



# Breast Cancer Risk and Screening in Transgender Individuals

David Roznovjak<sup>1</sup> · Andrew Petroll<sup>2</sup> · Chandler S Cortina<sup>3</sup>

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## Abstract

**Purpose of Review** There are over 1.4 million individuals who identify as transgender in the USA, and these individuals are frequently treated with cross-sex hormonal therapy (CSH) to acquire their desired phenotype. Simultaneously, breast cancer is one of the most common cancers in the USA, and there are mixed data on how CSH may influence breast cancer development in transgender individuals. Here, we review the barriers that exist to health access in this population, the current evidence of breast cancer risk in transgender individuals, and breast cancer screening guidelines for both transgender women and men.

**Recent Findings** A large portion of the transgender population report barriers that exist to accessing appropriate healthcare, some of which are directly related to poor interactions with healthcare providers. From both systemic reviews and large retrospective studies, it appears that while transgender females have a lower rate of breast cancer development compared to cis-gender females, transgender males have a higher rate of breast cancer development compared to cis-gender males. While several organizations have released screening guidelines for transgender persons, there is a lack of consensus on optimal screening regimens. In addition, there are no formal recommendations by the American Cancer Society or the United States Preventative Task Force for breast cancer screening in transgender persons.

**Summary** The risk of breast cancer development in transgender individuals is different compared to that of the cis-gender population. Further prospective data are needed to appropriately quantify these risks and to assess what is the appropriate breast cancer screening recommendations for this population.

**Keywords** Breast cancer · Breast cancer risk · Breast imaging · Transgender, disparities

## Introduction

Currently in the USA, there are at least 1.4 million adults who identify as transgender, defined as an individual whose sense of personal identity and gender does not correspond to their sex assigned at birth [1]. This identification may be accompanied by a change in physical appearance, possibly through interventions such as cross-sex hormonal therapy (CSH) and/

or gender-affirming surgical procedures [1]. Currently, there are mixed data on the risk of long-term CSH on the development of breast cancer in transgender individuals. In the year 2020 alone, an estimated 276,480 new cases of breast cancer will be diagnosed in the USA, including an estimated 48,530 cases of ductal carcinoma in situ [2]. Thus, it is imperative to understand the potential risk of CSH and current recommendations for breast cancer screening in the transgender population.

The current literature on breast cancer development in transgender individuals is primarily based on case reports, case series, systematic reviews, and large retrospective analyses and is largely lacking in prospective data. A 2018 systematic review identified a total of only 18 reported cases of breast cancer in transgender females and 8 cases in transgender males [3, 4]. As more cases have been published, a 2020 systematic review was able to identify only 23 cases in the English literature of transgender males with a diagnosis of breast cancer [5••]. Among all series, the majority of breast cancers were hormone-receptor (HR) positive and were found in individuals taking CSH [3•, 4•, 5•]. Here, we review barriers that this population faces to healthcare, the current

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✉ Chandler S Cortina  
ccortina@mcw.edu

<sup>1</sup> Medical College of Wisconsin, Milwaukee, WI, USA

<sup>2</sup> Division of Infectious Disease, Department of Medicine, Froedtert & The Medical College of Wisconsin Inclusion Health Clinic, Milwaukee, WI, USA

<sup>3</sup> Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, 8701 Watertown Plank Rd., Milwaukee, WI 53226, USA

evidence of breast cancer risk in transgender individuals, and breast cancer screening options for both transgender women and men.

### Section 1: Disparities and Healthcare Barriers for Transgender Persons

Despite an increase in visibility through better social acceptance and increased mainstream media coverage, transgender patients continue to suffer from significant health disparities including in cancer care and research [6, 7]. Many of these health disparities develop as a result of stigma and marginalization of the transgender community. Health disparities are further exacerbated by both decreased access to healthcare and patient avoidance due to their own negative experience(s) in healthcare settings [8]. Survey data show that approximately 41% of transgender patients report widespread discrimination in healthcare [8]. Discrimination can be seen on the institutional level as failures to recognize a person's gender and use their chosen name, failure to provide a safe and affirming space for transgender people (such as an appropriate restroom space), and a lack of appropriate patient educational materials [9]. Healthcare providers can contribute to discrimination through negative interpersonal interactions such as a provider's failure to use affirming language, overt refusal of care, micro-aggressions, or lack of transgender health knowledge [10]. In a survey study of 150 transgender men, 68% reported they had experienced some form of mistreatment in seeking healthcare and 47% have avoided seeking healthcare due to their negative experience(s) [10]. Similarly, in a separate survey, out of 452 transgender women, 40.7% reported they avoided seeking healthcare for similar reasons [11]. This indicates that the problem is multilayered and the barriers to access to healthcare is not the only hurdle to overcome [12].

Cancer research involving the transgender community is uncommon. A recent study demonstrated that from 2016 to 2020, among scientific research conducted with sexual and gender minority individuals, only 1.8% of studies were focused on cancer [6]. In addition to the lack of research and knowledge on cancer screening and treatment in the transgender population, there is strong evidence to suggest the incidence of cancer is higher in the transgender community due to increased risks, decreased cancer screening rates, and socioeconomic barriers [13]. A 2018 systematic review on cancer in the transgender population illustrated that the evidence quality was very low and did not provide enough information to definitively determine cancer prevalence rates, indicating the need for further research [14].

If healthcare providers feel uncomfortable treating transgender patients or do not understand how to appropriately care for them, this can also become a healthcare barrier. In a survey of 141 obstetrician and gynecologist providers across the USA, only 30% reported that they felt comfortable caring

for transgender patients. While 80.4% of these providers were willing to perform routine breast examinations on transgender women, 59.4% of providers did not know the recommendations for breast cancer screening for these individuals [15]. The present study demonstrates the gap in knowledge both of the current guidelines and the ability to effectively provide treatment to transgender patients.

### Section 2: Breast Cancer Risk in Transgender Women (Male to Female)

Feminizing cross-sex hormonal therapies (CSH) are thought to most drastically increase the potential risk for breast cancer development among transgender females [3]. This is largely drawn from evidence that elevated estrogen exposure in cis-gender males is associated with an increased risk of breast cancer development and that both increased duration and exposure to estrogen may play a pivotal role in the development and proliferation of neoplastic processes within the breast epithelium [16, 17, 18]. Previous data have shown that exogenous estrogen-based therapy in biological males does cause proliferation of breast ducts and lobules that is histologically identical to that of biological females [19, 20]. However, due to the small number of reported cases of breast cancer in transgender females, there is no current evidence to directly confirm that use of CSH definitively increases the risk of breast cancer development in transgender females compared to that of the general population [21, 22].

A single analysis from 2013 found the rate of breast cancer development in transgender females to be 4.1 per 100,000 person-years (PY) (95% CI 0.8–13.0) compared to 1.2 per 100,000 PY in cis-gender males and 170 per 100,000 PY for cis-gender females. While it did appear that transgender females had a higher rate of breast cancer development compared to cis-gender males, this finding did not remain significant on statistical analysis [23]. On the contrary, a large retrospective analysis from the Netherlands found that transgender females had a 46-fold increase in the risk of breast cancer development compared to that of cis-gender males (95% CI 27.2–75.4) but lower than in cis-gender females [24]. While transgender females have a higher incidence of breast cancer compared to cis-gender males, their breast cancer risk is much lower when compared to cis-gender females [3, 23, 24].

The first cases of breast cancer in transgender females were reported in 1968 by Symmers and colleagues in two 30-year-old patients [25]. The number of published cases has slowly grown over the past several decades, with the majority of publications occurring within the past 10 years. A 2018 systematic review of breast cancer cases in transgender females identified 22 published cases in the English language [3]. Tumors are usually estrogen-receptor (ER) positive, human epidermal growth factor receptor 2 (Her2) negative and are clinically detected as a palpable lesion on breast examination.

Mean age at time diagnosis of breast cancer was found to be 51.5 years (range of 30–69), which is significantly younger compared to median age of 68 seen in the cis-gender male population [3, 26]. The majority had taken or were currently taking estrogen-based CSH at the time of diagnosis, seven had a positive family history of breast cancer, and one patient was found to have a pathogenic germline variant in the *BRCA2* gene [3, 27].

### Section 3: Breast Cancer Risk in Transgender Men (Female to Male)

Transgender men commonly take exogenous androgen-based therapy to induce a masculine phenotype [28]. While testosterone therapy may confer an increased risk in breast cancer development, the current data do not demonstrate a clear risk [29, 30]. This theory is hypothesized to occur through the peripheral conversion of androgens by the enzyme aromatase to estrogen [31].

Over the past several years, three systemic reviews have been performed on the incidence of breast cancer in transgender men [4, 5, 32]. The most recent identified 23 cases, all of which had taken androgen-based CSH therapy [5]. Mean age at time of diagnosis was 42 years (range from 27 to 77) and the majority (74%) were hormone-receptor positive, 30% were Her2 positive, and one case was hormone-receptor and Her2 negative (triple-negative) [5]. The most common presenting symptom was a palpable mass and 39% were found incidentally at the time of chest-masculinization surgery. Notably, nine patients did have a significant family history of breast cancer, suggesting that a genetic or familial component may have been involved in risk development [5]. In the Netherlands registry of 1229 transgender men, four cases of breast cancer were identified over a 34-year period [24]. Median age at time diagnosis of breast cancer was 61 and when compared to the lifetime risk of breast cancer in cis-gender females, a 0.3-fold risk decrease was seen [24]. While breast cancer development in transgender males is lower than that of cis-gender females, the incidence is still higher than that of cis-gender males and the direct relationship between testosterone and breast cancer development remains unclear [33].

Chest masculinization surgery, often called “top-surgery,” is an elective cosmetic procedure that is sometimes perused by transgender males and should not be considered as a preventative oncologic operation given that native breast tissue may be left behind for appropriate chest contouring and cosmetics [34–36]. Several cases of breast cancer development has been reported in transgender males who have previously undergone chest masculinization procedures [37•]. In addition, when examining breast cancer specimens in transgender men on androgen-based therapy, androgen-receptor testing on tumor pathology should be considered given that it may influence adjuvant therapy treatment and future CSH treatment [36, 38].

### Section 4: Breast Cancer Screening and Imaging

Despite the sparse evidence on breast cancer risks in the transgender population, there are several organizations that have developed suggested guidelines for breast cancer screening in transgender patients that are publicly available (Table 1). All current guidelines recommend some form of breast cancer screening with mammography in transgender females beginning at age 50 after at least 5 years of hormonal therapy [39•, 40•, 41•, 42•, 43•, 44•, 45•]. However, individualized risk based on family history and personal history should be evaluated for consideration to begin screening sooner [39, 40, 43–45]. In those transgender men who have not undergone chest masculinization surgery, all guidelines recommend following

**Table 1** Summary of current chest and breast cancer screening guidelines for transgender individuals

Guideline entity:	Transgender males (female to male)	Transgender females (male to female)
University of California San Francisco [39, 40]	<i>Breast reduction or no chest surgery:</i> Screen based on cis-gender female guidelines. Consider MMG, MRI, or US. Engaged dialog between patient and provider	<i>No FH:</i> Age $\geq 50$ and at least 5–10 years of hormone therapy: screening MMG every 2 years <i>FH and or known gene mutation:</i> individual approach
Fenway Health [41]	<i>No chest surgery:</i> Follow screening for cis-gender females <i>Chest surgery:</i> Engaged dialog between patient and provider	Age $\geq 50$ and at least 5 years of hormone therapy: annual screening MMG
University Hospitals Cleveland Medical Center [42]	<i>Breast reduction or no chest surgery:</i> Screen based on cis-gender female guidelines	Age $\geq 50$ and at least 5 years of hormone therapy: screening MMG every 2 years
Susan G. Komen Puget Sound [43]	<i>Chest surgery:</i> Annual chest and axillary examinations. If only chest reduction, then annual MMG beginning at age 50 <u>No Chest Surgery:</u> Annual MMG beginning at age 50 <u>FH and No Chest Surgery:</u> Consider beginning annual MMG before age 50	<i>No FH:</i> Age 50 and on estrogen-based therapy for at least 5 years: screen with MMG yearly <i>FH:</i> Discuss risk with a healthcare provider to consider beginning prior to age 50 or prior to 5 years of estrogen-based therapy: screen with MMG yearly
Canadian Cancer Society [44, 45]	<i>Chest surgery and no chest surgery:</i> Screening MMG every 2 years age 50–69	Age 50–69 and on estrogen-based therapy for at least 5 years: screen with MMG every 2 years

*FH* family history, *MMG* mammogram

screening guidelines for cis-gender females. However, recommendations vary for those transgender men who have received a chest masculinization operation. Currently, there are no formal recommendations by the American Cancer Society or the United States Preventative Task Force on breast screening in transgender persons [46, 47].

If an abnormality is seen on screening imaging or on clinical examination, standard diagnostic breast imaging guidelines should be followed in conjunction with patients and clinicians [48]. Any lesion that is felt to be suspicious on examination or on imaging should be considered for tissue biopsy [49, 50]. When performing both screening and diagnostic clinical examinations and imaging assessments, it is imperative for healthcare providers to be knowledgeable of the appropriate terminology to use with patients, aware of the anatomical differences that may exist compared to cis-gender individuals, and offer an inclusive patient environment [48, 51]. A recent survey revealed that only 33% of transgender patients undergo breast cancer screenings, compared to 66% of cis-gender patients, indicating there is significant room for improvement in screening [52].

## Conclusion

While current research acknowledges that much is still unknown regarding the long-term sequelae of exogenous hormonal therapy has on breast cancer development, large-scale longitude prospective data are needed to appropriately estimate this potential risk. In addition, healthcare provider education on the barriers that transgender individuals face is needed to optimize access to care and the patient–provider relationship. Future efforts are needed to further assess the lifetime risk of breast cancer development in transgender individuals, educate healthcare providers on current care standards, and to develop optimal evidence-based breast cancer screening guidelines for this unique population.

## Compliance with Ethical Standards

**Conflict of Interest** The authors have no relevant disclosures to report. This article does not contain any studies with human or animal subjects performed by any of the authors. Author ICJME COI documents are included separately.

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