

The Risk of Breast Cancer Among Male-to-Female Transgenders: A Systematic Review

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Background. The health needs of the transgender population have not been well understood and have been an interest when it comes to research. There were several reported cases of breast cancer, specifically in male-to-female (MtF) transgenders or those who were born genotypic male but addressed themselves psychosocially as females. The characteristics, risk factors, and recommendations for breast cancer in this population have not been established, and thus the need to develop further research.

Methods. In this study, three independent reviewers conducted literature searches using various online databases for all types of studies in relation to breast cancer occurrences in MtF transgenders in adult patients during the publication timeline of 2016-2022. Studies were excluded if there were no confirmed histologic studies nor breast cancer screening recommendations on the said population.

Results. A total of 14 articles were included and categorized in which quality assessment for risk of bias was done accordingly. Most of the studies were case reports, case series, and literature reviews making the overall quality poor. Most of the MtF transgenders were diagnosed with breast cancer at a median age of 58.9 years. The use of cross-sex hormones for at least 5 years by a transgender women may contribute the most to the risk of developing breast cancer. Other possible risk factors include a family history of breast cancer and obesity with body mass index (BMI) >35. The level of risk of developing breast cancer is still uncertain, but chronic hormonal use may increase one's risk.

Conclusion. Due to the poor quality of the studies included, it is not possible at this time to quantify the risk of breast cancer among MtF transgenders. However, long-term use of cross-sex hormones (estrogen and/or progesterone) may be a contributing factor, but more large-scale studies are needed to establish the relationship. Most studies recommend mammography as the screening diagnostic modality at the age of 50 and older, with significant risk factors as identified annually or biennially. These recommendations still vary and are not yet well established by strong evidence due to various limitations, one of which is the uncertainty of the size of the MtF transgender population. Hence, further investigations are warranted and this study aims to uplift the recognition of breast cancer risk among the MtF transgenders.

Keywords. *Male-to-female transgenders, MtF, Breast cancer, Transgender*

Introduction

The most common malignancy among the general female population is breast cancer, which accounts for about 25% of all malignancies in this population, with a

lifetime risk of 12%, while only 0.1% lifetime risk was noted in the male population.^{1,2} Numerous risk factors for breast cancers have been recognized, namely, advanced age, family history of breast carcinoma, existing genetic mutations, breast density, overweight, obesity, nulliparous women, and tobacco and alcohol use.² However, the transgender population, specifically the male-to-female (MtF) transgenders, have unique health needs. There were several reports of MtF transgenders developing breast cancer, and this is becoming an

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interest in research.³ Although there are available systematic reviews concerning the breast cancer risk of the MtF transgender population, identifying the risk has been a challenge, and establishing guidelines for screening is fragmentary.

In this study, we aim to answer whether there is an increased risk for breast cancer among MtF transgenders as compared to the general female population. Furthermore, we will describe clinical presentations, identify risk factors, appraise and evaluate evidence-based recommendations from clinical studies on breast cancer early screening procedures, and determine the level of risk among the MtF population through a systematic review.

Materials and Methods

Eligibility Criteria

This study comprises all types of papers, including case reports, case series, cohort and cross-sectional studies such as randomized controlled trials, systematic reviews, and meta-analyses that included breast cancer occurrences in MtF transgender patients in the adult population during the publication timeline of 2016–2022, as earlier literature was incorporated into recent studies during this review. During study selection, duplication of the studies identified and included in other systematic reviews were removed. No language and publication status restrictions were imposed. Studies were excluded through the criteria of no MtF transgender patients and with either no confirmed breast cancer occurrence that is confirmed by histologic examination or no breast cancer screening recommendations on MtF transgenders.

Information Sources, Search Strategy, and Selection Process

The identification of studies was done in August 2022 through searching in the online databases such as Cochrane, Ovid, OpenAthens, PubMed, HERDIN, and grey literatures from Google scholar as provided by the Romeo P. Ariniego, MD, Library of De La Salle Medical and Health Sciences Institute. The search was done using MeSH terms as follows: "Transgender", "Transsexual", "Breast Cancer", "Male to Female Transgenders", "MtF Transgenders", "MtF Transsexual", "Breast Carcinoma", "Breast Malignancy", "Breast Neoplasm", and was reviewed by two individual reviewers. All studies that were identified and included from the search strategy were screened in duplicate by three independent reviewers. Full texts of potentially eligible studies who passed the level 1 screening were critically appraised to assess eligibility. Non-electronic versions were also requested, and all eligible study types were included. The updated PRISMA 2020 guidelines were followed. Disagreements were resolved by consensus strategy.

Data Collection Process and Data Items

The data were extracted from the reports independently by three reviewers. Data collected from the studies include the patient's age, breast cancer characteristics,

BRCA gene status, family history, hormone receptor status, and recommendations on breast cancer screening for MtF transgenders. The level or degree of risk of developing breast cancer were extracted and reported as to whether the risk increased or decreased. The corresponding authors were contacted for further information and to clarify any unclear data in their study. Qualitative data extraction and qualitative assessment were performed using the JBI checklist for each respective study.⁴

Study Risk, Reporting of Bias Assessment, and Certainty Assessment

Each included study was evaluated individually with the risk-of-bias tool to ascertain the validity of eligible studies. The eligible studies underwent a component-based assessment for quality and bias (including blinding of patients, healthcare providers, data collectors, outcome assessors, as well as the adequacy of randomization and concealment of allocation and the extent of loss to follow-up) as guided from the JBI checklist and adopted from the study of Hartley et al.,⁵ and were presented in graph and summary form. Disagreements among reviewers were resolved through a consensus strategy. Primary reviewers first discussed discrepancies, and if unresolved, a third independent reviewer was consulted. For persistent disagreements, a senior researcher provided the final decision based on pre-defined inclusion criteria and methodological quality. Glycemic Control Assessment (HbA1c)

HbA1c result from three time points (initial consult, 3 months and 6 months) were taken for each patient. A standard value of less than 7% HbA1c indicated desired glycemic control. At 6 months after the initial consult, the

Effect Measures and Synthesis Methods

The degree or level of risk of developing breast cancer in MtF transgender patients were described as the primary outcome of this review. It was described as to whether there was an increased or decreased risk of breast cancer. However, relative risk or incidence ratio for overall breast cancer risk for MtF transgender individuals were not calculated, due to the predominance of case reports and literature reviews, as well as the lack of an established total transgender population. Data synthesis was performed by using descriptive statistics such as mean difference for baseline characteristics. The evidence-based data were appraised using PRISMA.

range of HbA1c is 3.81 to 12.70 with a mean of 7.23 ± 1.30 . A total of 161 patients or 47.4% achieved glycemic control with less than 7% HbA1c.

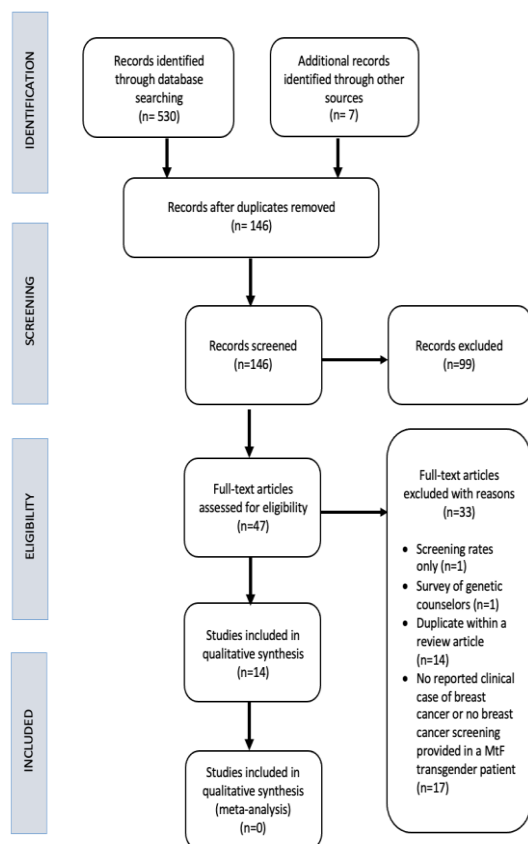
Results

Study Selection and Characteristics

During study selection, a total of 530 potential articles from database searching and 7 additional records from bibliography review and electronic library were identified. After duplicates between databases and other mentioned sources were removed, 146 titles, abstracts

and electronic dissertations were screened. The corresponding authors were emailed for a full text copy in articles that were only available as abstracts; however, no response was obtained. A full-text assessment for eligibility was done to 47 articles who have either documented clinical case of breast cancer or provided breast cancer screening in MtF transgender patients (Figure 1). One cross-sectional analysis article only compared the screening rates between different cancers such as cervical, breast, and colorectal cancer in MtF transgender patients. On the other hand, another descriptive article conducted a cancer risk survey among genetic counselors of MtF transgender patients. However, neither of these articles had evidence of breast cancer by histologic examination nor breast cancer screening recommendations, as so with most of the articles excluded. A total of 14 articles⁶⁻¹⁹ were included in qualitative synthesis, and each of their characteristics are shown in Table 1. The earliest article was published in 2018, and the most recent was published in 2022. Most articles were published in the United States (n=9), and the rest were published in India (n=1), Lebanon (n=1), Scotland (n=1), Canada (n=1), and Brazil (n=1). Most of the articles were case reports (n=6), in which two articles

Figure 1. Flow diagram of studies included in systematic review



Study Quality Assessment

A total of 14 articles were assessed for quality and risk of bias (Figure 2, Figure 3). The overall quality of the articles was poor, as most of these had unclear risk or high risk of bias when it came to quality assessments for results – specifically, biased sample selection (random samples or selection of consecutive series of patients when not clearly stated), loss to follow-up (no certain timeline of cancer status and plans), no blinded outcome (outcomes were assessed by persons with knowledge of the study), no adequate statistical adjustment (no statistical adjustment was performed), and no precision of results (no reported confidence intervals for outcome). Four articles had a high risk of bias for description of population, as the inclusion criteria were not defined, and one did not describe the age and natal gender. Two articles posed a high risk of bias to its exposure and outcome measurements, since one article reported a concomitant neoplasm and the other based its outcome on cisgender females. Five articles had a high risk of outcome measurement, since the results were generalized with female-to-male transgender or there was no mention of proper reference for the recommendations stated. Despite these, most of the articles had low risk of bias when it came to adequate exposure (described MtF transgender and possible exposure), and outcome measurement (mentioned histologic confirmation or screening methods for breast

Figure 2. Graph of quality assessment of included studies

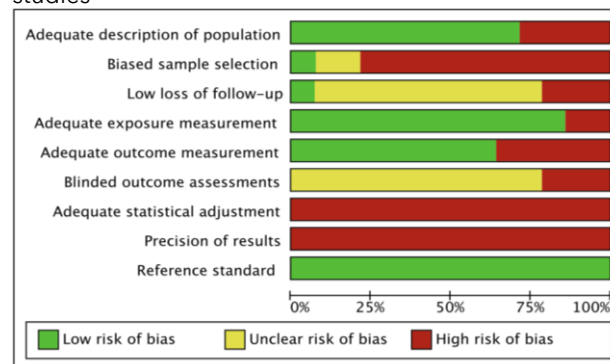
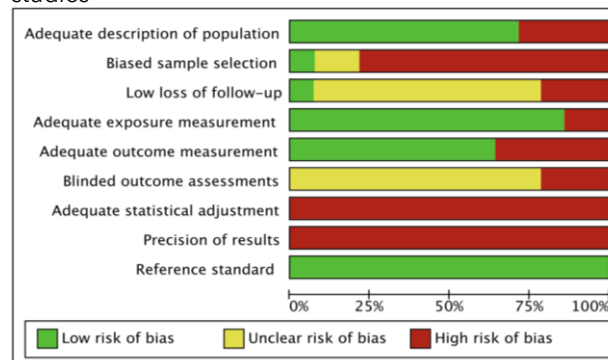


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Table 1. Eligible publications on MtF breast cancer

Author	Year	Location	Study Type	Breast cancer events/screening
Ali et al ⁶	2019	USA	CR	1
Stafford et al ⁷	2020	USA	CR	1
Nehlsen et al ⁸	2020	USA	CR and LR	1
Sieberg et al ⁹	2021	USA	CR	1
Phillips and Timek ¹⁰	2022	USA	CR	1
Cole et al ¹¹	2022	Lebanon	CS	21
Dente et al ¹²	2019	USA	LR	15
Brown et al ¹³	2021	USA	LR	+S
Iwamoto et al ¹⁴	2020	USA	LR	1
Goyal et al ¹⁵	2020	India	LR	+S
Ceres et al ¹⁶	2018	USA	SR	+S
Joint et al ¹⁷	2018	Scotland	SR	15 / +S
Meggetto et al ¹⁸	2019	Canada	SR	+S
Calas et al ¹⁹	2022	Brazil	SR	+S

+S, with screening recommendations; CR, case report; CS, case series; LR, literature review; NR, not recorded; SR, systematic review

Breast Cancer Characteristics and Clinical Presentation

Five case reports, one case series, and three systematic reviews focusing on MtF breast cancer were included in this review. Table 2 shows the articles that mentioned breast cancer characteristics in MtF transgenders, and the remaining had no mention of breast cancer characteristics but cited level of risk and screening recommendations (Table 3).

MtF transgenders were diagnosed with breast cancer at a median age of 58.9 years. Almost all the patients included in the study declared the use of either estrogen, progesterone, or a combination of both, and to some extent, the use of anti-androgens such as spironolactone for at least 5 years. Only three case reports mentioned family history of cancer, in which two specifically had breast cancer history, and two case reports cited that they

were Jewish descendants. Among the journals included, breast mass presenting as breast asymmetry or palpable mass was the most common presentation of breast cancer. Other presentations include skin changes, nipple discharge, and breast pain. Only two case reports reported mammogram screening and incidental finding and work-up leading to the diagnosis of breast cancer. The most common type of breast carcinoma among the included patients was invasive ductal carcinoma; however, there were reports of ductal carcinoma in situ and adenocarcinoma. One patient included in this review had a breast implant associated with anaplastic large cell lymphoma, while another had metastatic breast carcinoma which was initially presented as neck mass but later on work-up was revealed to be breast cancer in origin. Most of these tumors are estrogen receptor (ER) positive, progesterone receptor (PR) positive and HER2-neu negative subtypes; however, testing for *BRCA2* mutation was inconsistent and only three *BRCA* positives were reported.

Table 2. Characteristics of MtF breast cancer

Author	Age (years)	Breast cancer type	ER status	PR status	HER2 status	BRCA	Family history	Hormonal Use
Ali et al ⁶	54	BIA ALCL St III	NR	NR	NR	NR	None	Yes
Stafford et al ⁷	67	Ductal carcinoma in situ	Positive	Positive	NR	NR	Ovarian and gastric cancer	Yes, estrogen
Nehlsen et al ⁸	53	Invasive breast carcinoma	Negative	Negative	Negative	NR	None	33 years on estrogen
Sieberg et al ⁹	70	Invasive ductal carcinoma	Positive	Positive	Negative	Positive	Breast cancer	Yes, estradiol
Phillips and Timek ¹⁰	51	Metastatic breast carcinoma	Positive	Positive	Negative	NR	Breast cancer	NR
Cole et al ¹¹	30-74	DCIS	10 positive 8 negative 3 NR	8 positive 4 negative 9 NR	2 positive 9 negative 10 NR	1 positive 20 NR	NR	Yes but 2 patients had no report of use
Dente et al ¹²	30-65	Not recorded	6/12 positive 3/15 negative	5/11 positive 3/15 negative	2/6 HER2 neu 3/15 negative	0/2 positive	NR	Yes, estrogen and progesterone
Joint et al ¹⁷	NR	50% invasive ductal carcinomas, 15% adenocarcinomas, 10% ductal carcinomas, 10% unspecified breast carcinomas, 5% ductal carcinoma in situ, 5% secretory carcinomas, 5% primary tumor unconfirmed	52% positive	40% positive	NR	1/4 positive	NR	Yes, except for 1 patient

NR, not recorded

Risk of MtF Breast Cancer and Screening Recommendations

From the literature and systematic reviews that were included in this study, all journals recommended the use of mammogram as the screening method for breast cancer for patients with breast implants, and several studies suggested the screening mammogram for

transwomen patients who have been using cross-sex hormones like estrogen and progesterone of at least 5 years (Table 3).^{4,7,8,13,16,17} Furthermore, screening should start by at least 50 years old,^{4,13,16} in contrast to Brown et al., who recommended to start screening by age 40 years and even earlier (25-30 years old) if the transfeminine patient had a higher than average risk or 15 years of hormone use.

Table 3. Level of evidence and risk of MtF breast cancer

Author	Year	Study type	Population	Level of risk	Recommendations	Level of evidence
Dente et al ¹²	2019	LR	15 transwomen	There remains a knowledge gap in risk of breast cancer in transgender patients	Screen at age >50 years and >5 years of HRT with additional risk factors to consider: BMI >35 and family history of breast cancer	VII
Brown et al ¹³	2021	LR	Transwoman	Incidence was increased in transgender women who received hormone treatment	- Screening mammography in average-risk transgender women aged ≥40 years with >5 years of hormone use - Mammography as screening in higher-than-average-risk transfeminine patients aged 25-30 years or older with past or current hormone use for 15 years - Imaging is usually not appropriate for breast cancer screening in an average-risk transfeminine patient of any age with no or <5 years of hormone use	VII
Nehlsen et al ⁸	2020	CR, LR	Transwoman	Majority of male breast cancers are estrogen and progesterone positive; hence, maybe differentiate between male breast cancers and those driven by hormone administration. However, a small volume of literature suggests no significant increase in breast cancer incidence in the transgender female population	Mammography is the primary screening modality in patients who are on estrogen therapy.	VI

Iwamoto et al ¹⁴	2020	LR	Transwoman	NA	Screening mammography can be done every 2 years for BMI >35 or those taking CHS for 5-10 years.	VII
Goyal et al ¹⁵	2020	LR	Transwoman	There is a mixed review on the increased risk and association of CSH use in the development of breast cancer.	The recommendation is to do breast cancer screening if a patient is >50 years old and still on CSH or have >5 years of hormonal therapy and/or before cosmetic mastectomy	VII
Ceres et al ¹⁶	2018	SR	Transwoman	NA	Screening in patients aged >50 years with additional risk factors for breast cancer such as >5 years use of estrogen / progesterone therapy, family history of cancer, and BMI >35	V
Joint et al ¹⁷	2018	SR	15 transwomen	There is a greater risk for breast cancer on patients who used a combination estrogen + progesterone than estrogen alone, and the risk further increases if the use of CSH is longer (≥10 years)	More large-scale studies with extended periods of follow-up focusing on the potential long-term health effects and risk are recommended	V
Meggetto et al ¹⁸	2019	SR	Transwoman	One study suggested no significant change in the risk between MtF using hormonal therapy and the male population, while one study suggested that MtF using hormonal therapy had a higher incidence for breast cancer	Most of the reviewed studies recommended breast screening if a transwoman has CSH use, but this depends on the duration, presence of breast implants, age, orchiectomy status, and breast growth. Some recommended doing the screening mammogram if there is ≥5 years of CSH use and every 2 years	V
Calas et al ¹⁹	2022	SR	Transwoman	NA	Mammographic screening in transgender women undergoing hormone therapy, after 5 years of use, but there is no consensus regarding how often and at what age.	V

CSH, cross-sex hormone; Level V, evidence from systematic reviews of descriptive and qualitative studies; Level VI, evidence from a single descriptive or qualitative study; Level VII, evidence from the opinion of authorities and/or reports of expert committees; LR, literature review; NA, not applicable; NR, not recorded; SR, systematic review²⁰

The level of risk in this population was increased among those with hormonal treatment; the most prominent risk factor that was identified in the studies is the duration of

hormonal therapy. Nehlsen et al. cited that breast cancer possibly caused by hormonal administration may be difficult to justify without molecular markers, as majority of the patients were ER and PR positive. Other risk factors

mentioned in the literature include BMI, presence of breast implants, orchiectomy status, and breast growth. A mixed review or no significant change in the level of risk were cited in the study of Dente et al., Nehlsen et al., Goyal et al., and Meggetto et al.

Discussion

The MtF transgender population, or transwomen/trans females, are the ones who were born as male phenotype but identifies themselves psychosocially as female. This particular population has their special needs, most especially concerning their healthcare. Little is known with regard to the overall incidence and guidelines for screening of breast cancer in MtF transgenders, and it is still a work in progress in the field of research. To our knowledge, there are still no published reports of breast cancer in MtF transgenders in the Philippines. Brown and Jones have conducted a study with the transgender population and have identified a 0.2% incidence in their entire sample size for breast cancer, two of whom were MtF transgenders.²¹ Estimating the transgender population is challenging due to inconsistent data collection, stigma, and privacy concerns, leading to under-representation in research. Many health surveys and cancer registries lack gender identity data, making it difficult to assess breast cancer risk in MtF transgender individuals and develop evidence-based screening guidelines.

Most of the articles reviewed had breast cancer presentations during the late-middle adult years, which is also consistent with recent international literature during the late-middle (ages 45-64) to late adult stages (ages 65 and older).²¹⁻²³ In this review, the median age of breast cancer diagnosis in MtF transgender individuals (58.9 years) falls between that of cisgender women and men. According to the statistics from the American Cancer Society, the median age at diagnosis in cisgender women is approximately 62 years, while in cisgender men it is around 67 years.²⁴ This suggests that breast cancer in MtF transgender individuals may develop much earlier than in cisgender men but just slightly earlier or similar to cisgender women. The influence of long-term estrogen exposure, genetic predisposition, and other risk factors may contribute to this intermediate-risk profile (Table 4). Additionally, even at the first few medical consults, the possibility of malignancies was known, which were primarily confirmed as carcinoma. Factors that served as hindrance to health consult may have also posed an ancillary effect on why most of the diagnoses of breast cancer were during the late age. Joseph N has reported refusal of most MtF transgenders to seek medical care in the United States due to discrimination, harassment, or violence, or they had to teach medical providers about transgender care, but these were contrary to Philippine setting.²⁵ Healthcare services in the Philippines were reported by MtF transgenders to be easily accessible, but most consults were because of employment purposes.²⁵

Table 4. Summary of risk factors contributing to breast cancer development in MtF transgender individuals

Risk Factor	Description	Relative contribution to risk
Hormone therapy use	Long-term use (≥ 5 years) of exogenous estrogen may promote breast tissue proliferation and increase cancer risk	Significant
Genetic predisposition	Family history of breast cancer, in which individuals with <i>BRCA1/BRCA2</i> mutations have an elevated breast cancer risk similar to cisgender women	Major
BMI >35	Higher BMI is linked to increased estrogen levels and a higher risk of hormone-sensitive breast cancer	Elevated
Presence of breast implants	The presence of breast implants in MtF individuals has not been shown to increase breast cancer risk but may impair the accuracy of screening mammography	Minimal
Orchiectomy status	Undergoing orchiectomy reduces endogenous testosterone levels, which may influence breast cancer risk; however, the specific impact on MtF individuals remains unclear due to limited data	Uncertain
Breast growth	The degree of breast development achieved through hormone therapy may correlate with breast cancer risk, but current evidence is insufficient to establish a definitive relationship	Uncertain

Note: The relative contributions to risk are estimated based on available data and may vary among individuals. Further research is needed to quantify these risks accurately in the MtF transgender population. Significant - Strong association with breast cancer development; Major - Primary contributing factor with substantial impact; Elevated - Higher than moderate but not as significant as major risk factors; Minimal - Very little evidence of risk or negligible impact; Uncertain - Insufficient data or conflicting evidence on its effect.

This study identified key risk factors, including family history of breast cancer, hormone therapy use, and BMI >35 , which align with findings from existing literature (Table 3). Notably, hormone therapy use emerged as the most significant contributing factor across various

populations, including those in Southeast Asia.²⁶ This is consistent with prior research indicating that prolonged exposure to exogenous hormones can influence breast cancer risk through several biological mechanisms.²⁷ Exogenous estrogen administered during hormone

therapy binds to estrogen receptors in breast tissue, promoting cellular proliferation and potentially increasing the likelihood of malignant transformations. Additionally, genetic factors, such as *BRCA1* and *BRCA2* mutations may significantly increase breast cancer risk by impairing the body's ability to repair DNA damage and maintain genomic stability.^{2,5,28} Transwomen use cross-sex hormones to transition from their biological gender to their desired physique and gender, as hormones are the main reason for the development of one's secondary sexual characteristics. Interestingly, a study suggested that estrogen therapy had a minimal effect on the development of breast tissue, as only 10.7% of patients on estrogen therapy develop an "A" cup at 1 year of hormonal use.¹⁹ Additionally, while genetic predisposition and obesity are well-established risk factors, their relative impact may vary across different demographic and geographic populations.²⁹ These findings underscore the importance of tailored risk assessment and screening strategies based on regional and individual risk profiles.

In the Philippines, Winter et al. have reported that 69.4% of their participants have a history of hormonal use even at the early age of 13 years, and the majority did so without medical supervision.³⁰ Furthermore, a local study of Pang and Barrera also reported unsupervised hormonal use in all of their MtF transgender respondents in the Zamboanga peninsula, but their mean BMI was at 21.7, which was lower than the BMI level that may constitute a high risk for breast cancer.³¹ Unfortunately, there was no mention of their respondents' family histories. Limited access to supervised gender-affirming care poses significant ethical concerns, as many transgender individuals resort to unsupervised hormone use due to financial constraints, stigma, and a lack of specialized healthcare providers. This increases the risk of adverse health effects, including potential impacts on breast cancer risk, without proper monitoring or informed medical guidance. Expanding affordable and supervised care, improving provider training, and addressing societal barriers are essential for safer evidence-based treatment.

The screening recommendations vary from very limited studies, and they have no united consensus with regard to this particular population. Most of the literature gathered in this review recommend mammography as the basic screening modality and early screening at age >50 years, with significant risk factors as mentioned that would classify the patient as high risk for breast cancer.^{12,14-16} However, a consideration should be made since mammogram is less sensitive in detecting breast cancer in a person with breast implants than in a person without.³² To date, the recommendations on timing of screening is based on the recommendations of breast cancer screening in cisgender females, and until now there is no official recommendation in terms of the resources and ensure equitable access to care. Addressing these gaps will require standardized data collection, inclusive research methodologies, and

interval of screening mammography for transgender women, although Iwamoto et al. recommended to do the screening every 2 years provided that the risk factors identified are present, but there can be limitations in the mammogram if a patient is subjected to mastectomy. Moreover, breast imaging or mammography is not recommended for transgender women who have no hormonal use unless the patient has other known risk factors such as having Klinefelter syndrome.²⁸ The exact interval for screening is still unknown, but in some consensus and to our knowledge, they recommend annual or biennial mammography for MtF transgenders or may be earlier if with high risk factors.^{5,19,33,34} In spite of these recommendations, most of the studies were drafted from a cisgender women population or a pool of MtF transgender case series. This may be primarily because the exact population of MtF transgenders is still unknown, and so, current evidence-based recommendations are not sufficient. Making a scientific analysis for the data and definitive recommendation was unyielding. There is also difficulty in determining the level of risk among this population, for the same reason as mentioned. There are reports that were uncertain, but there are some that reported an increased risk of breast cancer among MtF transgenders who have a significant history of hormonal use.^{8,17,22}

The findings of this review are limited by the predominance of case reports and literature reviews, which restrict the general applicability of the results and are prone to bias and lack applicability to the large-scale population. There were vast, albeit limited, articles in international databases that were searched, but the majority had no evidence of breast cancer nor cited recommendations. Numerous gender identification and terminologies were also encountered that may have limited the study search. The term "transgender" was mentioned in the literature as an umbrella term for those person who were assigned male sex at birth and identify as female, including those who underwent transition, which refers to steps taken to alter outward appearance, and gender reassignment, which refers to steps taken permanently to alter one's phenotype and can be achieved by hormone treatment and surgery.^{8,12,17} The terminologies and definitions are still evolving, and these may be a substantial limitation involving this population. In addition, the primary limitation we encountered was the redundancy of the articles, since most of the studies were already included in a review. There were also articles that could not be easily accessed although available and limited resources have been exhausted. The lack of large-scale cohort studies or randomized trials emphasize the need for more rigorous research to accurately determine breast cancer risk in MtF transgender individuals and provide evidence-based screening recommendations. Without accurate estimates, healthcare systems may struggle to allocate

policies that encourage safe disclosure and participation in healthcare and research settings.

Future research on breast cancer risk in MtF transgender individuals should focus on longitudinal studies to assess the long-term effects of gender-affirming hormone therapy, comparing cancer risk with cisgender populations, and exploring genetic and molecular changes in breast tissue. Accurate estimation of the transgender population and improved data collection methods are essential for reliable statistical data. Additionally, further research should evaluate tailored screening guidelines, examine the impact of surgical interventions, and address socioeconomic and healthcare access disparities, to enhance prevention and early detection in this population.

The results of this study will amplify the awareness regarding the increased risk of breast cancer among male patients with gender reassignment, including an additional knowledge on the risk factors. The medical providers will be more knowledgeable regarding the health needs of the transgender population. And lastly, this study will aid in emerging guidelines and future research, since what is known is still fragmented because the denominator to the equation to develop significant evidence is yet to be unraveled.

Conclusion

Just like in cisgender females, a palpable mass is the most common presentation of breast cancer in MtF transgenders with breast cancer. *BRCA* mutation is uncommon, but ER/PR positive subtypes are the most prominent. Long-term use of cross-sex hormones (estrogen and or progesterone) may be a contributing factor for the development of breast cancer. Clinicians should assess potential risk factors when determining screening recommendations. Mammography is generally recommended starting at age 50, or earlier for patients at higher risk. Healthcare providers should recognize the unique breast cancer risks in MtF transgender patients and adopt an individualized approach to screening. Despite the lack of definitive guidelines, proactive risk assessment, informed discussions, and advocacy for inclusive research are essential to ensure early detection and equitable care. Future research should focus on the long-term effects of hormone therapy, accurate risk assessment, tailored screening guidelines, and healthcare disparities, to establish the relationship and quantify the risk.

Registration and Protocol

This review has not been registered at the time of data collection. However, its publication remains valuable as it synthesizes existing literature, identifies key gaps, and informs future research and clinical guidelines. A review protocol was done and was approved by the Technical Review Board of De La Salle Medical Health Sciences Institute - Center for Clinical Epidemiology and Biostatistics. This study was exempted from ethics committee approval.

Support

This study was undertaken as education research. No funding was received.

Competing Interest

No competing interests are declared by the authors.

Availability of Data, Code, And other Materials

Data collection form was adopted from the *JBIManual for Evidence Synthesis*. JBI. (n.d.). Retrieved November 30, 2021, from <https://jbi-global-wiki.refined.site/space/MANUAL>, and quality assessment was adopted from the study of Hartley RL, Stone JP, and Temple-Oberle C (2018). Breast cancer in transgender patients: a systematic review. Part 1: Male to female. *European Journal of Surgical Oncology*, 44(10), 1455-1462.

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