

Research Article

Comprehensive Approach in Multi-Disciplinary Preventive Care for Transgender Patients

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Keywords

- Transgender health screening
- Preventive care
- Health care access
- Guidelines

Abstract

Importance: Transgender individuals comprise a unique and interesting patient population for primary and sub-specialty care providers. Transgender individuals require standard screening for their assigned sex, screening for any hormonally-induced disorders during a transition, and any screening applicable to any at-risk behaviors. The purpose of this manuscript is to describe screening guidelines in the care of a transgender patient.

Methods: Data and literature for this review were identified through searches of PubMed from article using the following terms: “transgender”, “transgender screening”, “preventive care” in addition to terms related to each type of preventive health care screening including “breast cancer”, “anal dysplasia”, “cervical cancer”, “endometrial cancer”, “prostate cancer”, “smoking”, “metabolic diseases”, “psychiatric care”, “sexually transmitted diseases”, and “alcohol dependence”. Articles in English published between 2003 and 2019 were screened for relevance through abstract review.

Conclusions and Relevance: Physicians would benefit from clearer guidelines on management of preventive care for transgender patients. Beyond routine screening guidelines for both sexes, transgender patients should additionally be screened as based on their assigned sex at birth, any conditions that arise due to the transitioning process, and psycho-social conditions as summarized in Table 2 of this manuscript. Through this awareness, physicians can improve access to preventive care and better reduce the incidence of preventable chronic illnesses.

BACKGROUND

Transgender individuals comprise a unique patient population. These patients experience gender dysphoria, incongruence between their accepted gender and their anatomic sex [1]. In the United States, the prevalence of transgender individuals is roughly 1 to 1.4 million and has doubled in the last eight years [2].

Transgender individuals require standard screening for their assigned sex, screening for hormonally induced disorders, and screening applicable to at-risk behaviors. The importance of health maintenance of existing anatomy may be minimized by patients; however, it is the physician’s duty to ensure regular preventative health screenings.

Nearly half of transmen patients and roughly 1/3 of transwomen patients have delayed preventive care. They report multiple factors that limit effective health care, including harassment and lack of provider expertise in transgender care [3]. Furthermore, these patients seek gender-affirming medical

care and may avoid care that does not align with their preferred gender [3]. Providing proper preventive care is vital given that LGBTQ patients have elevated risk for risky behaviors, depression, anxiety, and suicidality [4]. These behaviors, including unsafe sex, smoking, excessive alcohol use, can increase lifetime risk of cancer and chronic illnesses.

METHODS

Data for this review were identified through searches of PubMed from article using the following terms: “transgender”, “transgender screening”, “preventive care” in addition to terms related to each type of preventive health care screening including “breast cancer”, “anal dysplasia”, “cervical cancer”, “endometrial cancer”, “prostate cancer”, “smoking”, “metabolic diseases”, “psychiatric care”, “sexually transmitted diseases”, and “alcohol dependence”. Articles were screened for relevance through review of abstracts. Relevant associated articles were further selected from search-generated articles. Only articles published in English between 2003 and 2019 were included.

INCIDENCE OF CHRONIC MEDICAL CONDITIONS IN TRANSGENDER PATIENTS

Given potential delays in preventative care that transgender patients face, this population may be at increased risk [3]. Moreover, cross-sex hormone therapy can cause side effects with long-term use, which can further impact chronic health statuses [5].

In a study of 230 transgender patients from 1979 to 2016 from the New York State Cancer Registry, Hutchison et al found that these patients were approximately three-fold more likely to be smokers at the time of cancer diagnosis. They were also five times more likely to have HPV- and HIV-related cancers [6]. Although Hutchinson et al focused on data from New York state, similar data from 46 other states and the District of Columbia also demonstrated that transgender patients were at greater risk of viral infection-related invasive disease [6,7]. In addition to risk conferred by viral infections, McFarlane et al were interested in the effect of gender-affirming hormone therapy on hormone-dependent cancers [8]. They conducted a systematic review of 43 studies, mainly including case reports, but also retrospective cohort studies and cross-sectional studies [8]. The cohort studies did not demonstrate any increased risk; however, the patients were young and the duration of hormone use may have not been long enough to accurately assess cancer risk [8]. However, case reports suggested that high-dose estrogen and anti-androgen treatment could increase the incidence of prolactinoma and meningiomas, respectively [8].

In terms of cross-sex hormone therapy, data on cancer prevalence in transgender patients is more readily available when compared to that on metabolic and psychiatric conditions.

However, a few articles address concerns of metabolic effects from hormone therapy, but the results are contradictory. While some studies demonstrate no increased risk, others suggest increased cardiovascular and thromboembolic risk secondary to estrogen use in male to female (MTF) patients [9-12].

In addition to metabolic effects of hormone therapy, Giltay et al also found that these patients may be at increased risk of suicide and drug abuse [11]. Similarly, a large Swedish cohort study (n= 324) found that patients after gender-affirmation surgery had increased mortality from suicide, more suicide attempts, and more inpatient psychiatric care [13].

USE OF CANCER SCREENING IN TRANSGENDER PATIENTS

For transmen with an intact uterus, less than 30% of these patients underwent a Pap test in comparison with 43% of cisgender American women [1,14]. Like with Pap screening, transgender men and women both have decreased utilization of mammography for breast cancer screening when compared to cisgender women. For instance, Kiran et al determined that these patients were less likely to have eligible screenings for breast, cervical, and colorectal cancer ($P < 0.001$, $P = .001$, and $P = .046$, respectively [15].

While many studies reported a decrease in screening rates for transgender patients, Tabac et al challenged this notion. In

a 2018 study of self-reported data, Tabac et al noted significant differences in health-related surveillance for cervical, breast, and prostate cancer in LGBTQ patients. Cervical and prostate cancer screening was lower in transgender and gender non-conforming patients. However, transgender men were more likely to have updated colorectal cancer screening and mammography screening when compared to their cis-gendered men and women. Tabac et al explained these findings by suggesting that trans men engaging in receptive anal sex are more readily offered colorectal screening. Evidence of increased rates of mammography screening in transmen appears to be a possible limitation of the study because the indication for mammography (pre-operative versus routine screening) was not delineated [3].

Current guidelines for cancer screenings are also not created for the specific needs of the LGBTQ community. Hudson et al collected data for 32 of the 50 National Comprehensive Cancer Network (NCCN) guidelines through emailed surveys to NCCN chairs. The study had an overall response rate of 62% with nearly 90% of those NCCN chairs reporting that neither self-reported sexual orientation nor gender identity were relevant to creation of NCCN guidelines [16].

A 2019 study of oncologists at the National Cancer Institute-Designated Comprehensive Cancer Centers. Schabeth et al surveyed 450 oncologists from 45 cancer centers across the United States. Of the 149 responses, there was an interest in additional education about the unique health needs of LGBTQ patients and about the gender identity of their patients [17]. Banerjee et al expanded this topic by studying the knowledge gaps of oncological health care personnel, including physicians, advanced practice professionals, and nurses. Of the 1253 providers, only 5% were able to correctly answer seven knowledge items on LGBTQ care, showing a lack of expertise [18]. Although these studies focus on oncology providers, other providers may also need additional education to best treat their transgender patients.

Breast Cancer Screening

The guidelines for breast cancer screening in transgender patients are not clear. Experts recommend that female-to-male (FTM) transgender patients without bilateral mastectomy utilize the current guidelines for cisgender women [19]. However, the guidelines for breast cancer screening for cisgender patients are conflicting based on four different medical associations, including the U.S. Preventive Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), American College of Radiology (ACR), and the American Cancer Society (ACS) [20]. USPSTF recommends that average risk women should begin mammogram screening every two years starting at age 50. On the other hand, ACOG, ACR, and ACS, recommend starting annual screening at age 40 for average-risk patients [20].

Other considerations in breast cancer screening for FTM patients include gender affirmation surgery and hormonal therapies. Patients who have undergone bilateral nipple sparing mastectomies are at a reduced risk of breast cancer, but like cisgender women, this risk is not zero. Given reported cases of breast cancer in FTM patients following mastectomies, consideration should at least be given to clinical chest exams

[21]. In those patients undergoing chest contouring, where more residual breast tissue is present, the risk is more unclear, and the ability to perform a mammogram is not always possible. By comparison, in cisgender women who have undergone breast reduction, there is data to show that the risk of breast cancer is decreased, and these women typically follow the previously mentioned society screening guidelines [22]. This suggests that in FTM patients who have had chest contouring, that screening mammogram should be considered if feasible, otherwise breast ultrasound or MRI may be of more utility.

When considering testosterone therapy in FTM patients, studies tend to indicate that there is a reduced risk for developing breast cancer. In a Dutch study examining 795 FTM patients that received testosterone (mean 20 years), there was only one reported case of breast cancer (20). They estimated the incidence for breast cancer to be 5.9 cases per 100,000 person-years. This was found to be considerably lower than the 154.7 cases per 100,000 person-years found in cisgender women but comparable to the rate in cisgender men [19]. While the number of patients who also underwent gender affirming surgery in this study is unclear, it seems to suggest that overall, FTM patients undergoing mastectomy and hormone therapy are likely at a decreased risk for breast cancer. In summary, taking this limited data into account in FTM patients, screening mammograms should be continued as per society guidelines in those patients who still have breasts; mammograms, if feasible, should be considered status post chest contouring; and clinical exams should be considered in those patients who underwent bilateral mastectomies, keeping in mind that testosterone therapy may also decrease the risk of developing breast cancer.

Recommendations for breast cancer screening in Male-To-Female (MTF) patients are also vague. Some physicians utilize the traditional breast cancer screening guidelines for these patients. Transwomen with a family history of breast cancer, age greater than 50 years old, high body mass index, or who have taken hormone therapy for at least five years are also more likely to be screened [19]. Gooren et al examined the rate of breast cancer in 2,307 MTF patients receiving estrogen therapy with or without androgen deprivation from 5 to over 30 years. The estimated rate was 4.1 per 100,000 patient-years which was similar to the rate in cisgender males [19]. Additionally, the Women's Health Initiative did not find an increased breast cancer incidence in women taking estrogen alone [23]. However, estrogen therapy causes the development of breasts with similar histology to that of cisgender females, implying that the same breast pathologies can occur in MTF patients taking estrogen [24]. Given this fairly conflicting data, it suggests that more information is needed in determining the role of screening mammogram in this specific population [19].

Endometrial Cancer Screening

Diagnostic screening is typically reserved for symptomatic patients using endometrial sampling and ultrasound imaging [3]. Interestingly, there should be a low threshold to sample symptomatic transmen on testosterone therapy. Both Grimstead et al and Khalifa et al characterized histologic features of androgen-mediated endometrial tissue changes in transmen,

finding these could confer an increased risk of endometrial carcinoma [21,22].

Cervical Cancer Screening

Previous literature suggests low cervical cancer screening rates for transgender men [6]. This issue could be attributed to the difficulties that transmen face at the gynecologist's office including fear, lack of desire to sit in the waiting areas, and pain associated with a speculum exam. Not only are these patients less likely to be up to date on Pap testing, but also the subsequent results are more likely to be inadequate or abnormal [14]. This propensity for inadequate testing has been attributed to testosterone-mediated atrophic changes of the cervical tissue, making dysplasia more difficult to assess on Pap testing [25]. Primary care providers should be cognizant of this when interpreting Pap testing results [25].

For transmen with a cervix, screening for cervical cancer follows standard guidelines for cisgender women. For patients between 21-29, a Pap test is recommended every three years.

From ages 30-65, co-testing with Pap test and HPV test should be done every five years.

However, a Pap test alone can be done every three years in this age group. Over 65 years of age, no further screening is required assuming a history of normal tests [14,23]. The above algorithm is appropriate for patients with consistently normal Pap testing, and abnormal results require further assessment and treatment as determined by American Society for Colposcopy and Cervical Pathology (ASCCP) [26].

Anal Dysplasia/Cancer Screening

There currently exists no standard anal dysplasia or anal cancer screening guidelines in place for normal to low risk individuals. However, it has been shown that in certain high risk groups, including those that are HIV+, men who have sex with men (MSM) and patients with a history of cervical dysplasia, have higher incidences of anal squamous neoplasms [24]. For example, in a study of HIV-positive men who have sex with men and HIV-positive transwomen, a history of greater than 20 sexual partners was associated abnormal testing [27].

Once a patient has been diagnosed with anal dysplasia by physical examination and biopsy, a number of different screening options exist, including anal cytology (anal Pap smear, HPV DNA testing, and high resolution anoscopy). None of these are standard of care or have proven to decrease rates of progression to anal cancer in comparison to the well-defined cervical cancer screening process. In a 2012 systematic review and meta-analysis, it was noted that rates of progression to anal cancer are substantially lower than those observed for cervical cancer [26].

Ovarian Cancer Screening

There are no standardized screening guidelines for ovarian cancer [7]. Some patients have genetic predispositions to develop ovarian cancer, such as biologic females with a family history of hereditary cancer syndromes. Genetic testing for BRCA1 and BRCA2 along with other rarer genetic conditions may be warranted in the appropriate clinical setting [28].

Prostate Cancer Screening

The American Urological Association recommends use of PSA (prostate-specific antigen) every 2 years along with DRE (digital rectal exam) in patients between the ages of 55- 69 who are of average risk. For those individuals deemed high risk, screening may be recommended between ages 40-54. They do not have a specific recommendation for patients considered "low risk," which would be patients on chronic androgen suppression [29]. There have been only approximately ten cases of prostate cancer in transgender women in the literature [30]. In transgender women who are currently on gender-affirming treatment, PSA levels should be suppressed. Therefore, even a level of 1ng/ml would be considered to be the upper limit of normal and warrant workup if the patient has elected for screening [31]. If a PSA is checked or a nodule felt on DRE, appropriate confirmatory testing includes trans-rectal or MRI-guided prostate biopsy [29].

USE OF METABOLIC AND PSYCHOSOCIAL SCREENING IN TRANSGENDER PATIENTS

In addition to lapses in cancer screening, there are also gaps in literature about other types of screening. In a systematic review of 41 publications on transgender preventive care, while studies mainly focused on HIV rates or risky behaviors, few addressed cholesterol screenings, routine STI examinations, and tobacco use, suggesting that there may be a need to increase awareness for non-cancer screenings [32].

Metabolic Screening

Both transmen and transwomen often use exogenous hormonal treatment to enhance desired sexual traits while suppressing or minimizing undesired characteristics. These types of medications can increase risk factors for chronic diseases, such as metabolic disease, osteoporosis, and venous thromboembolism.

For MTF patients, feminizing therapies include estrogens and anti-androgen therapy. Estrogen causes breast development, fat redistribution, decreased muscle mass, reduced testicular size, and reduced hair growth [33]. Additionally, anti-androgens, such as spironolactone, have breast augmentation effects. Long-term estrogen and anti-androgen use can be associated with lab abnormalities (Table 1) [27].

Dosing for estrogen depends on the route of administration. Initial dosages for sublingual estradiol, transdermal estradiol, and intramuscular estradiol are 1 mg/d, 100 mcg/d, and 2 mg weekly, respectively [33]. Maximum doses for estradiol are 400 mcg/d, 6 mg/d and 10 mg weekly, respectively [33]. The initial dose for spironolactone is 50-100 mg/d and maximum is 200 mg/d [33]. It is recommended that patients are seen roughly four times a year during the first year of estrogen treatment. During these visits, serum testosterone and estradiol levels are tested every three months for hormone dose optimization, and serum electrolytes are also tested every 2-3 months until stable. After the first year, patients are monitored at least once yearly. For FTM patients, testosterone therapy causes masculinizing effects including increased muscle mass, fat redistribution, voice changes, and male-pattern hair growth. Side effects may include vaginal atrophy, acne, baldness, hyperlipidemia, diabetes, and

Table 1: Changes Due to Hormone Therapy in Transgender Patients [42].

Laboratory Abnormalities	MTF patients	FTM patients
Red Blood Cell Mass	↓	↑
AST/ALT	-/↓	-/↑
Potassium	↑ (on spironolactone)	Not applicable
Total cholesterol	-/↑	-/↑
Prostate-specific antigen	↓	Not applicable

weight changes [33]. Testosterone therapy is also associated with higher erythropoietin production and polycythemia [31,34-36]. Large systematic review revealed clinically insignificant changes in blood pressure after initiation of testosterone therapy, but inconsistent changes in liver and renal function after therapy [34]. Therefore, masculinization requires monitoring for potential complications.

Like estrogen, dosing for testosterone is dependent on route of administration. Starting dosages for intramuscular testosterone, transdermal gel, and transdermal patch are 100mg every two weeks, 2.5 g/d, and 2.5 mg/d, respectively [37]. Maximum doses of these treatments are 200mg every two weeks, 10 g/d, 7.5 mg/d, respectively [37]. These patients should have monitoring every three months for mood symptoms, blood pressure, weight changes, and lab abnormalities. Specific labs of interest include hematologic, renal, and liver enzymes (Table 1). Estradiol levels are often checked until they decrease to 50 pg/mL, however, cessation of menstruation can also be used to indicate estrogen suppression [37].

AT-RISK BEHAVIOR SCREENING

It is important to discuss social history regularly as transgender patients may often face stress, anxiety, isolation, and discrimination. These issues can lead to an increased likelihood of risky behaviors, such as alcohol dependence, unsafe sexual practices, drug abuse, and smoking [4].

Mental Health Screening

Because many transgender individuals face discrimination, there is increased risk of trauma-related illnesses, depression, and increased suicidality. Therefore, these patients should be screened for depression using the Beck Depression Screening tool. Suicidality can be assessed with direct questioning. Providers should recognize that transgender patients experience positive life outcomes with transgender-centered care [38].

Alcohol Dependence

According to a 2011 Institutes of Medicine report, young and middle-aged transgender patients are especially vulnerable to alcohol misuse including binge drinking. Moreover, alcohol use may be associated with increased violence and victimization. Alcohol use screening tools, such as the Behavior Risk Factors Surveillance System, AUDIT-C screen, and the CAGE questionnaire, are can be used to determine dependence [36].

Table 2: Summary of Current Screening Guidelines for Transgender Patients.

	Female-to-Male (FTM)	Male-to-Female (MTF)
Breast Cancer	USPSTF: mammography every 2 years starting at age 50	USPSTF: mammography every 2 years starting at age 50
	ACOG, ACR, AC: annually starting at age 40	ACOG, ACR, AC: annually starting at age 40
Endometrial Cancer	No screening for asymptomatic patients	Not Applicable
	Symptomatic patients: transvaginal ultrasound & endometrial sampling	
Cervical Cancer	From age 21-29: Pap testing every 3 years	Not Applicable
	From age 30-65, Pap testing with reflex HPV testing every 5 years	
	Over 65 years, discuss with provider	
Anal Cancer	No standard screening for asymptomatic patients. Some experts use annual DARE in HIV+ patients.	No standard screening for asymptomatic patients Some experts use annual DARE in HIV+ patients.
	Symptomatic patients: DARE, Anal Pap test, HPV test, high resolution anoscopy	Symptomatic patients: DARE, Anal Pap test, HPV test, high resolution anoscopy
Ovarian Cancer	No standard guidelines for low-risk patients.	No standard guidelines for low-risk patients.
	Genetic testing for high-risk patients.	Genetic testing for high-risk patients.
Prostate Cancer	Not applicable	Patient-physician discussion about PSA testing and DARE
Metabolic Disorders	Hematologic, renal, and liver-specific blood work every 3 months.	Serum testosterone and estradiol levels every 3 months
	Blood pressure monitoring every 3 months	Serum electrolytes every 2-3 months until stable.
	Serum estradiol levels are checked until they reach 50 pg/mL	
Alcohol Dependence	Behavior Risk Factors Surveillance System	Behavior Risk Factors Surveillance System
	CAGE questionnaire	CAGE questionnaire
Sexual Transmitted Infections	HIV testing for ages 15-65 and/or high-risk patients	HIV testing for ages 15-65 and/or high-risk patients
	Gonorrhea, chlamydia, hepatitis C, and syphilis screening if no recent screening or presence of risky sexual behavior.	Gonorrhea, chlamydia, hepatitis C, and syphilis screening if no recent screening or presence of risky sexual behavior.
Lung Cancer	CT scan for current or former smokers with 30+ pack year history	CT scan for current or former smokers with 30+ pack year history
Abdominal Aortic Aneurysm	No screening required	Abdominal ultrasonography between ages 65-75

Sexual Practices

Patients should be actively counseled to encourage safe sex practices and in preventing sexually transmitted infections (STIs). They should be informed about the transmission and prevention of gonorrhea, chlamydia, HIV, Hepatitis C, and syphilis. Screening for these STIs should occur if the patient has no recent screening or indicates a history of risky sexual behaviour [39].

Smoking-Related Disorders

Given the risk of lung cancer, all adults should be screened and counseled on cessation of tobacco use. Lung cancer screening using a CT scan is reserved for current or former smokers with a 30+ pack year history [40]. In MTF patients who have smoked, abdominal aortic aneurysm screening should be completed using ultrasonography between the ages of 65-75 [41].

CONCLUSION

Transgender patients require specialized attention to address health concerns and understand screening guidelines and protocols for these patients. Beyond routine screening guidelines for both sexes, transgender patients should additionally be screened based on their assigned sex at birth as summarized in Table 2. By becoming aware of the LGBTQ care, physicians can impact the incidence of preventable chronic illnesses.

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