

ORIGINAL ARTICLE – GLOBAL HEALTH SERVICES RESEARCH

Tumors, Treatments, and Trust: Cancer Characteristics, Outcomes, and Screening Uptake in Transgender and Gender-Diverse Patients

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ABSTRACT

Background. More than 2.5 million adults in the United States identify as transgender or gender-diverse (TGD), but little data exist on cancer screening and care for this population. We examined cancer characteristics, screening adherence, genetic testing, and provider inclusive language for TGD patients with cancer.

Methods. This single institution retrospective cohort study identified TGD patients with cancer between 2000 and 2022. Demographic, clinicopathological, treatment, and screening data were collected, as well as data on gender-affirming care (GAC) and use of patients' personal pronouns in medical records. Descriptive statistics and regression analyses were used to report outcomes.

Results. Sixty unique patients with 69 cancer diagnoses were included: 63.3% were transgender women, 21.7% transgender men, 6.7% nonbinary, and 8.3% were genderqueer. Sixty-five percent had a family history of cancer. Only 46.2% of those who met genetic testing criteria were referred. On review of recommended cancer screening, colorectal screening had the greatest uptake (62%), followed by

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A. C. Istl, MD, MPH, FSSO, FRCSC e-mail: aistl@mcw.edu breast (48.3%), lung (35.7%), cervical (33.3%), and prostate (32%); 8.5% of cancers were diagnosed on screening. Individuals with Medicare had reduced odds of screening uptake (OR 0.07, 95% CI 0.01–0.58) versus private insurance. With respect to GAC, 73.3% used gender-affirming hormone therapy and 41% had gender-affirming surgery. After initiating GAC and asserting personal pronouns, 75% were referred to by incorrect name/pronouns in provider documentation. **Conclusions.** Our TGD cancer patient cohort had low rates of disease-specific cancer screening and inadequate genetic referrals. Many providers did not use appropriate patient names/pronouns. Provider and patient interventions are needed to ensure inclusive preventative and oncologic care for this marginalized population.

Persons who identify as transgender or gender-diverse (TGD) are individuals whose gender identity differs from the sex they were assigned at birth (Table 1).¹ Over the past decade, the number of people identifying as TGD has significantly increased worldwide; in the United States alone, an estimated 2.6 million people identify as TGD.² Transgender or gender-diverse persons face significant healthcare disparities due to systemic marginalization, discrimination, and a lack of inclusivity in clinical databases and trials.^{3–5}

The growing TGD population has led to an increased uptake of gender-affirming care (GAC).^{6,7} The goal of GAC is to enable TGD persons to align their physical bodies with their gender identity and is associated with improved mental health outcomes and quality of life.^{8–10} Gender-affirming care includes gender-affirming hormone therapy

Terms	Definition	Example
Gender identity	A self-identified characteristic based on one's internal sense of gender. May or may not be congruent with sex at birth or presenting gender	Man, woman, gender-queer, transman, transwoman, etc.
Legal sex	Sex or gender designation on legal documentation. May or may not be congruent with either sex at birth or gender identity*	Female, male, intersex
Sex assigned at birth	The sex designated at the time of birth based on chromo- some configuration and genital characteristics	Female, male, intersex
Cisgender	One's gender identity corresponds to their sex assigned at birth	Woman gender identity and female sex assigned at birth
Transgender	One's gender identity does not correspond to their sex assigned at birth	Woman gender identity but male or intersex assigned at birth
Nonbinary	One does not identify with any one gender presentation exclusively	May identify as both male and female or neither male nor female; may use they/them pronouns
Gender-queer [†]	An overarching term for those who do not identify as cis- gender or are gender nonconforming; may be inclusive of transgender individuals and other non-cisgender identities	Transgender, nonbinary, two-spirited, questioning
Gender-affirming hormone therapy	Feminizing or masculinizing hormone applications through oral medications, injections, or other methods, such as patches or creams	Estrogen, testosterone, progesterone
Top surgery	Feminizing or masculinizing surgery to alter the breasts and/or chest wall	Breast implants/chest feminization surgery; chest masculini- zation surgery
Bottom surgery	Surgery to remove or alter existing sex and reproduc- tive organs and/or reconstructive surgery to create new, gender-concordant anatomic structures	Resection: hysterectomy, oophorectomy, vaginectomy; orchiectomy/scrotectomy, penectomy Reconstruction: vaginoplasty, phalloplasty
Pronouns	Self-identified gender-oriented nouns referring to the person in question	She/her/hers, he/him/his, they/them/theirs

*Laws surrounding sex assignments on birth certificates and edits to documented gender on existing government identification vary across countries and states

[†]Not embraced by all gender non-conforming individuals given historical use in a derogatory fashion

(GAHT)—either testosterone- or estrogen-based—and gender-affirming surgeries (GAS) such as chest masculinization or feminization surgery, hysterectomy with or without oophorectomy, penectomy/orchiectomy, vaginoplasty or phalloplasty, and thyroplasty (Table 1). Gender-affirming care has significant health benefits for TGD persons, however, it is unclear how GAC may impact cancer risk or outcomes. In particular, it is unclear whether GAHT may alter the risk of hormonally driven malignancies, such as breast and prostate cancer.^{11–15}

Significant disparities in cancer screening have been identified in recent years among TGD individuals because of a lack of gender-inclusive screening guidelines and limited patient and provider understanding of screening options.^{16–18} Retrospective data has found that non-heterosexual and gender-diverse individuals are diagnosed with cancer at more advanced stages and have inferior oncologic outcomes compared to heterosexual and cisgender individuals.^{19–21} This is hypothesized to relate to inequities in cancer screening, appropriate referrals to genetic counseling services, and healthcare discrimination.¹⁷ The goals of this study are to describe a cohort of TGD patients with a cancer diagnosis, quantify the uptake of recommended cancer screening, and examine factors associated with appropriate cancer screening and referrals.

METHODS

Study Population

A single-institution retrospective cohort study was performed to identify non-cisgender patients with a cancer diagnosis over 22 years. Our institutional Clinical Research Data Warehouse platform was queried from January 2000 through July 2022 using ICD-9 and ICD-10 codes for sexual and gender identity diagnoses (previously termed disorders; ICD-9 302.0–302.9 and ICD-10 F64.0–F64.9) as well as diagnoses associated with malignancy (ICD-9 140–239.99 and ICD-10 C00–D49). Charts were manually reviewed. Patients with noninvasive disease were excluded, with the exception of individuals diagnosed with ductal carcinoma in situ (DCIS) of the breast or melanoma in situ since these entities are treated as early-stage invasive disease.^{22,23} In 2018, our system's electronic medical record (EMR) began incorporating self-identified gender data into patient charts. To maximize cohort inclusion, patients identifying as transgender women (TGW), transgender men (TGM), gender nonbinary (NB), gender fluid, genderqueer/queer, other, or patients who chose not to disclose gender were included in our candidate cohort along with individuals with an ICD-9 or ICD-10 sexual or gender identity diagnosis. Duplicates from the previous data query were removed. This study was reviewed and approved by our institutional review board. Electronic patient charts were manually reviewed by three study team members to confirm that patients self-identified as non-cisgender (gender identity differed from sex assigned at birth) and had a documented solid organ or hematologic malignancy.

Data Collection

Individual demographic, clinicopathological, treatment, screening, and surveillance data were manually extracted from eligible patient charts. Duration of follow-up was calculated from date of cancer diagnosis to date of death or last documented follow-up as of March 2022. Healthcare provider documentation in the EMR was manually analyzed for use of appropriate pronouns and names after initiation of GAC or documented declaration of the patient's name and/ or personal pronouns. All charts were reviewed and data was verified by two authors.

Screening Parameters

Recommended cancer screening was assessed for each patient based on age, organ inventory, family history, smoking history, and GAC. Indications for colon, breast, cervical, prostate, and lung cancer screening were reported based on recommendations set forth by the United States Preventative Services Task Force (USPSTF).^{24–28} Given that the USP-STF does not specify breast cancer screening guidelines for persons not assigned female sex at birth or for persons who have undergone gender-affirming chest masculinization surgery, we used recommendations set forth by University of California—San Francisco for those individuals.²⁹ Screening uptake during any time period was based on contemporary screening recommendations and therefore may have changed during a patient's analysis time if guidelines evolved. Any such changes were accounted for in the data collection and analysis. Indications for referral to genetic counseling services were based on current National Comprehensive Cancer Network (NCCN) guidelines for each diagnosed malignancy.^{30,31}

Statistical Analysis

Categorical variables are reported as frequencies and continuous variables are reported as measures of central tendency with standard deviations or interquartile ranges as appropriate based on population distribution. Multivariate logistic regression analyses included variables with statistical significance on univariate analysis ($\alpha = 0.05$) and clinically relevant outcome variables. Odds ratios (OR) with corresponding 95% confidence intervals (CI) were reported. Data were analyzed by using Stata statistical software³² and are reported in concordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.³³

RESULTS

We reviewed the electronic medical records for 2267 TGD patients, of which 60 individuals met the specified inclusion criteria (Table 2). Most patients (63.3%) identified as transgender women (TGW), 21.7% as transgender men (TGM), 6.7% as nonbinary (NB), and 8.3% identified as another gender (Fig. 1). Median age at cancer diagnosis was 45.5 years (IQR 31–57). Most patients were non-Hispanic white (76.7%) and had a previous or current history of tobacco smoking (55.2%). After initiation of GAC and declaration of personal pronouns or name in the EMR, 75% of patients were referred to by the incorrect name or pronouns in provider documentation.

Cancer Characteristics

Distribution of primary disease sites in our cohort is depicted in Fig. 2. The most common malignancies were nonmelanomatous skin cancer (NMSC), lymphomas, and thyroid cancers. Fifty-five percent (55%) of patients presented with stage I cancer, 7.1% with stage II, 21.4% with stage III, and 19.1% with stage IV; only one patient had in situ disease. A total of six (8.5%) cancers were detected on screening. Recommended treatment varied based on underlying disease site, histology, and stage. Median time to first cancer treatment was 31 days (IQR 18-49). Seven patients (11.7%) had multiple cancer diagnoses over the course of their follow-up. Of the seven patients with multiple cancers, four had multiple metachronous primaries of the same disease site (two with nonmelanoma skin cancers, one with head and neck squamous cell carcinomas (SCC), and one with gastrointestinal neuroendocrine tumors (NET)).

TABLE 2 Demographic and cancer characteristics

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	Incorrect pronouns/name used in EMR [‡] , $N(\%)$	45 (75)	

TGW transgender woman; *TGM* transgender man; *BMI* body mass index; *SD* standard deviation; *IQR* interquartile range; *EMR* electronic medical record.

*60 unique patients with 69 cancers.

[†]Percent of diagnosed cancers.

[‡]In medical provider documentation after initiation of gender-affirming therapy and declaration of preferred name/pronouns

The other three had combinations of GI, prostate, and hematologic malignancies; all were transgender women.

Specific Cases Relevant to Organ Inventory

Breast

Five patients were diagnosed with breast cancer. Four (80%) had hormone-receptor-positive disease, of which all were recommended adjuvant endocrine therapy; however, only 50% agreed to endocrine therapy. Data on gender, breast cancer characteristics, and therapy are summarized in Table 3.

Gynecologic

Two TGM were diagnosed with stage I uterine or ovarian cancer at age 24 and 34 years, respectively. The patient diagnosed with ovarian cancer had been on GAHT for 5 years and, of note, had not had appropriate cervical cancer screening. The individual diagnosed with uterine cancer had no history of GAHT or GAS; their cervical screening was current.

Urologic

Two TGW were diagnosed with stage I prostate cancer at ages 60 and 74 years; neither case was screen-detected. One patient had not received any prostate cancer screening; screening data were unavailable for the other. Two TGW were diagnosed with stage I testicular cancer at ages 17 and 33 years. Both were treated with orchiectomy and started GAHT after their cancer diagnosis.

Cancer Outcomes

Follow-up after diagnosis ranged from 1–12 years; median duration of follow-up was 3.5 years (IQR 1.5–4). Ten patients (16.7%) died during the study's follow-up period: eight died secondary to their cancer diagnosis, including six who presented with *de novo* stage IV metastatic disease.

Pathogenic Germline Genetic Testing

A total of 13 patients (22.4%) were eligible for pathogenic germline genetic testing based on NCCN guidelines, of which six (46.2%) were referred to genetic counseling services and



FIG. 1 Gender identity distribution in study population. *TGM* transgender man; *TGW* transgender woman

FIG. 2 Disease site distribution in study population (site, N). NMSC nonmelanomatous skin cancer; H&N head and neck; SCC squamous cell carcinoma; CRC colorectal cancer; CLL chronic lymphocytic leukemia; GI gastrointestinal; NET neuroendocrine tumor; HL Hodgkin's lymphoma; RCC renal cell carcinoma: ALL acute lymphocytic leukemia; CML chronic myeloid leukemia; SCLC small cell lung cancer; AML acute myeloid leukemia; NSCLC non-small cell lung cancer; CNS central nervous system tumor; Esoph esophageal, GB gallbladder; HCC hepatocellular carcinoma



underwent testing. Two individuals were found to have identifiable genetic mutations. One NB patient, diagnosed with breast cancer, was positive for a variant of unknown significance of the *FLCN* gene that did not affect treatment or surgical management. The other patient was a TGM who had previously undergone gender-affirming chest masculinization surgery before diagnosis with invasive ductal carcinoma. He was positive for a pathogenic *BRCA1* gene variant and had bilateral oncologic mastectomies.

Screening Recommendations and Uptake

Based on organ inventory, age-appropriate guidelines, use of GAHT, and relevant risk factors, breast cancer screening was indicated for 49.2% of patients, prostate screening for 40.7%, cervical screening for 25%, colorectal screening for 58.6%, and lung cancer screening for 24.1%. Screening uptake for the study population is summarized in Fig. 3. When evaluating factors predictive of appropriate screening, none of gender identity, race, family history of cancer, or use of GAHT were associated with screening uptake on univariate or multivariate analysis. Notably, individuals who had Medicare insurance had a reduced odds of completing indicated cancer screening on multivariate analysis compared to individuals with private insurance (OR 0.07, 95% CI 0.01–0.58, p < 0.05; Table 4).

Gender-affirming Therapy

In patients for whom data on GAC was available (n = 55), 73.3% of patients used GAHT with a median duration of 6 years (IQR 2.6–10). Of those using GAHT, 61%

started therapy before their cancer diagnosis and 40.7% also underwent GAS: 32.7% had top surgery and 28% had bottom surgery. Seventy-five percent of patients were referred to by the incorrect name or pronouns in provider documentation after undergoing GAC.

DISCUSSION

This single-institution retrospective cohort study of TGD patients with a cancer diagnosis identified low rates of disease-specific cancer screening, genetic counseling referrals, and appropriate name/pronoun use in clinical documentation. This is the largest single-institution study of TGD patients with a cancer diagnosis and provides granular data and novel insights into opportunities to improve cancer screening uptake, enhance clinical cancer care, and further our understanding of gaps in oncology for TGD persons. The censorship of TGD patients from large databases and rare dedicated study efforts to date have left us with sparse data to guide interventions that could overcome barriers to care. Emerging data consistently demonstrate disparate healthcare outcomes for TGD individuals relative to the cisgender population.^{5,17,34} These disparities arise from social, legal, and economic factors, intersect with race, ethnicity, gender presentation, and sex at birth, and lead to healthcare avoidance and identity concealment.^{35–39} In a cancer care setting, one National Cancer Database study of 589 presumed non-cisgender persons found that TGD individuals were diagnosed more commonly at a later stage of disease and had worse survival than their cisgender counterparts.²⁰

Gender	Sex at birth	Top surgery	Age at Dx	Screening- detected	ER status	PR status	Adjuvant ET	GAHT before Dx	Hx of oopho- rectomy	Genetic testing results
RB	н	No	29	No	I	I	Not applicable	No	No	FLCN p.P311L (c.932C>T) VUS
TGW	Μ	No	49	No	+	+	Yes	No	MAB	Negative
TGM	ц	Yes	37	No	+	+	Yes	8.9y	Yes	BRCA1 c5177_518 0delGAAA (p.R1726Kfs^3)
Other	Ц	No	45	Yes	+	+	No	No	No	Not tested
TGW	Μ	No	76	Yes	+	+	No	45y	MAB	Negative

Organ-based Screening and Gaps in Evidence

In both our study and the only other cohort study of TGD patients with cancer, 16-20% of cancers diagnosed in the TGD population were cancers for which routine screening guidelines exist (breast, cervical, prostate, colon, and lung).⁴⁰ Another 24% of cancers in both studies were those for which screening is recommended in high-risk patients (anal cancer, hepatocellular carcinoma, skin cancers, and ovarian cancer). These data indicate clear opportunities to improve screening and diagnosis for TGD persons. With respect to uptake, our study found dismal rates of recommended screening adherence in the TGD population: 48% for breast cancer, 33% for prostate and cervical cancer, 62% for colorectal cancer, and 36% for lung cancer. To put our data into context, National Cancer Institute survey data found that 75.5% and 86.5% of respondents in the general population adhered to breast and cervical cancer screening guidelines.⁴¹ Other cross-sectional population studies, including those in low-income individuals, have documented cervical cancer screening uptake rates of 75% and 65-81% uptake of mammography for breast cancer screening.^{42,43}

Survey responders are more likely to have engaged in positive screening behaviors, and therefore, these studies may overestimate the true rate of uptake. However, as we evaluate screening rates and consider opportunities for improvement, there are fundamental factors that warrant consideration. First, primary care physicians (PCPs) recommend screening schedules set by various bodies (the American Cancer Society, the United States Preventative Services Task Force, the National Comprehensive Cancer Network), whose recommendations vary and evolve with time.⁴⁴ As such, screening recommendations vary across providers - a phenomenon that has been demonstrated in other studies in Wisconsin, where the majority of our study cohort resides.⁴⁵ Second, a lack of screening awareness, aversion to discussing screening procedures, financial strain, continuity of care, and access to care all constitute significant barriers to effective and timely screening uptake across disease sites.^{42,43,46} TGD patients are more vulnerable to these challenges than the general population, because (1) clear guidelines have not been established for organ-inventory based screening in TGD patients, (2) providers may not understand how to apply existing guidelines after GAC, and (3) TGD patients are not always educated on organ-specific screening.⁴⁷ Finally, distress associated with having a prostate, cervix, or breasts may make it difficult for TGD patients to approach these conversations with their care provider, especially in a medical system where non-cisgender patients have been, and may still be, inexcusably pathologized.

Breast cancer in particular presents a unique challenge in the TGD population. Breast cancer risk in TGD persons is estimated to be higher than cisgender men, but lower than in FIG. 3 Number of patients for whom screening was indicated, stratified by disease site, and corresponding percent uptake in TGD cohort



TABLE 4 Multivariate analysis of factors predictive of screening uptake

Variable	OR (95% CI)	р
Gender		
TGW	ref.	
TGM	0.38 (0.06-2.39)	0.306
Race		
White	ref.	
Black	2.23 (0.56-8.93)	0.257
Insurance status		
Private	ref.	
Medicare	0.07 (0.01-0.58)	0.014
Medicaid	0.28 (0.04–1.90)	0.191

OR odds ratio; *CI* confidence interval; *TGW* transgender woman; *TGM* transgender man; *ref* reference category

cisgender women.^{12,48} Recent studies have found that TGD patients present with breast cancer at later stages and have worse overall survival compared with cisgender women.¹⁹ While several organizations have put forward recommendations for breast cancer screening in these patients, 17,29,48 there is limited high-level data to inform guidelines andwhere expert consensus guidelines exist-primary providers may not know where to find them. As a result, many patients and providers remain unaware of screening options. This leads to insufficient screening referrals and lower rates of uptake. For patients who already have a breast cancer diagnosis, the management of adjuvant endocrine therapy in balance with GAHT adds a layer of complexity. Uptake of recommended endocrine therapy was only seen in half of TGD breast cancer patients with hormone-receptor positive disease in our cohort, and a recent survey found that >50% of TGD persons would not stop GAHT in the setting of a hormone-receptor positive breast cancer.⁴⁹

For other genital/reproductive cancers, data are similarly sparse. The incidence of prostate cancer in TGD individuals is not entirely clear. The United States Veteran's Affairs Hospital System data suggest that prostate cancer occurs in 33 out of 10,000 TGW, but it is likely underdiagnosed and there is conflicting data on prostate cancer risk in those on GAHT.^{50,51} The cases in our series were not screen-detected, despite both patients meeting screening criteria. Granular studies dedicated to better understanding the experiences of TGD with these specific diagnoses are needed to clarify how we monitor, screen, and optimize care for these patients.

Genetic Testing

The role of pathogenic germline genetic testing has increased substantially in recent years.⁵² Recently, many national organizations are calling for genetic testing in all patients with a cancer diagnosis.⁵³ However, only half of the patients in our cohort who met NCCN criteria for genetic testing were referred to genetic counseling services. The identification of pathogenic mutations provides valuable opportunities for improving personal cancer care, including (1) enhanced cancer surveillance, (2) options for riskreducing surgery, (3) prevention-focused medications and lifestyle changes, (4) targeted systemic therapy options, and (5) improved therapeutic decision-making during current or future cancer treatment.^{54–57} The identification of pathogenic germline variants may also have a significant impact on decisions around gender-affirming surgeries, such as riskreducing mastectomy and oophorectomy for transmasculine patients.47

Inclusive Language

Finally, the role of the patient-provider interaction warrants emphasis in any discussion on the treatment of sexual and gender diverse people in the healthcare system. Inaccurate provider language, whether conscious or unconscious, is a source of trauma for TGD patients and leads to distrust and avoidance of the healthcare system.^{36–39} Our study found that 75% of patients were referred by the incorrect name or pronouns after initiation of GAC or declaration of preferred name or personal pronouns in the EMR. Provider education on inclusive language including correct name and pronoun use is an actionable target to ensure equitable cancer care. The need for inclusive language in healthcare also extends to screening services, as certain individuals may be denied cancer screening based on their sex assigned at birth rather than their gender and/or current organ inventory.^{17,50} A recent analysis of insurance coverage for screening mammography in the United States identified that only 6.2% of insurance policies in 2023 specifically provided screening mammography coverage for TGD individuals.⁵⁸ Ensuring gender-inclusive language in insurance policies and screening guidelines will likely expand screening access and minimize the social and financial barriers to appropriate cancer screening examinations.

Limitations

Because of limited sample size, we were unable to examine potential associations between variables such as GAHT and specific cancer types. Additionally, while our search was intended to capture all TGD individuals with a cancer diagnosis from our data infrastructure, there are likely patients who were not captured due to misdocumentation in the EMR or patient hesitancy to share their gender identity for fear of discrimination. Nevertheless, this investigation is the largest single retrospective cohort study of non-cisgender patients with a cancer diagnosis and identifies several opportunities for future clinical interventions to reduce cancer disparities and improve patient outcomes.

CONCLUSIONS

Our cohort study of TGD patients with cancer demonstrates disparate screening and genetic testing outcomes as well as a pervasive use of incorrect language by providers. Underlying mechanisms for these disparities have been discussed. Data from organ-specific cohort studies in the TGD population are needed to support the development of nationally recognized organ inventory-specific screening guidelines. Additionally patient and provider education initiatives related to cancer screening recommendations and inclusive language, as well as interventions to enhance screening uptake, are needed to reduce disparities and optimize oncologic outcomes in TGD patients.

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