

Acute Clinical Care for Transgender Patients

A Review

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IMPORTANCE *Transgender* is an umbrella term used to describe individuals whose gender identity and/or gender expression differs from assigned sex at birth. There are an estimated 1.4 million transgender adults in the United States, and this number is increasing. Clinicians will increasingly be caring for transgender patients. Topics considered in this narrative review include terminology, how to address transgender patients, obtaining an inclusive history that takes into account gender-affirming surgery, managing hormone therapy and other clinical issues, consideration for hospitalized patients, interpreting laboratory values in the setting of hormone use, legal issues, and considerations for health systems.

OBSERVATIONS Best practices in caring for a transgender patient include using a patient-identified name and pronoun, using gender-neutral terminology until the appropriate term is identified by the patient, and obtaining a surgical history inclusive of an anatomic inventory. Gender-affirming hormones can modify disease-specific risk factors or confer risk for in-hospital complications. They can also cause changes in laboratory values; however, studies are limited to observational studies and case series. Some data are derived and extrapolated from cisgender populations. There are also unique systems-based concerns, including lack of procedures for standardized collection of gender identity and lack of sufficiently comprehensive electronic health record platforms. Vulnerabilities exist for hospitalized transgender patients in the transition from the inpatient to outpatient care that require dedicated institutional efforts to address.

CONCLUSIONS AND RELEVANCE Clinicians should learn how to engage with transgender patients, appreciate that unique anatomy or the use of gender-affirming hormones may affect the prevalence of certain disease (eg, cardiovascular disease, venous thromboembolism, and osteoporosis), and be prepared to manage specific issues, including those related to hormone therapy. Health care facilities should work toward providing inclusive systems of care that correctly identify and integrate information about transgender patients into the electronic health record, account for the unique needs of these patients within the facility, and through education and policy create a welcoming environment for their care.

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Transgender is an umbrella term commonly used to describe individuals whose gender identity and/or gender expression differs from assigned sex at birth.¹ Although accurate census data are limited, there are an estimated 1.4 million transgender adults in the United States, or 390 adults per 100 000,^{2,3} and this number has been increasing.⁴ Studies⁵⁻⁹ have consistently shown health care outcome disparities for transgender individuals, including higher rates of mental health disorders, substance abuse, and disability. Transgender patients also have impaired access to and acceptance into health care.¹⁰

The 2015 US Transgender Survey⁵ is the largest available survey of transgender adults; it examined 27 715 respondents via an anonymous online questionnaire available in English and Spanish. The survey was distributed to more than 400 organizations across

the United States and US territories; the number of respondents but not the response rate was reported.

The survey⁵ showed that 33% of transgender respondents who saw a clinician in the year prior reported at least 1 negative experience related to being transgender, including verbal harassment or refusal of treatment because of gender identity, while 23% of all respondents avoided seeking medical care because of fear of being mistreated. This barrier may lead transgender individuals to initially be seen with more advanced illness, thus increasing the likelihood that urgent management within an acute care setting will be required.

Despite increasing transgender awareness and advocacy among the public,¹¹ the field of transgender medicine is in its infancy.¹² There is also a dearth of formal education in transgender health in undergraduate and graduate medical education,¹³⁻¹⁶ so that clinicians may

Table 1. Gender Identity Terminology and Definitions^{21,22}

Terminology	Definition
Sex	The sex (male or female) assigned to a child at birth, most often based on external anatomy. Also referred to as birth sex, natal sex, biological sex, or assigned sex at birth
Gender	A social construct used to classify a person as male, female, or along a masculine to feminine spectrum
Gender identity	A person's deeply held internal sense of being male, female, some combination of the 2, or neither. Unlike gender expression, gender identity is not visible to others
Gender expression	An external manifestation of gender, expressed through a person's name, pronouns, behavior, clothing, voice, or body characteristics
Pronoun	Individuals may use he/his or she/hers or use gender-neutral pronouns, such as they/theirs or zie/zirs
Cisgender	An individual who gender identifies as their birth sex
Transgender man/transman/FTM	A transgender person whose birth sex is female but whose gender identity is male
Transgender woman/transwoman/MTF	A transgender person whose birth sex is male but whose gender identity is female
Genderqueer/gender nonbinary	A term used by people who experience their gender identity and/or gender expression as falling outside the category of man and woman. The term is not a synonym for transgender and should only be used if someone identifies as such
Gender transition	The process of coming to recognize, accept, and express one's gender identity. Most often, this refers to the period when a person makes social, legal, or physical changes (sometimes referred to as <i>gender affirmation processes</i>)
Gender-affirming hormone therapy	The administration of hormones to a patient who wishes to match secondary sex characteristics to their gender identity. Also referred to as cross-sex hormone therapy
Gender-affirming surgery	Modification of the body to be congruent with one's gender identity. Also referred to as sex reassignment surgery or gender-confirming surgery
Transsexual	Sometimes used in medical literature or by transgender people to describe those who have transitioned through medical interventions. Transsexual is not a synonym for transgender and should only be used if someone self-identifies as such
Intersex	An identity term used by some individuals with disorders/differences of sex development. Some intersex individuals identify under the transgender umbrella, while others do not
Terminology to Avoid	
Sex change/preoperative/postoperative	Terminology that overemphasizes the role of surgery in the transition process. It is preferable to use the term "transition," which is inclusive of medical and surgical interventions
Biologically/genetically male/female	Terminology that emphasizes biology over gender identity. It is preferable to use "assigned male/female at birth"
"Real" name	Terminology that emphasizes the legal name over the chosen name. It is preferable to use "chosen name" or "name used"
Transgendered	The extraneous "-ed" is not necessary for the adjective transgender and leads to tense confusion and grammatical errors (ie, would not say "lesbianed" so thus would not say "transgendered")
Tranny	A derogatory term used to refer to transgender individuals. While some transgender people may use this term to refer to themselves, others find this term offensive
Hermaphrodite	A derogatory term used to refer to intersex individuals
Transvestite	A derogatory term previously used to refer to an individual who wears clothing associated with a different sex

Abbreviations: FTM, female to male; MTF, male to female.

struggle to provide appropriate care to transgender patients.¹⁷ Available guidelines focus on longitudinal care of transgender individuals, particularly the initiation and maintenance of gender-affirming therapy.^{18,19} In this narrative review, we discuss the acute clinical care of transgender patients, whether in the hospital, the emergency department, or urgent care. Among the topics we consider are terminology, how to address transgender patients, obtaining an inclusive history that takes into account gender-affirming surgery, managing hormone therapy and other clinical issues, considerations for hospitalized patients, interpreting laboratory values in the setting of hormone use, legal issues, and considerations for health systems. The longitudinal care of transgender individuals has been considered elsewhere.¹⁸

Terminology

Although the terms are often used interchangeably, sex and gender are distinct. Sex is assigned at birth as male or female based on external anatomy. Gender is a social construct rooted in a particular culture's associations with masculinity or femininity.²⁰ Gender

identity refers to an individual's internal identity across the gender spectrum, such that a person may identify as male, female, male and female, or neither. Although gender identity is internal, gender expression is visible. Gender expression is the way in which a person communicates their gender identity to the world (through clothing, speech, behavior, etc). Sexual orientation is a separate concept, which characterizes emotional or sexual attraction to others. Some transgender individuals identify themselves as sexual minorities (ie, lesbian, gay, bisexual, etc); others identify as heterosexual (Table 1). A recent newspaper article also summarizes the vocabulary.²³

Clinicians can signal to the patient their understanding of these distinctions. Asking what name the patient uses in the initial meeting communicates an understanding that transgender individuals often use names different from the listed legal name. In addition, using gender-neutral terminology, such as "significant other" or "spouse" rather than "husband/wife" or "parent" rather than "mother/father," provides the patient with the opportunity to identify the appropriate term. Patients are often willing to answer more direct questions about sexual orientation and gender identity, despite clinicians' perceived fear of causing offense.^{24,25} For transgender individuals,

Table 2. Questions to Elicit More Comprehensive Gender Identity Information²⁷

Questions	Responses
What is your gender identity?	<ul style="list-style-type: none"> • Male • Female • Transmale/transman/FTM • Transfemale/transwoman/MTF • Genderqueer/gender nonconforming • Different identity [please specify] • Decline to answer
What is the sex listed on your original birth certificate? or What sex were you assigned at birth?	<ul style="list-style-type: none"> • Male • Female • Other • Decline to answer
What gender pronouns do you currently use?	<ul style="list-style-type: none"> • He/him • She/hers • They/them • Something else [please specify]
What name do you currently use? or What is your name?/How would you like me to address you?	Name used: _____

Abbreviations: FTM, female to male; MTF, male to female.

failing to be identified by chosen name or pronoun can have a deleterious influence on satisfaction and quality of care²⁶ (Table 2).

Although electronic health record (EHR) systems are increasingly expanding their capacity to capture chosen name and pronoun,^{27,28} lack of a consistent, dedicated space for this information may present an additional barrier to patient-centered care. Without consistent space in the EHR, this information, if collected, may be lost as the patient sees different clinicians or receives care in different facilities. It would be beneficial to expand all EHR systems to include fields for chosen name and pronoun and to educate clinicians and staff on how to collect this information in an appropriate manner.

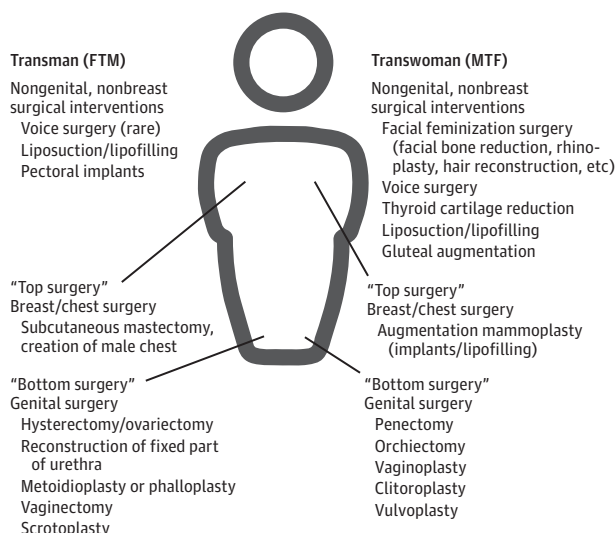
Clinical Considerations

Anatomic Inventory

An essential part of caring for transgender patients is whether the patient has undergone any gender-affirming surgical procedures, also known as sex reassignment surgeries. Such knowledge can inform risk factors for diseases and possible diagnoses related to the patient's current anatomy. This is sometimes referred to as taking an anatomic inventory or organ inventory during the initial medical history.²⁷

Transgender patients may be reluctant to disclose information about surgical procedures or medical treatment out of fear of discrimination or inappropriate treatment.⁵ Clinicians can proactively explain the medical justification for seeking this information and state that the disclosed information will be treated confidentially in accord with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).²⁹ Although there is no single best practice for eliciting an anatomic inventory, clinicians as part of the surgical history can ask if the patient has undergone any gender-affirming surgical procedures. If the answer is yes, more detailed questions can be asked about current anatomy.

The Figure shows options for gender-affirming surgical procedures.^{19,30} The decision to undergo any of the available procedures is personal and depends on the individual's goals for gen-

Figure. Gender-Affirming Surgery Options¹⁸

Gender-affirming surgery options are defined as: (1) Voice surgery: feminization surgery can involve increasing vocal fold tension, reducing vocal cord mass, or both to elevate pitch. Masculinizing surgery involves a relaxation thyroplasty to reduce vocal cord tension. (2) Metoidioplasty: surgery uses local genital tissue without skin grafting to create a phallus. (3) Phalloplasty: surgery uses a skin graft, typically from radial forearm or anterior lateral thigh, to create a phallus. FTM indicates female to male; MTF, male to female.

der transition, affordability depending on insurance coverage, and availability of trained surgeons.⁵ In the 2015 US Transgender Survey,⁵ 25% of the respondents reported having some form of transition-related surgery, while 49% had ever received hormone therapy. Common surgical complications include infection or scarring after chest surgery and frequent urinary tract infections, urethral strictures, or fistulas after genital surgery.^{18,19}

In hospital systems without a designated area in the EHR for an anatomic inventory, clinicians should consider storing this information in the medical and surgical history sections of the medical record.³¹ As institutions develop their EHR, consideration should be made to include decision support driven by surgical history on all patients, so that an anatomic inventory can be generated regardless of a transgender identity.

Hormone Therapy Interactions and Adverse Effects

The goal of gender-affirming hormone therapy is to more closely align an individual's physical appearance with their gender identity. Feminizing therapy is taken to produce female secondary sex characteristics and suppress or minimize male characteristics; the goal of masculinizing therapy is the opposite.¹⁸ Estrogens are the primary class of medications used for feminizing therapy and include oral, parental, and transdermal methods of delivery.³² Antiandrogens, such as spironolactone, cyproterone acetate, or 5 α -reductase inhibitors, may also be used, often as adjunctive medication, to suppress testosterone.¹⁸ Testosterone is the mainstay of masculinizing therapy and is available in oral, buccal, injectable (subcutaneous or intramuscular), implantable pellet, or transdermal forms.¹⁸

Gender-affirming care has been defined as medically necessary by the American Medical Association,³³ the American Psychological Association,³⁴ the American College of Obstetricians and Gynecologists,³⁵ the Endocrine Society,³² and the World Professional Association for Transgender Health.^{36,37} Gender-affirming therapy may improve mental health and quality of life.³⁸⁻⁴¹ During a hospitalization, outpatient hormone therapy should be continued, even if it is not on the hospital formulary.

Medications transgender patients may take as part of the gender transition process can inform disease-specific risk factors, such as hypertriglyceridemia or osteopenia, or confer risk for in-hospital complications, such as venous thromboembolism (VTE).¹⁹ However, many medication risks for transgender patients are extrapolated from data in cisgender populations receiving similar therapies or based on smaller observational studies or case series of transgender patients. Alteration or discontinuation of gender-affirming hormone therapy should involve a discussion of potential risks and benefits with the patient or surrogate, informed by the current limited data from transgender populations.

Estrogens

The greatest concern for transgender individuals receiving estrogen therapy is the elevated risk of venous thromboembolism. Data on thrombogenic effect are conflicting,⁴² with the risk of VTE depending on the formulation of estrogen in conjunction with the presence of additional risk factors (eg, tobacco use or personal history of VTE). The findings of a recent cohort study⁴³ suggest the risk may also depend on duration of estrogen use. That study found that transgender women had a higher incidence of VTE relative to cisgender men and cisgender women and demonstrated that the risk difference increased over time: 2-year and 8-year risk differences for VTE in transgender women were 4.1 (95% CI, 1.6-6.7) and 16.7 (95% CI, 6.4-27.5) per 1000 persons relative to cisgender men and 3.4 (95% CI, 1.1-5.6) and 13.7 (95% CI, 4.1-22.7) relative to cisgender women. Forms of particularly thrombogenic estrogen, such as ethinyl estradiol, should not be prescribed for transgender women because of heightened VTE risk. However, some people who obtain hormones from nonprescription sources, such as underground pharmaceutical dealers, may still take these formulations. Transdermal estrogen appears to confer less risk of venous thrombosis for transgender patients, potentially by avoiding first-pass metabolism in the liver that can increase hepatic protein synthesis, including procoagulant factors.^{44,45} The results of a case series⁴⁶ of 251 transgender patients, 18 with activated protein C resistance and 1 with protein C deficiency, suggest that transdermal estrogen may be safe, even for individuals with this hypercoagulable state.

We are unaware of evidence for the routine cessation of estrogen treatment when in the hospital or around the time of surgery. Suggestions for interruption of estrogen have been based on opinion, not evidence, and are contrary to practice in other areas of hormone therapy, such as contraception or menopausal hormone therapy.⁴² If there remains high concern for risk of VTE, the estrogen dose can be reduced or the estrogens administered transdermally, if this approach is not already being used.¹⁸

When considering VTE prophylaxis for hospitalized patients, the Padua risk assessment model accounts for the use of ongoing hormone treatment.⁴⁷ However, in the derivation of the Padua model,

there was no mention of indication for hormone therapy in study participants, with sex of the study patients stated as binary (male/female). Therefore, it is unclear if this derivation included transgender individuals.

The findings of another study⁴⁸ suggest that transgender women receiving estrogen may have an elevated risk of cardiovascular and cerebrovascular events compared with cisfemale controls. The risk of such transgender women may better align with that of cisfemale controls, although the study did not control for confounding factors, such as tobacco use. The more recent cohort study by Getahun et al⁴³ that controlled for confounding factors (tobacco use, body mass index, blood pressure, and cholesterol level) found similar incidence of ischemic stroke in transgender women relative to cisgender men and cisgender women and found similar incidence of myocardial infarction to cisgender men. The potential for elevated risk should be discussed with transgender women who are seen with cardiovascular issues or who are undergoing perioperative evaluation. To our knowledge, there are no studies with robust information on the relative or absolute risk for cardiovascular disease in transgender women; such data would be important for decision making.

Commonly used risk stratification tools, such as the Revised Cardiac Risk Index,⁴⁹ the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) risk prediction,⁵⁰ or CHADS₂-Vasc⁵¹ (congestive heart failure, hypertension, age >75 years, diabetes, prior stroke/transient ischemic attack) scoring systems, do not take into account the use of estrogen therapy. Therefore, it is not known whether transgender women receiving estrogen therapy should be afforded an additional "female" point in CHADS₂-Vasc scoring. Extrapolation of available studies^{42,43,52} suggests that this may only be a consideration in individuals with additional risk factors for VTE, such as ongoing tobacco use.

In addition to potential thrombogenic risks, estrogen therapy may be associated with drug-drug interactions; however, available studies have examined oral contraception in cisgender women rather than with gender-affirming hormone regimens. In a 2016 systematic review,⁵³ the results of pharmacokinetic studies on the use of oral contraceptives in cisgender women suggested estrogen interactions with some antiretroviral therapies used to treat HIV, including protease inhibitors, nonnucleoside transcriptase inhibitors, and cobicistat. However, that review found insufficient evidence to draw conclusions about drug-drug interactions between gender-affirming hormone therapy and antiretroviral therapy. For transgender women requiring antiepileptic drugs, there may be an interaction between enzyme-inducing antiepileptic agents, such as phenytoin or carbamazepine, which increase hepatic metabolism of estrogen, or lamotrigine, for which estrogens increase the metabolism.⁵⁴ The interactions have been suggested by extrapolations from oral contraceptive data. If there is concern that newly introduced medications may increase estrogen metabolism (lowering drug efficacy), one approach would be to monitor estrogen levels and, when needed, to compensate for decreased levels by increasing estradiol dosing. However, this approach has not yet been formally studied.

If estrogen supplementation has to be discontinued in the hospital, for example because of a diagnosis of an estrogen-sensitive cancer, tapering therapy can postpone but not prevent development of vasomotor symptoms in patients who have had an orchiectomy.

Although abrupt cessation of estrogen supplementation may cause substantial discomfort, a study⁵⁵ of postmenopausal cisgender women found no significant adverse reactions from that practice. Further studies are needed to examine issues of coagulability, cardiovascular, and cerebrovascular risk in transgender individuals receiving gender-affirming estrogen regimens.

Antiandrogen Therapy

Antiandrogen agents are an integral adjunct to estrogen therapy for transgender women who desire maximal feminization and have not undergone orchiectomy. Chronic antiandrogen therapy is typically discontinued after orchiectomy.

The potassium-sparing diuretic and antiandrogen medication spironolactone, a drug primarily used for patients with heart failure or liver disease, may also be used for chronic antiandrogen therapy. However, dosing of spironolactone in gender-affirming therapy may be 2- to 4-fold higher than for patients with heart failure or liver disease, with regimens in a dosage range of 100 to 400 mg daily, not 25 to 100 mg daily.^{18,56} Spironolactone given at gender-affirming dosages may increase potassium levels, reduce volume status, or exacerbate acute kidney injury in the setting of an illness; however, the effects of such dosages have not been formally studied to date. Active monitoring of potassium and renal function in the acute setting and dosage adjustments, when needed, are important. If spironolactone therapy is discontinued, the dosage does not require tapering.

Cyproterone acetate is a synthetic progestogen with potent antiandrogen activity. Although not approved by the US Food and Drug Administration, it is approved in other nations, such as the United Kingdom and Canada. Some transgender individuals use this synthetic progestogen. Although often well tolerated and effective, the use of cyproterone has been associated with a risk of deep vein and arterial thrombosis, as well as rare cases of fulminant hepatotoxicity.⁵⁷

Gonadotropin-releasing hormone (GnRH) analogues, such as leuprolide acetate, are neurohormones that block the GnRH receptor, decreasing the release of luteinizing hormone and follicle-stimulating hormone. Such agents may be used for suppression of puberty in pediatric or adolescent transgender patients or for suppression of menstruation in transgender men.^{19,32} There are limited data on prolonged use of GnRH analogues in adults, although deleterious effects on bone mineral density may be seen.³²

Finasteride or dutasteride, 5 α -reductase inhibitors, are used for transgender women unable to tolerate spironolactone, those who seek partial feminization, or those who continue to exhibit virilized features after complete androgen blockade or orchiectomy.¹⁸ These medications may also be prescribed for transgender men experiencing androgenic hair loss as a result of testosterone therapy. There are no additional considerations in using these agents other than what is known for cisgender men, where it can lead to dizziness or orthostatic hypotension, although targeted studies in transgender patients have not been performed to date.

Testosterone

The use of testosterone therapy in transgender men may be associated with a thrombogenic erythrocytosis.¹⁸ The potential risk of subsequent venous blood clots related to polycythemia led the US Food and Drug Administration⁵⁸ in 2014 to issue a warning on

testosterone products. However, a 2017 systematic review and meta-analysis⁵⁹ of testosterone use in transgender men found insufficient outcomes data to allow meaningful assessment of VTE risk.

The same systematic review and meta-analysis⁵⁹ found that transgender men receiving testosterone had significantly higher serum triglycerides and low-density lipoprotein levels and lower high-density lipoprotein levels compared with the period before they were taking testosterone. Two studies,^{43,48} one in 2013 and one in 2018, found no evidence of differences in rates of cardiovascular or cerebrovascular disease among transgender men receiving testosterone therapy compared with cisgender controls. We are unaware of other studies on this topic.

Chronic testosterone therapy in cisgender men may suppress endogenous testosterone production, leading to symptoms (eg, weight changes and depression) if testosterone treatment is discontinued. However, this is thought to be less of a risk for transgender men because the degree of endogenous testosterone production is lower than that of cisgender men. If testosterone supplementation needs to be discontinued in the hospital (eg, in the setting of polycythemia), abrupt cessation in transgender men who have undergone oophorectomy may cause fatigue and mood changes, as well as hot flashes. Although physiologically safe, we are unaware of reasons to routinely discontinue chronic testosterone therapy during hospitalization.

Interpreting Laboratory Values

Interpretation of a transgender patient's laboratory values may be affected by type and duration of hormone therapy (Table 3).⁷² For example, both estrogen and testosterone alter the hematocrit reading; transgender women receiving estrogen tend to have lower hematocrit readings compared with before initiation of hormone therapy, while transgender men receiving testosterone tend to have higher hematocrit readings. Creatinine levels also decrease in transgender women taking hormone therapy, while creatinine levels can increase in transgender men taking hormone therapy. Knowledge of a patient's birth sex, anatomic inventory, and hormone status are important to interpret reference laboratory ranges and to separate normal from abnormal values.

The EHR may be misleading if potentially abnormal values are identified based on a patient's legal sex and not their gender identity with or without concurrent hormone therapy. In some instances, the EHR may even discount biomarkers that are thought to be sex specific, such as prostate-specific antigen in a transgender woman, or inhibit a clinician from ordering particular studies, such as a pregnancy test in a transgender man, if the patient is classified as having the "incorrect" (although self-identified) gender.⁷²

Considerations for Hospitalized Patients

Clinicians and staff should recognize that a transgender patient may not be open about their transgender status and must ensure that discussions pertaining to transgender identity, hormone therapy, or gender-affirming surgical procedures remain private,

Table 3. Laboratory Value and Risk Factor Interpretations in Transgender Persons Receiving Hormone Therapy Relative to Values or Risk Before Hormone Therapy^a

Laboratory Values	Transgender Women Receiving Hormone Therapy	Transgender Men Receiving Hormone Therapy
Hematocrit	Decreased ⁶⁰⁻⁶²	Increased ⁶²⁻⁶⁶
Creatinine	Decreased ^{60,61,63} (most pronounced after gender-affirming surgery)	Increased ^{62,63,67}
Potassium	No change ^{60,63} or slight increase (if receiving spironolactone) ⁶³	Not applicable
Total cholesterol	No change ^{59,60,62,63,68} or increased ⁶⁹	No change ^{59,62,63,66,68} or increased ^{65,69} or slight decrease ⁶⁴
LDL	No change ^{59,68} or decreased ^{63,69}	Slight decrease ⁶⁴ or increase ⁵⁹ or no change ^{63,69}
HDL	No change ^{59,68} or slightly increased ^{60,63} or decreased ⁶⁹	No change ^{63,64,68} or decreased ^{59,65,66,69}
Triglycerides	Increased ^{59,60,69} or no change ^{63,68} or decreased ⁶² (latter seen after gender-affirming surgery)	No change ^{62-64,68,69} or increased ^{59,65}
AST/ALT	No change ^{60,63} or decreased ⁶² (latter seen after gender-affirming surgery)	Increased ^{62,65} or no change ⁶⁴
Alkaline phosphatase	No change ⁶⁰ or decreased ⁶⁷	Increased ⁶⁷
Prostate-specific antigen	Decreased ^{62,70}	Not applicable
Prolactin	Within normal reported range ⁶²	Decreased ⁶⁵
Risk Factors		
Bone mineral density (spine)	Decreased ^{52,60,62,71}	No change ^{52,62,65} or decreased ⁶⁷
Thromboembolic events	Increased risk may be linked with oral estrogen ^{48,52,59,62,71}	No increased risk ^{48,52,59,62,71}
CHD risk	Increased risk may be linked with oral estrogen ^{48,52,59,62,71}	No increased risk ^{48,52,59,62,71}
Hormone-related cancer	No known risks ⁶² but need to monitor for prolactinomas and breast cancer when receiving estrogen, as well as prostate cancer ^{48,52,71}	No known risks ⁶² related to hormone therapy but need to monitor for ovarian cancer, endometrial cancer, and breast cancer. ^{52,71} After gender-affirming surgery, residual breast tissue remains a cancer risk, even after bilateral mastectomy ^{48,52,71}

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; CHD, coronary heart disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

^a Study details include the following: Weinand and Safer,⁵² 2015: review of multiple studies; Wierckx et al,⁴⁸ 2013: 214 transgender women receiving hormone therapy for a mean of 7.7 years (65% after gender-affirming therapy) and 138 transgender men receiving hormone therapy for a mean of 9.4 years (86% after gender-affirming therapy); Maraka et al,⁵⁹ 2017: meta-analysis of multiple studies totaling 3231 transgender women and 1500 transgender men, with treatment periods ranging from 3 months to 41 years of hormone therapy (gender-affirming surgery state not reported); Roberts et al,⁶⁰ 2014: 55 transgender women receiving hormone therapy for a median of 4 years; van Kesteren et al,⁶⁷ 1998: 20 transgender women and 19 transgender men receiving hormone therapy a mean of 25 months after gender-affirming surgery; Lapauw et al,⁶¹ 2008: 23 transgender women receiving hormone therapy and at least 5 years after gender-affirming surgery; Wierckx et al,⁶²

2012: 50 transgender women and 50 transgender men after gender-affirming surgery and hormone therapy for at least 10 years; Colizzi et al,⁶⁹ 2015: 79 transgender women and 43 transgender men followed for 2 years receiving hormone therapy; Fernandez and Tannock,⁶³ 2016: 33 transgender women and 18 transgender men followed for up to 18 months receiving hormone therapy; Mueller and Gooren,⁷¹ 2008: review of multiple studies; Jacobbeit et al,⁶⁴ 2009: 17 transgender men followed for a 3-year period and by the end of the study, 13 of these patients had undergone gender-affirming surgery; Wenisch et al,⁷⁰ 2014: 30 cisgender men followed for 56 days after luteinizing hormone-releasing hormone analogue injection; Deutsch et al,⁶⁸ 2015: 16 transgender women and 31 transgender men followed for 6 months after initiating gender-affirming hormone therapy; Pelusi et al,⁶⁶ 2014: 45 transgender men followed for 12 months receiving hormone therapy; and Mueller et al,⁶⁵ 2010: 45 transgender men followed for 2 years on hormone therapy.

including to family members, unless otherwise requested. Of the 14 688 participants in the 2015 US Transgender Survey⁵ who had disclosed their gender identity to their families, 10% reported subsequent violence from a family member because of their transgender status, and 8% reported subsequent eviction from home. Clinicians and health care facilities should strike a balance between confidentiality and the benefit of having a wide range of hospital personnel address the patient respectfully using a name and gender identity determined by the patient.

When transgender patients are admitted to the hospital, they should be placed in a private room or, if none are available, in a shared room according to their gender identity rather than their legal sex.²⁹ However, such practices may not be routine, in which case clinicians should proactively address these issues with nursing and ancillary staff. Transgender patients may experience additional stress as inpatients because of replacement of personal clothing or other usual means of gender expression with uniform

hospital gowns; when possible, flexibility about such practices may be desirable.

Transgender patients may face socioeconomic hardships.⁷³ Compared with the general US population, transgender individuals have higher unemployment rates and lower socioeconomic status.⁵ Given increased rates of unemployment, individuals may be less likely to have employer-based health insurance or a clearly identified primary care clinician. Even transgender patients with adequate health insurance may have difficulties in obtaining high-quality primary care. A 2017 study⁷⁴ found that only 50.6% (80 of 158) of primary care providers surveyed were willing to prescribe gender-affirming hormone therapy for transgender patients. There are also concerns about transgender individuals' experiences in skilled nursing and rehabilitation facilities, such as invalidation of transgender identity in the setting of disability, and their safety within such facilities.⁷⁵ Early involvement of social workers and discharge planners with knowledge of outpatient or rehabilitation services for transgender individuals is important.

Table 4. Future Directions for Research and Education in the Acute Care of Transgender Individuals

Stages of Acute Care	Research or Educational Initiative
Presentation to acute care	Describe the most common diagnoses that lead to acute care for transgender individuals
	Assess if transgender individuals are seen at later stages of illness compared with cisgender peers
	Analyze cardiovascular and/or cerebrovascular risk in the setting of gender-affirming hormones, controlling for appropriate risk factors
	Describe the effect of gender-affirming hormones on hormone-sensitive conditions, such as migraine, epilepsy, or autoimmune disorders
	Evaluate strategies for eliciting an anatomic inventory to derive evidence-based best practice
	Assess patient, health care provider, nursing, and staff attitudes on standardized gender identity collection in the acute setting
Admission to the hospital	Describe transgender patients' current experiences during hospitalizations
	Evaluate hospital administration attitudes and perceived barriers to caring for transgender patients in the acute setting
	Assess health care provider, nursing, and staff perceived barriers to providing care for transgender patients in the acute setting
	Describe the effect of changes in the electronic health record on transgender patient experiences and health outcomes
	Evaluate ongoing changes in electronic health records to determine evidence-based best practices for trans-inclusive platforms
	Disseminate and educate health systems about existing guidelines for trans-inclusive hospital policies
Acute clinical care	Validation of risk prediction models in transgender individuals
	Evaluate perioperative risk of venous thromboembolism in transwomen receiving estrogen
	Educate comanagement hospitalists on the most common postoperative complications after gender-affirming surgery
	Characterize normal laboratory ranges for transgender individuals based on gender-affirming hormones/surgical procedures in a large cohort
	Create processes and education for ordering studies that are "sex specific" in the acute setting, such as pregnancy tests
	Evaluate current frequency of training in transgender health for health care providers, nursing, and staff in the acute setting
Discharge considerations	Describe transgender individuals' experience in rehabilitation centers or skilled nursing facilities
	Assess rehabilitation providers' and staff's perceived barriers to caring for transgender patients
	Evaluate appropriate timing for resumption of gender-affirming hormones if this treatment was stopped during a hospitalization
	Educate social workers, case managers, and discharge coordinators about unique psychosocial needs of transgender patients and connect to local transgender resources

Legal Issues and Health System Considerations

Structural issues within a medical office or health system may impede the access of transgender individuals to equitable care; resolving such issues may require dedicated leadership. For example, lack of standardized procedures for collecting gender identity can make transgender patients "invisible" within a health system.⁷⁶ Physicians, nurses, and other staff often receive little to no formal training in transgender health, potentially leading to insensitive or discriminatory behavior. Lambda Legal and the Human Rights Campaign,²⁹ national organizations committed to the full recognition of civil rights for lesbian, gay, bisexual, and transgender individuals, have proposed best practices for transgender-affirming hospital policies. Examples include ensuring that hormone therapy is provided for transgender patients in a manner consistent with prevailing standards of care, including gender identity/expression in health facilities' nondiscrimination policies, and ensuring that transgender patients have safe access to restrooms in accord with their gender identity. However, such practices have not been widely adopted.²⁹

As of 2016, sexual orientation and gender identity data are required elements to be reported yearly to the US Department of Health and Human Services (DHHS) Health Resources and Services Administration (HRSA) Uniform Data System.²⁹ As of 2015, all EHR systems labeled under the DHHS Meaningful Use program as certified EHR technology are required to have the capacity to record sexual orientation and gender identity information, although this rule does not require institutions to actually collect this information.^{77,78} The challenge now is to not only obtain this information and incorporate it into the EHR but to also

use it to improve patient care, while preventing stigma and discrimination.²⁸ Online education modules and resources for improving care delivery environments for transgender individuals are available without charge; these can be personalized for specific acute care settings. Examples are the training provided by the National LGBT Health Education Center,⁷⁹ which is affiliated with Fenway Health (an LGBT-focused health center in Boston, Massachusetts), or by GLMA: Health Professionals Advancing LGBT Equality,⁸⁰ an association of LGBT health care professionals.

Conclusions

An increasing proportion of physicians are likely to care for transgender patients. Research on specific clinical issues for transgender patients is limited and primarily consists of case series, observational studies, or data derived and extrapolated from studies of cisgender patients. Additional investigation is needed on a wide breadth of topics (Table 4). Clinicians should learn how to engage with transgender patients, appreciate that unique anatomy or the use of gender-affirming hormones may affect the prevalence of certain disease (eg, cardiovascular disease, VTE, and osteoporosis), and be prepared to manage specific issues, including those related to hormone therapy. Health care facilities should work toward providing inclusive systems of care that correctly identify and integrate information about transgender patients into the EHR, account for the unique needs of these patients within the facility, and through education and policy create a welcoming environment for their care.

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