually performed on an outpatient basis, but in some circumstances, it may require an overnight hospital stay. Intravenous sedation is generally used for the procedure. A midline incision is made in the scrotum, through which the testes are removed and the spermatic cords are cut as short as possible [120].

The patient should occasionally massage the incision (as needed) for one to two weeks after surgery to prevent scarring and adhesions. The scrotal skin can be kept supple by stretching and moisturizing the area on occasion. Postoperative pain is usually minimal. The patient is prescribed antibiotics to prevent infection, and a thin coating of an antibiotic ointment is applied to the incision site twice daily for two weeks. After two weeks, the area may be treated with aloe vera as needed. All activity is limited for the first 24 hours, and no heavy lifting should be done for two weeks [120].

Orchiectomy has the lowest complication rate of all GCSs [121]. One potential complication of the procedure is scrotal hematoma, which usually resolves spontaneously but may require aspiration, drainage, or even surgical removal to achieve the best result. If the scar does not heal properly, a skin graft may be necessary for subsequent vaginoplasty.

Voice Surgery

Some MTF transgender individuals will choose to undergo voice feminization surgery, particularly if voice therapy has not achieved satisfactory results. There are varying degrees of satisfaction, safety, and long-term improvement in patients who have had such surgery. The WPATH recommends that individuals undergoing voice feminization surgery consult a voice and communication specialist in order to maximize the surgical outcome, help protect vocal health, and learn non-pitch-related aspects of communication [71]. Voice surgery procedures are followed by sessions with a licensed and/or credentialed voice and communication specialist [71].

Historically, the most commonly performed surgery to raise the fundamental frequency of the voice was cricothyroid approximation. The procedure is commonly performed under local anesthesia with monitored anesthesia care. A small incision is made in the natural skin fold of the neck, and the thyroid cartilage is pushed against the cricoid cartilage that lies below it. The two cartilages are held together with sutures or metal clips. This increases the tension on the vocal cords by stretching them posteriorly, causing them to vibrate at a higher pitch. Postoperatively, patients are placed on vocal rest for 10 days to allow for the stretching of laryngeal soft tissues and reduce the risk of edema. Potential complications include difficulty swallowing, sore throat, and frequent throat clearing. Long-term follow-up has shown inconsistent results. Following surgery, the voice frequently has a falsetto quality. Some patients will experience a re-stretching of their vocal cords, even though the surgical sutures remain tight, which results in a drop in frequency back to the male range. If stretching occurs, it is usually evident within one to two months of the procedure [122].

Feminization laryngoplasty (FemLar) is a newer surgical technique that reshapes the larynx to make it smaller and the vocal cords shorter. In this procedure, a strip of the thyroid cartilage is removed, making the larynx smaller. The vocal cords are then stretched, and the front one-third to one-half of the cords are removed. A thyrohyoid elevation may also be performed at the same time to feminize a portion of the resonance chamber (pharynx). A thyrohyoid elevation consists of passing sutures around the hyoid bone to hold the larynx in an elevated position in the neck and shorten the pharynx. This surgery carries some significant risks, including potential loss of vocal range and volume. The vocal cords may also heal with an asymmetric tension, resulting in a rough voice. Granulomas may form on the inside of the larynx; these are either coughed out or removed. Other risks include infection, bleeding, and an occluded airway due to postoperative edema [122].

The Wendler laser reduction glottoplasty involves CO_2-laser de-epithelialization of the anterior commissure of the vocal cords and the anterior one-third of the two vocal folds. The two vocal folds are sutured, and fibrin sealant is applied to strengthen the stitches. Neither the larynx nor the muscles around it are altered; only the folds and cords are changed. Laser reduction glottoplasty is less invasive than either a cricothyroid approximation or FemLar. However, the changes are usually less impressive than with the other techniques, and the procedure is more effective in younger individuals [123].

Gender-Confirmation Surgery

GCS, also known as gender-affirmation surgery or sex reassignment surgery, should only be performed on individuals who have two referrals from qualified mental health professionals, have had 12 continuous months of hormone therapy (with some exceptions), and have had 12 continuous months of living in their identified gender role [71]. The primary goals of GCS for MTF individuals include the creation of a sensate and aesthetically realistic vulva, including the clitoris, labia minora and majora, and vagina; creation of a urethral opening that allows a downward urinary stream; creation of a stable and sensate neovagina with adequate dimensions for penetrative sexual intercourse; and preservation of orgasmic capability.

In most cases, GCS consists of several procedures, including bilateral orchiectomy, partial penectomy (penile dissection), vaginoplasty, labiaplasty, and clitoroplasty, that are performed in a single session. However, some surgeons prefer a two-stage approach, performing the labiaplasty and clitoroplasty after the initial vaginoplasty has fully healed. Construction of the neovagina is typically done using the inverted penile skin. However, in some cases, a segment of the rectosigmoid colon or skin grafts from the abdomen, buttocks, hips, or scrotum are used when sufficient vaginal depth cannot be achieved using penile tissue alone [124; 125]. Scrotal skin is generally used to create the labia.

Vaginoplasty using rectosigmoid colon segments has become increasingly popular, as it results in a functional, self-lubricating, deep neovagina with relatively few surgical complications. As the use of puberty-suppressing hormonal treatment in preadolescent patients has become more routine, penile and scrotal hypoplasia is common, making vaginoplasty with this tissue infeasible [126]. Some surgeons have begun to offer sigmoid vaginoplasty to all MTF individuals with a phallus length of less than 11.4 cm [127].

As a prerequisite to GCS surgery, patients often undergo genital electrolysis to remove hair from the scrotum and base of the penis in order to prevent intravaginal hair growth in the neovagina [116]. If the individual smokes, smoking cessation is recommended for at least one month prior to surgery and six months following surgery. Some surgeons also require that the patient's body mass index be less than 28 [128]. Two to four weeks before the surgery, estrogens are discontinued to prevent potential thromboembolic events. Any other medications that may inhibit blood clotting are also discontinued. The day/evening before surgery, a bowel preparation is necessary to evacuate the bowels. Some institutions

also recommend a skin scrub using chlorhexidine prior to surgery, and prophylactic antibiotics may be administered either the night prior to surgery or just before incision. The patient is kept NPO (nothing by mouth) after midnight prior to surgery, which is common to most surgical procedures [116].

Preoperative medical clearance for surgery typically includes a history and physical, CBC, an electrocardiogram (EKG) if the individual is older than 50 years of age, and a chest x-ray if the individual is a smoker or is older than 50 years of age. Cardiology clearance is needed if the patient has current or previous coronary heart disease, a pacemaker, automatic internal defibrillator, or arrhythmias [117].

A longitudinal incision is made in the perineum dorsal from the scrotal base to about 3 cm from the anus. Blunt dissection creates a space for the neovagina between the rectum and the bladder. The neovagina is positioned posterior to the prostate, which is left intact during this procedure [124]. The scrotum and testes are incised and an orchiectomy performed, with the skin preserved to form the labia majora. The spermatic cords are cut and ligated at the level of the external inguinal ring. Penile skin is dissected away from the corpora, and the urethra is divided from the cavernosa and cut at the usual female length. The urethra is then sutured through an opening at the female position. The penile skin is inverted to form the neovagina [31].

The labia are constructed using existing male genital skin segments. The labia minora are fashioned from the penile skin, or prepuce, while the labia majora are created using scrotal skin [124]. There are multiple techniques noted in the literature for creation of the neoclitoris. Most use a segment of the glans penis that remains attached to its dorsal nerve and blood vessels, known as the sensate pedicled clitoroplasty technique [124; 125; 129].

A prosthesis is inserted into the neovagina during surgery to maintain side-to-side junction of the penile skin flap and any other skin grafts used to create the vaginal walls while also maintaining maximum vaginal dimensions. This prosthesis is removed approximately five days after surgery, but regular dilation of the neovagina must be continued for the remainder of the individual's life in order to maintain vaginal depth and width [124]. Dilation techniques and schedules vary, but typically begin at three times daily and are gradually spaced to longer intervals [87]. Some recommend the use of progressively larger dilators to gradually widen and maintain the neovagina [117].

Hospital stays for GCS vary from two to eight days. Because many patients travel long distances to have GCS, there may be an additional stay at a local recovery or guest house for an additional two to six days after discharge from the hospital. Generally, patients are able to ambulate and resume a regular diet on the second postoperative day. Patient-controlled analgesics, antibiotics, compression hose, stool softeners, and anticoagulants may be prescribed [124]. A Foley catheter is inserted prior to surgery and left in place until approximately five to six days following vaginoplasty. Ice packs may be placed over the surgical site for the first 24 hours to reduce edema. Intraoperative venous thromboembolism prophylaxis in the form of subcutaneous heparin and sequential compression devices is essential [114].

The level of discomfort improves daily, and by the time individuals are discharged home, they are often no longer taking pain medication. It is recommended that the patient do no heavy lifting or straining for the first two weeks following surgery, followed by a gradual return to normal activity. Individuals may return to work in four to six weeks [120]. Surgeons generally recommend that sexual intercourse not be attempted for 8 to 12 weeks postoperatively [120; 130].

Potential complications of GCS include bladder damage, nerve injury, rectovaginal fistula, urethrovaginal fistula, urethral stenosis, vaginal stenosis, granulation tissue, and vaginal prolapse [117]. In a retrospective review of 117 patients who underwent penile inversion vaginoplasty, the most common complications were granulation tissue (26%), intravaginal scarring (20%), and prolonged pain (20%) [131]. The majority of patients (90%) were satisfied with the outcomes despite complications.

The main risk of GCS is rectal wall tear resulting in rectovaginal fistula, which is estimated to occur in 1 of 400 vaginoplasties [117]. This complication may develop in the immediate postoperative period or following discharge from the hospital. Symptoms include intestinal distress and intrusion of intestinal fluids, gases, and feces into the vagina. For a small fistula, the only clue may be a brown discharge. If rectovaginal fistula is suspected, a tampon may be inserted into the vagina and an enema of clear water with food coloring administered to determine if the tampon is stained [130]. Some fistulas spontaneously resolve as the neovagina heals. A liquid or low-residue diet will help during the healing process, and dilation and sexual intercourse should be discontinued. If the fistula does not heal spontaneously, surgical repair with skin grafts may be indicated.

Urethral stricture or stenosis is another common complication that usually presents as inability to or difficulty voiding, dysuria, diminished stream, and/or increased time and effort to urinate. If urethral stricture or stenosis occurs following the removal of the Foley catheter, the catheter should be reinserted for an additional two to three days until urethral swelling subsides and the patient is able to void without problem. Rarely, surgical revision may be required [124]. Urethral swelling or irregularities resulting in urine spray generally resolve several weeks following surgery.

The patient should also be monitored for partial or complete flap necrosis, which presents early in the postoperative course as non-blanching erythema or mottling of the skin that becomes progressively darker. If this is suspected, the surgeon should be notified immediately [124].

Vaginal bleeding and/or discharge may be a sign of hypergranulation. This complication can be treated with the application of silver nitrate or Monsel's solution. Some experts recommend treatment with intravaginal estradiol until the issue has been resolved [130].

Vaginal stenosis is often related to a lack of adherence to the vaginal dilation regimen [132]. Conservative treatment is gradual dilation with lidocaine 2% jelly or lidocaine (2.5%)/prilocaine (2.5%) cream to lubricate the dilators. Estradiol vaginal tablets or cream may also be used to soften the tissue [130].

Since the WPATH Standards of Care have been in place, there has been a steady increase in patient satisfaction with the outcome of GCS. The vast majority of follow-up studies have shown an undeniable beneficial effect of GCS on postoperative outcomes such as subjective well-being, cosmesis, and sexual function [71]. A meta-analysis of 32 studies found that positive results were achieved, both aesthetically and functionally, in most cases [125]. One study reported 90% of patients were satisfied with both aesthetic outcomes and orgasmic capability, although only 58% acknowledged sexual intercourse at that time. Orgasmic capability following vaginoplasty ranges from 63% to 92% [124].

Researchers from one facility reported maintenance of sexual sensation in 98.6% and achievement of orgasm (at least occasionally) in 94% of 71 MTF individuals after an average of 4.2 years following vaginoplasty [124]. A separate study reported decreased orgasmic ability but 75% more sex, resulting in high overall sexual satisfaction [124].

Due to the massive reconstruction necessary in vaginoplasty, postoperative orgasms may be more difficult to achieve. In some cases, transdermal testosterone or a phosphodiesterase-5 enzyme inhibitor (e.g., sildenafil, tadalafil, vardenafil) may improve a patient's ability to achieve orgasm [130].

Procedures that maintain attachment of the dorsal portion of the glans penis to the dorsal neurovascular bundle result in lasting neoclitorides and higher levels of sexual satisfaction [125]. Higher risk of sexual dissatisfaction is associated with techniques in which reattachment of the glans onto the dorsal neurovascular bundle was attempted.

An estimated 87% of MTF individuals experience improved psychosocial function following GCS [133]. A study of 247 MTF individuals showed that those who had GCS surgery had higher mental health quality of life ratings than those who did not have surgery. The mental health quality of life in postoperative individuals was not significantly different to that of the general female population [118]. In one study with a small sample of 19 patients who had received GCS (18 MTF, 1 FTM) two to five years previously, the subjects reported improved sexual experience and improved ability to initiate and maintain relationships [134].

An estimated 1% to 2% of individuals who have had GCS regret it; MTF patients with late (adult)-onset gender dysphoria are at the greatest risk for regret [18]. This may be a reflection of difficulties in making the transition to a different gender because of personal appearance or limited social skills. It is imperative for patients with late-onset gender dysphoria who have lived in their natal sex for a long time to understand the importance and impact of actually living as the other sex before undergoing GCS [18].

The costs of GCS range from $7,000 to $30,000 [20]. The estimated cost of GCS surgery (completed in one stage with penile inversion, clitoroplasty, and labiaplasty) plus hospital stay in a Philadelphia, Pennsylvania, transgender center is $19,500. In addition, breast implants are approximately $8,100 and facial and body augmentation surgeries range from $3,500 to $10,600. Due to the high cost of surgery and the paucity of surgeons, many transgender individuals in the United States seek care in Thailand or Canada. In Thailand, the total for all of these procedures can range between $9,000 and $20,000 [20].

SURGICAL MANAGEMENT FOR FTM TRANSITION

Surgical procedures commonly sought by FTM individuals include bilateral mastectomy and chest reconstruction ("top surgery") and bilateral salpingo-oophorectomy, hysterectomy, and metoidioplasty [87]. Less common procedures include phalloplasty, scrotoplasty, testicular implants, or vaginectomy ("bottom surgery") [108]. Many FTM individuals never undergo genital surgery, aside from hysterectomy or salpingo-oophorectomy [71]. In a survey of FTM individuals, the majority wanted to have or already had "top surgery," but only a slim majority desired metoidioplasty; a vast majority did not want phalloplasty, citing the cost, morbidity, donor site scarring, and relatively poor results of the procedure [39].

Some procedures can be combined, but it is advisable to limit surgery time to less than eight to 10 hours. For instance, a mastectomy, hysterectomy, and metoidioplasty can be performed in one session. Some clinics are able to perform a transvaginal hysterectomy, oophorectomy, vaginectomy, metoidioplasty, and scrotoplasty with testicular prosthesis in a single seven-hour procedure [117].

Eligibility for "top surgery" includes persistent, well-documented gender dysphoria, age of majority, capacity for decision making and giving informed consent, and one referral from a mental health professional [71]. Eligibility does not require hormonal treatment. Criteria for hysterectomy and ovariectomy include these requirements plus an additional referral from a mental health professional, control of any significant mental health concerns, and 12 months of continuous hormone therapy. If the patient desires a metoidioplasty or phalloplasty, he must also have lived in his chosen gender for 12 continuous months [71].

Preoperative medical clearance for surgery typically includes a history and physical, CBC, a pregnancy test or proof of hysterectomy, an EKG if older than 50 years of age, and a chest x-ray if a smoker or if older than 50 years of age. Cardiology clearance is needed if the patient has coronary heart disease, a pacemaker, automatic internal defibrillator, or arrhythmias. Generally, testosterone should be discontinued two weeks prior to surgery to lessen postoperative bleeding and hematoma, as testosterone affects the clotting cascade and increases antithrombin III. Preoperative cessation of testosterone may decrease the risk of hematoma by 50% [117].

Mastectomy

The presence of breasts in FTM individuals causes significant gender identity discomfort, and these patients, particularly those who have significant breast development, wear a breast binder daily in order to better pass as male. In many cases, binding is one of the first physical acts in the FTM transition process [135]. Bilateral mastectomy is the most common surgical procedure performed in FTM individuals [121]. Indeed, it may be the only surgical treatment undertaken by some FTM individuals because it greatly increases their ability to pass as a man and greatly improves their psychologic and social functioning [136].

There are two basic mastectomy techniques used in FTM surgery, based on the patient's anatomical classification: the periareolar, or "keyhole," approach with or without liposuction, or the double incision method using free nipple grafts. The periareolar technique is used when there is small or moderate breast size with little skin redundancy. For marked breast size with skin redundancy, the inframammary fold double incision technique is used [117].

Mastectomy is an outpatient surgery unless medical conditions require hospitalization, in which case an overnight stay for observation is indicated. The procedure takes two to three hours to perform, depending on the amount of skin and symmetry of the breasts [136].

The patient is discharged home with analgesics and antibiotics as well as a tensor bandage around the chest, which is kept in place for about one month. The compression garment helps to achieve a symmetric outcome. The patient may shower after three days with wound-closing adhesive strips kept in place, patted dry, and left intact until they fall off on their own in seven to 10 days. In some cases, home care nursing may be necessary to empty and monitor surgical site drains, which are removed at a follow-up visit three to seven days after the procedure. To prevent or minimize scarring, topical application of onion extract gel (Mederma), silicone gel (Scar Fade), or silicone sheeting or tape may be useful.

Moderate postoperative edema is normal, as is erythema that does not exceed 1 to 2 cm beyond the incision. It is not uncommon to see or feel the suture knots at the end of the incision, which may be trimmed if they work their way to the skin surface [124]. The patient is generally able to resume normal routines within one to two weeks, but should avoid strenuous activity for three to four weeks [136]. Potential complications following mastectomy include seroma, hematoma, infection, areolar spreading (with the keyhole technique), or nipple hypo/hyperpigmentation (usually temporary) [117].

CHARACTERISTICS OF PHALLOPLASTY AND METOIDIOPLASTY		
Feature	**Phalloplasty**	**Metoidioplasty**
Penile length	7 inches	1–6 inches
Surgical stages	1 to 3	1
Length of surgery	11 hours	2 to 4 hours
Days in hospital	5 to 7	2 to 5
Orgasm	Possible	Possible
Erection	Possible	Not possible
Penetration	Possible	Not possible
Ejaculation	Not possible	Not possible
Procreation	Not possible	Not possible
Void standing	Possible	Possible
Usual cost	$40,000–$150,000	$5,000–$20,000

Source: [117] *Table 6*

FTM individuals who received top surgery report a higher quality of life than FTM individuals who have not received surgery [50]. The prices of subcutaneous mastectomies/mammoplasty range from $5,000 to $7,900 in the United States [20].

"Bottom Surgery"

"Bottom surgery" includes procedures such as hysterectomy, salpingo-oophorectomy, vaginectomy, metoidioplasty/phalloplasty, scrotoplasty, and urethral lengthening. The timing of these procedures varies by surgeon; some perform the hysterectomy and salpingo-oophorectomy in one procedure along with genital reconstruction, while others complete the hysterectomy, salpingo-oophorectomy, vaginectomy, and urethral lengthening in the first session, followed by a separate metoidioplasty or phalloplasty four to six months later [136].

Hysterectomy

Hysterectomy with oophorectomy is generally performed as a total laparoscopic hysterectomy procedure. Vaginal hysterectomy or a laparoscopically assisted vaginal hysterectomy is difficult in transsexual women who have been taking testosterone, as this treatment results in a small, non-compliant, and atrophic vagina [137].

Vaginectomy

Vaginectomy is often performed in combination with metoidioplasty or phalloplasty. It involves removal of the vaginal mucosa, with approximation of the levator ani muscles to obliterate the dead space. The procedure is relatively safe, with few complications (e.g., reopening of the surgical site) [108; 117].

Metoidioplasty

In some cases, the clitoris becomes sufficiently hypertrophied after testosterone exposure to serve as a microphallus. Otherwise, a phalloplasty or metoidioplasty may be performed (***Table 6***). The choice of technique may be restricted by anatomical or surgical considerations or the patient's financial considerations. If a patient wishes to have a phallus of good appearance, the ability to urinate while standing, sexual sensation, and/or coital ability, there are several separate stages of surgery and frequent technical difficulties that may require additional operations. Even metoidioplasty, which in theory is a one-stage procedure for construction of a microphallus, often requires more than one surgical procedure, and the goal of standing micturition with this technique cannot always be ensured [71].

Metoidioplasty involves elongation and reconstruction of the hormonally enlarged clitoris as a small neophallus with erectile function, analogous to penile tissue. During this procedure, the clitoris is released from its surrounding tissue and a flap of skin from the labia minora is wrapped around the clitoris to create a small phallus. The resulting neophallus is sensate. With ring metoidioplasty, a variation of the simple metoidioplasty, the urethra is lengthened using a flap of tissue from the anterior vaginal wall and labia minora to create the urethral extension. This carries urine to the distal end, similar to a natural penis. This procedure is less complex than a phalloplasty, has fewer complications, and has the benefit of providing greater erogenous sensation. However, the resulting neophallus is often not large enough to use for sexual penetration. Using this technique results in an average phallus length of 5.7 cm, with a range of 4–10 cm [136]. Testicular implants may be placed in the labia majora as part of the procedure.

If urethral lengthening is not performed, patients are kept in the hospital overnight. If urethral lengthening is performed, it may require a suprapubic catheter for two to four weeks until the urethra heals. For simple metoidioplasty with testicular implants, recovery time is about three weeks. Ring metoidioplasty and hysterectomy have a six-week recovery period.

Possible complications of metoidioplasty include hematoma, urethral stricture or fistula, urinary incontinence, spraying or dribbling urine (usually due to inflammation), bleeding, flap necrosis, and rarely, infection [108; 117]. Other problems that may arise include migration of testicular implants, reopening of a vaginectomy, or hypergranulation along suture lines [108].

Phalloplasty

The goal of phalloplasty is the creation of a neophallus that is aesthetic and has tactile and erogenous sensation, the ability to urinate from a standing position, and the ability to penetrate (with implantation of a penile prosthesis). Ideally, the procedure should result in minimal donor site morbidity and be completed in one to two operative procedures [117]. In phalloplasty, free or pedicled flaps of tissue removed from the radial forearm, myocutaneous latissimus dorsi, osteocutaneous fibula, and/or anterior lateral thigh or groin/abdomen are used to construct a neophallus. A scrotum may be constructed from the labia majora along with implantation of testicular prostheses.

In a pedicled flap, tissue is left attached to the donor site and simply transposed to a new location, keeping the pedicle intact as a conduit to preserve blood supply to the tissue. The advantages of a pedicled flap phalloplasty include decreased operative time, lower failure rates, and more easily concealed donor sites. In the pedicled pubic phalloplasty, the penis is created from a flap of anterior abdominal wall skin (11 cm wide and 12 cm long) that is anchored at the clitoris [138]. The neourethra is fashioned from skin from the labia majora. Both the neourethra and the flap are rolled over an 18 French catheter and anastomosed to the native urethral meatus. The penis created in this manner is sometimes rigid enough for penetrative sexual intercourse without a prosthesis. However, the disadvantages are a less aesthetic appearance and less sensation, making insertion of a penile prosthesis riskier [117].

In a free-flap procedure, the surgeon uses a flap of tissue (usually from the forearm) rolled into a tube to create the urethra, which is then rolled within a larger flap that includes fat and skin to make a "tube within a tube," resulting in an adult-sized phallus that transmits urine. The ulnar side of the forearm is generally used because of the reduced hair growth [136]. Alternatively, a radial artery-based forearm free flap graft may be used to create a urethra [139].

The advantages of a free radial forearm flap include the relative hairlessness of the donor site, the pliability of the flap, increased erogenous sensation, and the ability to do the urethral reconstruction in a single session. The disadvantages are that the donor site cannot be closed primarily and may be difficult to conceal and a rigid prosthesis is usually required for penetration. With the introduction of perforator flaps, the anterolateral thigh flap has begun to replace the radial forearm free flap as first choice. Benefits of the anterolateral thigh flap are a hidden donor area and lack of microsurgical expertise requirement. Possible complications include flap failure, urethral fistula, urethral stricture, and stiffener-related problems [140]. When combined with radial forearm free flap urethral reconstruction, anterolateral thigh flap phalloplasty has been shown to be a feasible alternative for FTM patients who desire a less conspicuous scar [141].

In an attempt to preserve nerve function, and therefore erotic sensation, the pre-existing clitoris is often de-epithelialized and covered by the base of the newly created phallus. The most common complications of this procedure are urologic fistula or stricture. In a survey of 287 patients, virtually all had tactile sensation after one year and 80% reported erogenous sensation. Establishing anatomic and functional stability of the neophallus can take about one year, at which time an erectile prosthesis may be inserted [117].

Various procedures have been developed to provide rigidity for penetration, including insertion of autologous cartilage or bone, rigid implants, or an inflatable prosthesis, but these procedures, and their outcomes, remain problematic [18]. A hydraulic erectile prosthesis is the best option for achieving the possibility of sexual intercourse, though there is a high complication rate due to infection. The life expectancy of this type of implant is about 50% after four years [142].

General surgical risks of phalloplasty include infection, deep vein thrombosis, pulmonary embolism, and death. In a review of 7,905 transgender patients, phalloplasty had the largest rate of complications, mainly from infection and delayed wound healing [121]. Prevention of these complications may be possible with appropriate postoperative interventions, such as sequential compression devices; management of intravenous hydration; turn, cough, and deep breathing; close monitoring of patient status and medication regimen; and ambulation as ordered [136]. The donor site also requires careful assessment. An occlusive dressing is maintained over the donor site for five days, followed by a sheet of gauze that assimilates into the eschar and may be trimmed as it peels up from the edges over the next two weeks. Sensation and function are often impaired in the hand distal to the flap donor site, but this generally resolves within a few weeks. However, approximately 5% of patients require long-term physical therapy to fully recover, so sensation and movement of the donor site should be monitored [136].

A major complication of phalloplasty is partial or complete flap necrosis, which can lead to loss of the neophallus. This often presents early in the postoperative course as a blanching erythema or skin mottling that becomes continually darker. Postoperatively, the phallus is monitored hourly for temperature, color, turgor, pulse, and capillary refill for two days to assure that vascularity is maintained. If signs of necrosis occur, the surgeon should be notified immediately.

Urethral fistulas occur in up to 45% of phalloplasty procedures [124]. This is characterized by urine flow from sites other than the urethral opening. It should be assessed, but urethral fistulas often resolve spontaneously after two to three weeks. They should be kept clean and monitored during this period.

Fistulas that do not heal require surgical revision. Urethral stricture presents as a progressive inability to urinate and may be accompanied by fistulas. Both stricture and fistulas commonly occur at the site where the neourethra is anastomosed to the existing urethral meatus. Correction requires dilation under anesthesia, and if this is unsuccessful, surgical revision will be necessary.

After hospital discharge, the patient is usually seen in the office in five to seven days, at which time the catheter is removed and antibiotics may be discontinued if healing is adequate [136]. It is also important to inspect the phallus and scrotum (if scrotoplasty was done simultaneously), as well as the skin and vein graft sites.

Scrotoplasty

Scrotoplasty is the surgical creation of a scrotum. This procedure is considered very important to many FTM individuals; a survey of 200 FTM individuals undergoing GCS found that 96% desired scrotoplasty, compared with 52% who desired phalloplasty [124]. This procedure is accomplished by hollowing out the labia majora to create the scrotal space and inserting testicular implants. Risks specific to scrotoplasty, while rare, include implant ejection, rupture, and migration or dislocation, which may require surgical removal and replacement later on [108; 124]. Some surgeons will perform scrotoplasty simultaneously with metoidioplasty or phalloplasty, while others prefer to do the scrotoplasty in a separate procedure, using tissue expanders for three to six months to create space for the testicular prostheses. The incision site should be monitored for increased drainage, visible extrusion of testicular prostheses or erectile prosthesis, and inflammation or changes in the size and shape of the scrotum.

SATISFACTION AND SEXUAL FUNCTION FOLLOWING SURGICAL TRANSITION

Generally, there is high satisfaction with GCSs in both MTF and FTM individuals. Of those who are unsatisfied, dissatisfaction is related to long-term complications and functional/aesthetic outcomes [143]. Factors associated with surgical regret include [144]:

- Age older than 30 years at first surgery
- Personality disorders
- Social instability
- Dissatisfaction with surgical results
- Skipping the "real-life experience"
- Improper hormone therapy
- Surgical approval letters from inexperienced mental health providers
- Poor partner or family support

Psychologic symptoms and life dissatisfaction at baseline are associated with treatment dissatisfaction at follow-up, emphasizing the importance of a thorough and accurate psychologic assessment prior to GCS [143].

There has been very little research on sexual function after GCS, and data are largely the result of self-reports. Not surprisingly, there is a correlation between sexual function and the quality of the neovagina or neophallus. While not all postoperative transsexual patients are orgasmic, they tend to report experiencing much greater sexual satisfaction [97]. One small survey conducted in the United Kingdom reported high overall satisfaction and no regret starting genital GCS among 10 FTM patients who had previously undergone suprapubic pedicle-flap phalloplasty and 15 who had undergone radial forearm flap phalloplasty. All patients who could achieve orgasm before GCS could achieve orgasm after surgery and the vast majority reported preserved erogenous sensation [145].

LIFELONG PREVENTIVE AND PRIMARY CARE

Very little has been published regarding the unique ongoing healthcare needs of patients who have undergone gender confirmation. In general, health care should be based on the treatments the patient has received and at what stage he or she may be in the gender transition. Health promotion awareness and health screening will vary somewhat, but generally the patient will have the same needs as most adult patients in a primary care setting; the patient's gender confirmation process will have little effect on many aspects of health care [81]. Basic preventive services, like sexually transmitted infection testing and cancer screening, can be provided without specific expertise in transgender care [57]. Keep in mind that in some cases, older transsexual individuals may not disclose their transgender history to their healthcare providers, as they initially sought treatment at a time when it was common for providers to use very strict guidelines to determine who could and could not receive treatment [30].

ROUTINE CARE FOR MTF PATIENTS

For the MTF patient, the routine physical exam includes a breast exam, prostate exam, and Pap test.

Breast Exam

Annual breast exam, including mammogram, is indicated in MTF women who are older than 50 years of age who have been taking estrogen for five or more years [57]. While this is recommended as a screening protocol, the actual risk is likely no different than in natal males. In a series of 2,200 MTF individuals studied between 1975 and 2005, there were no cases of breast cancer reported [99].

When breast cancer does occur among MTF individuals, the onset of symptoms (usually a palpable mass) occurs earlier than in natal females, at an average age of 51 years [146]. The most common type of cancer in this population is adenocarcinoma, accounting for 59% of all reported cases. There is no evidence to suggest that estrogen administration results in an increase in breast cancer. Given an earlier age at presentation, consideration should be given to starting breast cancer screening before 45 years of age. In addition, breast implant-associated anaplastic large-cell lymphoma is a concern for MTF individuals who have had breast implants. Clinicians should have a high degree of suspicion when these patients present with late periprosthetic fluid collection [146].

Prostate Exam

Prostate examinations should be performed as part of an annual physical examination [57]. The prostate gland is not removed in GCS; however, because the patient has likely been on estrogen, the prostate is generally atrophied. The risk of prostate cancer is small, as estrogen inhibits the effect of testosterone. There has been a case report of benign prostatic hyperplasia in an MTF individual 25 years after GCS and continuous estrogen therapy. The patient required transurethral resection of the prostate gland due to obstruction of urinary flow [147]. The authors hypothesize that mutations of androgen receptors on the prostate can cause the receptors to work "normally" even in the absence of androgens. As such, performing a transvaginal digital prostate exam on an MTF individual may be of value [148].

Pap Test

Opinion varies regarding the need for Pap testing in postoperative MTF individuals. On one hand, there is no possibility of cervical dysplasia. However, the penile skin that lines the vagina can show the same cytologic findings as biological females. Cytologic samples from postoperative MTF individuals have shown a greater incidence of inflammation than in natal women, and only about 4% of MTF individuals have identical cytology to natal women [149]. Because the glans penis is used to create a clitoris, a Pap test of this area may be used to screen for squamous cell carcinoma. While cancer of the glans penis is rare, the glans is more prone to cancerous changes than the skin of the penile shaft, and intraepithelial neoplasia of the glans is more likely to progress to invasive carcinoma than is intraepithelial neoplasia

of other penile skin [57]. It is theorized, though not proven, that the incidence of HPV in postoperative MTF individuals is similar to that of men [148].

Bone Health

Bone health should be monitored in MTF individuals according to guidelines for female patients. However, the risk of osteoporosis is low, particularly if the individual has been maintained on estrogen supplementation.

Genitourinary Health

Postoperative MTF patients may present with symptoms of vaginitis, with or without malodorous discharge. In a study of postoperative MTF individuals, there was a higher incidence in inflammation in the neovaginas than in the vaginas of cisgender women, probably due to the fact that penile skin is normally ectopically located [150]. Screening for bacterial vaginosis in MTF patients is complicated by the fact that the microflora of the neovagina includes mixed species of gram-negative and gram-positive bacteria normally found either on the skin, in the intestinal microflora, or in a bacterial vaginosis microflora. Also, the mean vaginal pH of the neovagina is 5.8, as opposed to the more acidic microflora of the biologic vagina, which is 3.8 to 4.5 [150].

Postoperative MTF individuals who are sexually active with men may experience a build-up of sebum, lubricant, semen, and sometimes granulation tissue in the neovagina, resulting in a malodorous vaginal discharge. If present, treatment consists of metronidazole and fluconazole and douching with plain water [130].

Aging postoperative MTF patients may have increased risk for genitourinary complications caused by the compounded effects of aging and postsurgical complications [30]. Complaints of frequency, hesitancy, urgency, and dysuria should be followed up as with other patients, keeping in mind that the complaints could be prostate-related.

Prolactinoma

It is recommended that MTF transgender patients receiving estrogen therapy have an annual prolactin level assessment and visual field examination to screen for prolactinoma [57]. Prolactinoma is the result of a benign adenoma of the pituitary gland and results in hyperprolactinemia, hypopituitarism, headaches, and bilateral loss of vision.

ROUTINE CARE FOR FTM PATIENTS

For the FTM patient, any residual female organs will require lifelong modified physical exams and risk screenings. These patients may require occasional modified pelvic exams and/or mammograms, and both the provider and the patient may have difficulty finding a comfortable clinical environment [37]. For FTM individuals, gynecologic examinations can heighten their emotional conflict between self-perception and physical anatomy. Respectful communication that maintains dignity, agency, and control is central to mitigating distress during pelvic exams [146]. The routine physical exam should include a breast exam, Pap test, and assessment of bone health and other possible effects of long-term testosterone supplementation.

Breast Exam

Among FTM individuals who have not had a mastectomy, the risk of breast cancer is likely similar to cisgender females. Those who have had mastectomy seem to have a lower risk of breast cancer, possibly due to GCS, but this is based on limited research [151]. Excess exogenous testosterone can be converted to estrogen, which has been linked to breast cancer [152]. As such, regular examination of remaining breast tissue is indicated. Although a mastectomy may have been performed, the axillary lymph nodes should be examined for enlargement. If a mastectomy has not been performed, annual mammograms are recommended.

Pap Test

For patients using androgen therapy who have not had a complete hysterectomy, there may be an increased risk of endometrial and ovarian cancer [57]. Therefore, a regular Pap test is indicated. It is important to be sensitive when performing a pelvic exam on a transsexual man. As noted, FTM individuals often experience emotional and psychologic distress with pap testing due to gender dissonance. This may be given as a reason for avoiding gynecologic examinations altogether [146]. It may be difficult to get a good sample, as the cervix will be atrophic; intravaginal estrogen cream can be used a few days prior to the Pap test to improve results.

Other interventions to consider are the use of a pediatric or long, narrow speculum; use of non-interfering lubricant on the speculum; application of topical lidocaine to the vaginal introitus; and informing FTM individuals of the likelihood of Pap test results being unsatisfactory [153; 154]. In some cases, providers may consider the use of sedative-hypnotics (e.g., benzodiazepines) prior to testing [154].

EVIDENCE-BASED PRACTICE RECOMMENDATION

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 and have a higher rate of inadequate cytologic sampling. 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.

(https://transcare.ucsf.edu/sites/transcare.ucsf.edu/files/Transgender-PGACG-6-17-16.pdf. Last accessed July 13, 2021.)

Level of Evidence: Expert Opinion/Consensus Statement

Long-Term Effects of Testosterone Therapy

Aging FTM patients may have an increased risk of cardiovascular disease and diabetes due to the effects of long-term testosterone and should be screened accordingly [30]. A small amount of research indicates that FTM individuals on long-term testosterone therapy do not have an increased risk of low bone mass [155]. Part of testosterone is converted to estradiol at levels that will support bone mineral density [99]. Dual-energy x-ray absorptiometry screening is suggested for FTM individuals older than 65 years of age, or after 50 years of age if not on testosterone [156].

CONSIDERATIONS FOR ALL TRANSGENDER PATIENTS

After GCS, hormone therapy will be continued. The usual dose of estradiol in MTF individuals is approximately 50 mcg per day, and in FTM patients, the dose of testosterone is typically the same as that used preoperatively: 200 –250 mg every two weeks in parenteral form or 5–10 g per day in gel form [18]. However, large, long-term studies are needed to assess the long-term risk of disease, especially cardiovascular disease and cancer, particularly in older patients and in those who have had prolonged exposure to sex hormones. Another unresolved question is whether there is an age at which cross-sex hormone treatment should be discontinued [18].

Continued psychologic counseling may help individuals consolidate their sense of self and cope with issues of disclosure, love, and work in the new role. Some individuals deal with issues of disappointment and grief over lost opportunities, loss of youth, or loss of relationships due to transitioning [7].

Sexual orientation varies as widely among the postoperative transgender population as it does in the general population. Postoperatively, FTM individuals generally have a preference for a female partner with a heterosexual orientation who is typically feminine, although a minority identify as gay males and seek out male partners [157]. In one study, female partners of FTM individuals reported being

as satisfied as women in a control group who were partnered with biological males [158]. Researchers found that intercourse in the couples with a FTM partner was usually initiated by the transsexual partner, whereas in the traditional heterosexual couples, the initiation was evenly distributed [158]. Female partners of FTM individuals explain that the success of their relationship is due to respect, honesty, trust, love, understanding, open communication, and the fact that the transsexual partner knows and understands women. The main drawback reported was the inability to have biologic children [158].

Conversely, postoperative MTF individuals are more heterogeneous in their choice of sexual partner. An estimated 60% are attracted to women and identify as lesbian or bisexual [39].

MANAGEMENT OF TRANSGENDER CHILDREN AND ADOLESCENTS

With greater public awareness of transgender issues, more adolescent and pre-adolescent children are expressing a desire to be a member of the opposite sex. While gender dysphoria in children does not necessarily continue into adulthood, its persistence into adolescence increases the likelihood that it will continue [71]. In the United States, informed consent laws prevent minors from consenting to their own medical treatment until 18 years of age unless they have the consent of a parent or guardian [159]. Because of this, providers traditionally waited to provide treatment until transgender children reached the age of legal consent to medical treatment, even though these adolescents made it clear that they found their pubertal physical changes unbearable [21]. Gradually, some providers have decided to treat individuals younger than 18 years of age with hormones to either suppress puberty or bring about the physical changes of the desired gender, provided there is parental consent. Multidisciplinary teams in the Netherlands have been pioneers in the treatment of transgender children [160].

When transgender children begin school, they begin to suppress cross-gender activities, as pressure from peers, parents, and schools quickly represses these unwanted behaviors. Children then become secretive. The behavior can be changed, but the internal sense of gender remains. However, for 75% to 80% of children who exhibit gender dysphoria, the disorder does not persist into adolescence, and complete gender role change and hormone treatment is not recommended in prepubertal children [17].

In general, psychologic therapy and support can assist transgender children/adolescents to complete developmental tasks on schedule, achieve self-acceptance and understanding, and manage and cope with social problems (e.g., peer and/or family conflict) and the stress of the change process [159]. Three models of therapy for children who display gender dysphoria have been described. The first of these is affirming approaches, based on the concept that being transgender is not a mental illness [28]. This approach encourages the child's exploration of gender identity and assists the child and his or her family to explore interventions such as social transitioning and hormone therapy. Dreger defines this approach as the "accommodation" mode [161]. The second treatment approach involves supportive therapies—a "wait and see" approach to determine how the child's gender identity unfolds. With this approach, there are no gender-related interventions. The third approach is a "corrective" approach that seeks to align the child's gender identity with his or her biological sex. This approach is also described by Dreger as the "therapeutic" model that views the child's gender dysphoria in terms of familial dysfunction and seeks to guide the child into a less stressful, more sustainable family environment and gender identity [161]. This last approach has been generally dismissed or condemned by organizations like the APA [162].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American Academy of Child and Adolescent Psychiatry recommends that clinicians should be aware of current evidence on the natural course of gender discordance and associated psychopathology in children and adolescents in choosing the treatment goals and modality. It is important to distinguish those who display only variation in gender role behavior (gender nonconformity, which is not a DSM diagnosis) from those who also display a gender identity discordant from their socially assigned birth gender and biologic sex.

(https://www.jaacap.org/article/S0890-8567(12)00500-X/fulltext. Last accessed July 13, 2021.)

Level of Evidence: Expert Opinion/Consensus Statement

In a qualitative study of FTM individuals, an early childhood sense of body-mind dissonance was the first sign of a transgendered identity [163]. Specifically, young FTM individuals believe themselves to be boys, prefer to play as boys, and balk at imposed feminine dress. This resulted in feelings of anger, frustration, and confusion for children as well as their parents. In American society, female children are often allowed more latitude in their dress, mannerisms, and play. The label of "tomboy" does not carry the same stigma that the label "sissy" carries for boys. As a result, in FTM individuals, gender dysphoria tends not to become an issue until puberty, with the onset of unwanted physical and emotional changes. At this time, FTM individuals often describe female secondary sex characteristics and menstruation as "repugnant" and "humiliating" [163].

In MTF individuals as well, gender dysphoria generally intensifies when adolescents develop unwanted secondary sex characteristics. Many gender dysphoric adolescents actually begin living in their true gender upon entering high school and desire hormones and surgery at that point. High levels of emotional distress, major depression, suicidality, and gender-related psychologic and physical abuse during early adolescence were reported in a large study of MTF individuals [42]. The depression is thought to be a product of the strain and confusion associated with forming a sexual identity that is at odds with societal norms. This research strongly suggests that psychologic and physical abuse play a major role in the incidence of depression.

Mallon and DeCrescenzo provide an overall review of the developmental needs of transgender children and adolescents and offer many suggestions for responding to the child in a healthy manner [164]. One such suggestion is that parents develop a "script" they can use to answer questions from neighbors and friends to decrease the possibility of harm to a transgender child. Because many transgender children who are not met with empathy and compassion become runaways or end up in foster care or the judicial system, much education needs to be done in these arenas as well.

Although it may be difficult for a parent to come to terms with having a transgendered child, it is possible; most parents report a resiliency beyond what they had imagined [116]. Parents worry about facing rejection by their families and the community and a general fear of the unknown. Despite these fears, many parents eventually accept their child's transition. For parents, a successful transition entails holding onto the essence of the love they had for their child and the moral worth of their child [116]. Parents who struggle with feelings related to their child's transgender identity could benefit from joining a support group of other parents of transgender children in order to obtain education, perspective, and strength from those who have faced similar challenges. These parents can then be a better resource for their children and more effectively engage in honest and open dialogue [116].

HOMELESSNESS

Because of estrangement from their families, lack of affordable housing, mental health and addiction problems, and emotional and physical abuse, as many as one in five transgender youth become homeless, and transgender youth are disproportionately represented in the homeless population of the United States [48]. Most homeless shelters are segregated by birth sex, regardless of the individual's gender identity, and homeless transgender youth may even be ostracized by agencies that serve their LGB peers. Moreover, transgender youth have fewer legal protections from job and housing discrimination than other sexual minorities and often face additional complications in obtaining appropriate care. Lack of stable housing can compound problems in gaining or maintaining employment, further lessening life stability. Evidence suggests that because of this lack of housing or employment, many homeless transgender people turn to survival sex, which obviously increases their risk for exposure to sexually transmitted infections and becoming victims of violence. Street youth may also go to great lengths to access body-altering substances (e.g., illegal silicone injections, hormones) because they wish to halt the development of secondary sex characteristics [48].

MEDICAL TREATMENT

Notice

Since 2021, several states have passed laws limiting or banning gender-affirming care for patients younger than 18 years of age; some states have proposed limiting care in patients up to 26 years of age. As always, it is important that healthcare professionals consult state board rules and laws governing their practice to ensure they are practicing legally.

Medical interventions for transgender children and adolescents fall into three categories or stages: fully reversible interventions, which include puberty-suppressing hormones; partially reversible interventions, which include cross-gender hormones; and irreversible interventions, which are surgical procedures. It is recommended that treatment progress from one stage to another with enough time for the patient and her or his family to fully integrate the effects of each stage [71].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Endocrine Society suggests that adolescents who meet diagnostic criteria for gender dysphoria/gender incongruence, fulfill criteria for treatment, and are requesting treatment should initially undergo treatment to suppress pubertal development.

(https://academic.oup.com/jcem/article/102/11/3869/4157558. Last accessed July 13, 2021.)

Level of Evidence: Weak recommendation based on low-quality evidence

Some providers believe that adolescents with gender dysphoria should experience the initial changes of their biologic, spontaneous puberty because their emotional reaction to these first physical changes has diagnostic value. However, to these youth, experiencing full biologic puberty is undesirable. Not stopping the development of secondary sex characteristics may result in emotional impairment, and the physical outcome following intervention in adulthood is less satisfactory than intervention before puberty, creating lifelong disadvantages. In males, these permanent changes include the development of laryngeal prominence, low voice, large jaws and brow, large stature, and male hair patterns. In females, these changes include short stature and large breasts. Pubertal suppression maintains end-organ sensitivity to sex steroids observed during early puberty, enabling satisfactory cross-sex body changes with low doses and avoiding irreversible characteristics that occur by mid-puberty [17]. By blocking, delaying, or "freezing" puberty, time is "bought" for providers to thoroughly explore the child's request for GCS [21]. The WPATH recommends commencing treatment when adolescents have reached early-to-advanced puberty (Tanner stage 2 to stage 4) [71].

Suppressing the effects of puberty is commonly done with GnRH agonists. GnRH agonists, commonly goserelin and leuprolide, initially overstimulate the secretion of gonadotropin, during what is called the flare period. Ultimately, this down-regulates and inhibits the secretion of gonadotropin, which in turn inhibits release of LH and FSH. In males, this suppresses the production of testosterone and sperm. In females, this suppresses ovulation and estrogen production.

GnRH agonist administration should begin before it is too late to reverse the physical changes of puberty. This is possible during Tanner stage B3 (breast bud extending beyond areola) in girls and during Tanner stage G3 (increase in testicular volume of ≥4 mL, with measurable nocturnal testosterone values) in boys. After testosterone production commences (testicular volume ≥10 mL), virilization becomes irreversible [18].

Prolonged pubertal suppression using GnRH agonists may continue for a few years. The effects are reversible and should not prevent resumption of pubertal development if treatment is stopped. In males, spermatogenesis will resume, along with the development of male secondary sex characteristics. In females, ovulation will occur, though there are not enough data to predict the timing [17]. There are no good data yet of the long-term effects of leuprolide on children with gender dysphoria, but the effect of GnRH agonists on bone density is being studied [161]. Due to the delay in bone density accrual in patients undergoing pubertal suppression, healthcare providers are advised to follow the patient's bone health annually and to consider annual dual-energy x-ray absorptiometry [165]. It is believed that when either cross-sex hormone therapy is initiated or biologic puberty is allowed to take place, bone mineral density will increase [21].

Laboratory work should be done prior to the initiation of therapy to establish baseline levels of gonadotropins, sex hormones, and metabolic determinants. This would include fasting glucose, cholesterol, and renal and hepatic studies. Measurements of height, weight, sitting height, hip and waist circumferences, and Tanner pubertal stage can be recorded initially and re-evaluated periodically to track growth and development [159].

To date, there seem to be no ill effects of GnRH agonists on social, emotional, and school functioning, but potential effects may be too subtle to observe during the follow-up sessions by clinical assessment alone [21]. One potential disadvantage in treating MTF individuals early in puberty is that the penis and testes will not fully develop, making surgical creation of a vagina from penile and scrotal tissue more difficult [71].

Some experts recommend initiating cross-sex hormone therapy at 16 years of age, using a gradually increasing dose schedule [17]. Others advocate using age 16 as a guideline but also considering starting cross-sex hormones earlier on a case-by-case basis after reviewing the potential risks and benefits with the youth and the parents [28]. In MTF individuals, hormone therapy would start with 17β estradiol at 5 mcg/kg per day and increase every six months to a maximum of 2 mg per day [28]. In FTM individuals, treatment starts with intramuscular injections of testosterone at 25 mg/m2 every two weeks, increasing the dose every six months to a maximum 100 mg/m2 every two weeks. At first, the dosage may not be high enough to suppress endogenous hormone secretion, so the recommendation is to continue treatment with GnRH agonists until gonadectomy is performed. Surgery should be deferred until individuals reach the legal age of majority and have lived continuously in their desired gender for 12 months. In the case of FTM patients, chest surgery could be carried out earlier, preferably after some time of living in the desired gender role and after one year of testosterone administration [71].

In the first year of cross-sex hormone therapy, patients should be monitored every three months, particularly while their hormone dosages are being adjusted, to maximize desired effects, minimize negative effects, and screen for complications [28]. Individuals may be monitored less often after they achieve stability in their dosing and are progressing well in their transition.

Beginning treatment for gender dysphoria at puberty appears to be associated with better psychologic outcomes than beginning treatment in adulthood, by which time irreversible secondary sex characteristics may pose lifelong barriers to successful sex reassignment. Additionally, limited observational data from transgender youth have indicated that gender dysphoria is reduced and relationships and academic skills are improved when therapy is started early [18]. The first longitudinal study of 55 transgender youth (22 MTF and 33 FTM) who received puberty suppression, cross-sex hormones, and in some cases GCS, was performed in the Netherlands in 2014 [160]. The researchers reported that gender dysphoria and body-image difficulties persisted through puberty suppression but remitted after the administration of cross-sex hormones and GCS. None of the individuals reported regret during puberty suppression, cross-sex hormone administration, or after GCS. Psychologic functioning improved steadily over time, and overall well-being was comparable to non-transgender peers. In fact, a higher percentage of the transgender study group was pursuing higher education than the general public. The researchers speculated that this success was not only due to the medical treatment but also due to access to care (covered by health insurance) and the involvement of a multidisciplinary team of mental health professionals, physicians, surgeons, and supportive parents [160].

EDUCATION OF HEALTHCARE PROFESSIONALS

Transgender care is generally lacking in medical school curricula. Among 132 U.S. and Canadian medical schools surveyed in 2011, the median reported combined hours dedicated to LGBTQIA content was five hours [166]. One-third of medical schools reported no hours of LGBT content during clinical years, and less than 40% of medical schools taught transgender-related content, such as GCS, body image, or transitioning, despite research that shows that medical students who have clinical exposure to LGBTQIA patients during their training perform more comprehensive histories, have a more positive attitude toward these patients, and possess greater knowledge of LGBTQIA healthcare concerns than students with little or no clinical exposure [56]. In addition, the results of one survey indicate that, contrary to official American Public Health Association policy, public health schools seldom offer planned curricula that address comprehensive LGBT health [167]. Barriers to increased transgender health exposure include limited curricular time, lack of topic-specific competency among faculty, and underwhelming institutional support [168].

Coverage of transgender care is also lacking from most nursing education. A review of the top 10 nursing journals from 2005 to 2009 found only eight articles (out of nearly 5,000) that focused on LGBT issues and only one that mentioned transgender issues [169]. None of the eight articles came from U.S. researchers. As stated, in 2010, the National Student Nurses Association adopted a resolution to include LGBT content in nursing school curricula to improve cultural competence, with additional resolutions adopted in 2015, 2016, 2019, and 2021 [68].

The American Association of Colleges of Nursing's *The Essentials of Baccalaureate Education for Professional Nursing Practice* does not directly address transgender health in the curriculum [170]. Likewise, the Quality and Safety Education for Nurses initiative excludes transgender issues as well [171].

The consensus model for Advanced Practice Registered Nurse (APRN) Regulation includes six populations for APRN licensure: adult/gerontology, pediatric, neonatal, family/individual, psychiatric/mental health, and women's health/gender-related. As of 2021, there were no specialty examinations available to nurses who may be interested in specializing in care for the LGBT community [172]. The American College of Nurse-Midwives supports the WPATH guideline and expects midwives to become knowledgeable about the healthcare needs of transsexual, transgender, and gender non-conforming people. With proper training, midwives may provide hormone therapy for transgender individuals [173].

Fifty percent of transgender individuals surveyed reported having to teach their medical providers about transgender care [72]. Having transgender people educate medical students will not transform the healthcare delivery system to accept transgender persons [63]. Instead, active participation by transgendered individuals in public health research, policy making, and teaching healthcare providers techniques to provide acceptable care is recommended. The ACA has provided funding for LGBT cultural competency trainings, which have been implemented in the health departments of large cities, with training underway for staff of the National Health Service Corps [59].

CONCLUSION

Transgender individuals have unique health needs. This population exhibits a high prevalence of HIV and other sexually transmitted infections, victimization, mental health issues, and suicide. In addition, transgender individuals are less likely to have health insurance than heterosexual or LGB individuals. Improving the health of sexual minorities is a goal of Healthy People 2030, which calls for recognition of transgender health needs as medically necessary and points out that transgender care is virtually absent from medical and nursing school curricula.

This course has provided a basic overview of the care of individuals experiencing gender dysphoria. With this information, it is hoped that healthcare professionals will address the unique healthcare needs of transgender individuals, overcoming the barriers to care and providing these patients with the best and most sensitive care possible.

RESOURCES

Centers for Disease Control and Prevention
Lesbian, Gay, Bisexual, and Transgender Health
https://www.cdc.gov/lgbthealth/health-services.htm

University of California, San Francisco
Center of Excellence for Transgender Health
https://prevention.ucsf.edu/transhealth

The Fenway Institute
https://fenwayhealth.org/the-fenway-institute

FTM International
http://www.ftmi.org

Gay and Lesbian Medical Association
http://www.glma.org

Gender Spectrum
https://www.genderspectrum.org

Human Rights Campaign
Transgender Visibility Guide
https://assets2.hrc.org/files/assets/resources/transgender_visibility_guide_042013.pdf

Lambda Legal
Creating Equal Access to Quality Health Care for Transgender Patients: Transgender-Affirming Hospital Policies
https://www.lambdalegal.org/publications/fs_transgender-affirming-hospital-policies

Mazzoni Center (Philadelphia)
https://www.mazzonicenter.org

National Center for Transgender Equality
https://transequality.org

Sylvia Rivera Law Project
https://srlp.org

The Joint Commission
Advancing Effective Communication, Cultural Competence, and Patient- and Family-Centered Care for the Lesbian, Gay, Bisexual, and Transgender (LGBT) Community: A Field Guide
https://www.jointcommission.org/assets/1/18/LGBTFieldGuide.pdf

Transsexual and Transgender Roadmap
https://www.transgendermap.com

TransYouth Family Allies
http://www.imatyfa.org

Trans Care BC
http://transhealth.phsa.ca

Transgender Law Center
https://transgenderlawcenter.org

World Professional Association for Transgender Health
https://www.wpath.org

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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