Gender- and Sexual Orientation–Based Inequities: Promoting Inclusion, Visibility, and Data Accuracy in Oncology

Ash B. Alpert, MD, MFA[1,2]; N.F.N. Scout, PhD[3]; Matthew B. Schabath, PhD[4]; Spencer Adams, BS[5]; Juno Obedin-Maliver, MD, MPH[6]; and Joshua D. Safer, MD[7,8]

overview

Sexual and gender minority (SGM) people, including agender, asexual, bisexual, gay, gender diverse, genderqueer, genderfluid, intersex, lesbian, nonbinary, pansexual, queer, and transgender people, comprise approximately 10% or more of the U.S. population. Thus, most oncologists see SGM patients whether they know it or not. SGM people experience stigma and structural discrimination that lead to cancer disparities. Because of the lack of systematic and comprehensive data collection, data regarding SGM cancer incidence, outcomes, and treatment responses are limited. Collection of data regarding sexual orientation, gender identity, transgender identity and/or experience, anatomy, and serum hormone concentrations in oncology settings would drastically increase collective knowledge about the impact of stigma and biologic markers on cancer outcomes. Increasing the safety of oncology settings for SGM people will require individual, institutional, and systems changes that will likely improve oncologic care for all patients.

Sexual and gender minority (SGM) people, including agender, asexual, bisexual, gay, gender diverse, genderqueer, genderfluid, intersex, lesbian, nonbinary, pansexual, queer, and transgender people and others who are not cisgender and/or heterosexual (Table 1 for definitions), experience stigma and structural discrimination.[1–7] These experiences have a profound impact on health, health care seeking, and health care experiences.[8–10] At least 7% of U.S. adults self-report SGM identities, 1% as lesbians, 1% as gay, 4% as bisexual, and 1% as transgender. In addition, 16% of generation Z adults, who were born from the mid-1990s to the early 2010s, report they are SGMs.[11]

Although SGM subpopulations are often assumed to be separate (e.g., lesbians are cisgender, transgender people are heterosexual), gender identity, sexual attraction, behavior, and identity are distinct for any given person. For example, some transgender women are lesbians and some queer men are transgender.

Given experiences of stigma and structural discrimination, many SGM people likely do not self-report as such.[12,13] These population statistics thus likely reflect only a small proportion of the people who are SGM. Nearly all oncology clinicians are thus likely treating SGM people of various ages, whether they realize it or not. All oncology clinicians must therefore become versed in issues faced by SGM people, particularly barriers to oncologic care, and mechanisms to intervene.

SGM people experience multiple barriers to cancer screening and prevention that likely translate into disparities in cancer incidence and outcomes.[14,15] For example, one-third of transgender people had negative experiences with clinicians in the past year, and one-fourth avoided needed health care because of fear of mistreatment and one-third did so because they could not afford it.[10]

Assumptions about the cancer risks of cisgender women who have sex with women may also lead to clinicians providing inappropriate recommendations regarding cervical cancer screening. For these and other reasons, the rate of cervical cancer screening may be lower in this population than in cisgender heterosexual women.[16–18] Similarly, transgender people have decreased cancer screening, likely because of a combination of a multitude of barriers to care.[14,19,20] Decreased screening or delayed evaluation of symptoms could lead to late presentations of cancer and thus worse outcomes for SGM people.[21–24]

Stigma and oppression likely also manifest in disparities in cancer morbidity and mortality via multiple other mechanisms, including increased rates of HIV, mental distress, and mental illness as well as increased experiences of violence and higher stress levels, termed *allostatic load*.[8,10,25–35] Minority stress—in other words, the stress associated with experiences of discrimination and marginalization, in this case related to sexual orientation or gender identity—has been directly linked to cancer

Author affiliations and support information (if applicable) appear at the end of this article.

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PRACTICAL APPLICATIONS

- Approximately 10% of U.S. adults self-report being sexual and gender minorities (SGMs). Most oncologists thus care for SGM people whether they know it or not.
- SGM people face barriers to primary care, including cancer screening, and this may lead to later-stage presentations of cancer and worse outcomes.
- Data are sparse regarding cancer incidence, outcomes, and treatment responses for SGM people. Collection of data regarding sexual orientation, gender identity, transgender identity and/or experience, anatomy, and hormone concentrations would drastically improve the body of knowledge regarding cancer in SGM populations and data precision for all patients.
- Hormone therapy and surgeries increase quality of life and decrease suicidality for transgender people who want them. No data exist to suggest that hormone therapy worsens cancer outcomes. Any conversations regarding continuation or discontinuation of hormone therapy in the setting of cancer treatment should thus weigh known benefits against potential, yet unproven risks.
- Increasing the safety of oncology settings will require systems, institutional, and individual changes and should include ensuring (1) nondiscrimination policies are in place that cover sexual orientation and gender identity and expression; (2) care services are nongendered; (3) correct name, pronouns, and gender are used for patients in clinical encounters and electronic health records; and (4) oncologists engage in shared decision-making with patients regarding oncologic interventions.

incidence, cancer-related treatment side effects, and the expression of genes and pathways linked to cancer.[8,36,37]

In addition to stigma and discrimination, assumptions about relationships, gender, pronouns, anatomy, and physiology create barriers to care for SGM people. These assumptions may be particularly salient in oncology for several reasons.

First, cancer diagnosis and treatment can be experienced as a trauma—in other words, an experience that creates intense feelings of fear and distress—and may be accompanied by sequelae, including intrusive thoughts, hyperreactivity, and other symptoms of post-traumatic stress disorder.[38,39] For SGM people with cancer, encountering clinicians' incorrect assumptions about their gender and/or sexual orientation is also stressful.[40–42] When encountering such assumptions, patients must choose between the dangers of being known to be SGM and the distress and/or dysphoria related to not being described or seen correctly. These decisions may be especially painful in the context of the fear and grief associated with a life-threatening illness.

Second, because cancer diagnoses and treatments often have life-and-death consequences, stigma that prevents patients from accessing efficacious treatment in the context of oncologic care can be deadly.[40]

Third, some cancers are specific to anatomy that is conflated with gender (e.g., ovarian or testicular cancer), and the language used regarding these cancers may include assumptions linking anatomy and gender.[41,43] For example, educational materials may reference "men with prostate cancer" or "women with uterine cancer" and thus render invisible transgender, gender-diverse, and intersex people. Similarly, specific cancer centers may have gendered designations, such as "women's cancer center," which exclude patients who do not fall into those gender categories.

Fourth, gender-affirming hormones and surgeries are lifesaving interventions for transgender people who seek and use them.[44,45] Data are sparse regarding the risks or benefits of continuing hormone therapy in the setting of cancer treatment of patients with hormonally driven or hormonally different cancers, such as cancers with differing rates in cisgender women and men.[46–48] In the absence of quality data, oncologists and transgender patients are left to weigh the unknown, potential risks of hormone therapy in the setting of cancer treatment against the known benefits. Oncologists may recommend halting hormone therapy despite the benefits to patients' safety, mental health, and quality of life.[41]

Given these factors, cancer morbidity and mortality are likely higher in SGM populations than in cisgender and heterosexual populations. Because of the lack of systematic and comprehensive data collection, however, SGM cancer incidence and outcome data are limited, particularly in regard to transgender populations.[49] National efforts are underway to fill gaps in data.[50] Known cancer disparities among SGM people include higher rates of specific cancer types, including increased rates of melanoma in cisgender gay men. Increased rates of Kaposi sarcoma, lymphomas, and anal cancer are also seen in SGM subpopulations at increased risk for HIV, including cisgender gay men and transgender women.[51] Little research has been done to assess the needs of SGM people of color across the cancer continuum, and this is an area in need of ongoing research.[52,53]

TABLE 1. Gender Identity and Sexual Orientation Terminology

Term	Definition
Transgender	A person whose gender identity differs from that commonly associated with their sex assigned at birth
Transgender man	A man who is transgender
Transgender woman	A woman who is transgender
Cisgender	A person whose gender identity is the same as that commonly associated with their sex assigned at birth
Nonbinary	A person who does not identify exclusively as a man or a woman
Sex assigned at birth	A designation typically made upon examining the external genitalia of a baby
Gender identity	The way a person sees themselves in terms of femininity, masculinity, both, neither, or something else
Gender	A broad term that is a multidimensional social construct that is culturally based and historically specific and includes socially prescribed and experienced dimensions of femininity, masculinity, both, neither, or something else*
Lesbian	A woman who is emotionally, romantically, or sexually attracted to other women
Gay	A person who is emotionally, romantically, or sexually attracted to people of the same gender
Bisexual	A person who is emotionally, romantically, or sexually attracted to people who are men or women
Queer	An umbrella term used for people who are not heterosexual and/or not cisgender
Intersex	People who have anatomy that does not fit into typical binary notions of sex assignment (sometimes labeled differences of sexual development or DSD)
Sexual minorities	People who are not heterosexual, including people who may not identify as gay, lesbian, or bisexual
Gender minorities	People who are not cisgender, including people who do not identify as transgender
Organ inventories	A means to query a patient's current anatomy
Gender-affirming hormone therapy	Use of estrogen, testosterone, or other hormones to better align one's body with one's sense of self
Agender	People who don't identify themselves with any particular gender or who have a neutral or undefinable gender; also called genderblank, genderfree, genderless, gendervoid, nongendered, ungendered, or null gender. Considered to be an identity under the nonbinary and transgender umbrella terms.†
Pansexual	Term used to describe people who have romantic, sexual, or affectional desire for people of all genders and sexes‡

*Johnson et al.[131]
†Nonbinary wiki: Agender. Available at: https://nonbinary.miraheze.org/wiki/Agender. Accessed April 29, 2022.
‡University of California, San Francisco LGBT Resource Center. General definitions. Available at: https://lgbt.ucsf.edu/glossary-terms. Accessed April 29, 2022.

ASCO is committed to reducing cancer disparities faced by SGM people. In keeping with this commitment, in 2017, ASCO outlined suggested steps for oncology clinicians, cancer centers, and other treating institutions.[54] In this article, we introduce the reader to key concepts and terminology, describe gaps in data and how to fill them, explore what is known about SGM cancer disparities, make suggestions to decrease barriers to oncology care, and outline specific training objectives and resources for oncology clinicians to enhance care of SGM people. See Table 2 for a list of recommendations to improve the safety of oncology spaces for SGM people and the Sidebar for a list of educational resources for oncology clinicians and institutions.

RESEARCH IN SGM POPULATIONS: HOW DO WE GET ACCURATE DATA COLLECTION?

Sexual and Gender Minority Cancer Research Challenges and the Importance of Comprehensive Data Collection

Research efforts to address the inadequate evidence base regarding cancer incidence, treatment efficacy, and outcomes for SGM people across the life span are urgently needed to assess and address cancer disparities.[49,55,56] Innovative methods are critically needed to overcome long-standing barriers to sufficiently powered SGM

TABLE 2. Resources for Sexual and Gender Minority Cultural Humility Trainings in Oncology*

Resource	Description	Website or Citation
Building the Next Generation of Academic Physicians SGM Cancer Care	Workshops for SGM cancer researchers	http://bngap.org/sgm-cancer-care-2021-workshop
Curriculum for Oncologists on LGBTQ+ Populations to Optimize Relevance and Skills (COLORS) training	A series of four 30-minute online training modules for oncology clinicians	https://colorstraining.org/
A Guide to Best Practices in LGBTQI+ Cultural Competency Training	Best practices in SGM cultural humility training	https://whitmanwalkerimpact.org/cultural-competency-trainings/
Human Rights Campaign Healthcare Equality Index	A grading system for SGM inclusiveness. Healthcare institutions can request annual assessment.	www.hrc.org/healthcare-equality-index
Integrating multicultural orientation framework into cancer care	Guidance regarding assessing and improving cancer care for SGM people	Raque et al[162]
National LGBT Cancer Network	A nonprofit organization that provides education, training, and advocacy to improve the lives of SGM people who have been diagnosed with cancer	https://cancer-network.org/
National LGBTQIA+ Health Education Center	Fenway Institute's offerings of SGM cultural humility training	https://www.lgbtqiahealtheducation.org/
Together, Equitable, Accessible, Meaningful (TEAM) Cancer Care for Sexual and Gender Minority (SGM) Patients Training	George Washington University Cancer Center's annual SGM training. Practices apply as an agency, committing to send four representatives through a series of self-paced online training sessions, supplemented by virtual technical assistance sessions with project staff.	https://cancercenter.gwu.edu/training-and-education/professional-education/team-together-equitable-accessible-meaningful
Welcoming Spaces	A series of eight online, 45-minute, oncology-focused trainings that qualify for the Human Rights Campaign's Healthcare Equality Index standards and offer continuing education credits for a wide variety of different health professionals. Welcoming Spaces is particularly focused on training the full staff team; modules 1-5 provide both the social base for clinical providers and the appropriate trainings for nonclinical office staff, such as front desk or administrative staff. The final three trainings are focused on clinical care for gynecologic oncologists treating transgender people. Welcoming Spaces will be free for all people to take for 2021; after that, it will move to a fee model.	https://cancer-network.org/welcoming-spaces/

Abbreviation: SGM, sexual and gender minority.
*Citations for these trainings are included in the text.

SIDEBAR. RECOMMENDATIONS FOR ONCOLOGY CLINICIANS AND INSTITUTIONS TO PROMOTE SEXUAL AND GENDER MINORITY INCLUSION

Recommendations for individual oncology clinicians

Introduce yourself with your name and pronouns, and query the same information from all patients and then use that name and those pronouns consistently, in person and in documentation.
Avoid gendered language when asking about partners.
Avoid gendered language when referring to specific cancers (e.g., "women's cancers").
Engage in shared medical decision-making, particularly in settings in which patient priorities differ from guidelines or in discussing gender-related care (e.g., hormones, surgeries) in the setting of cancer treatment.

Recommendations for oncology institutions

Ensure the availability of all-gender restrooms.
Ensure nondiscrimination policies cover sexual orientation and gender identity and that clear and accessible grievance policies exist for patients who experience discrimination.
Ensure intake forms are inclusive of sexual and gender minority (SGM) people by ensuring that there is no language that makes presumptions about anatomy based on gender (e.g., "for women only: when was your last period?").
Ensure intake forms are inclusive of SGM people by including answer options inclusive of SGM identities (e.g., questions about gender include nonbinary, agender, genderfluid, genderqueer, and/or other options).
Engage in comprehensive data collection, including querying sexual orientation, gender identity (including whether someone is transgender), and anatomy, and consider checking hormone levels.
Ensure clinical trial criteria do not exclude participants based on gender, hormones, or HIV status unless clinically indicated.
Ensure names of clinics and other settings are not gendered.
Ensure gowns and other clothing items provided are gender-neutral and/or that multiple options exist from which to choose.
Ensure SGM cultural humility training is required for all staff and clinicians.

oncologic research. Until comprehensive data collection is widely adopted, either voluntarily or through a national mandate, researchers primarily rely on pooling existing data across institutions to develop real-world evidence and accurately document SGM cancer disparities. If instead cancer registries and national probability-based surveys comprehensively collected relevant data for people with cancer across the life span, researchers would be able to begin to answer pressing questions and to address SGM cancer disparities.[55,57]

Lack of comprehensive data collection also prevents acknowledgment of SGM people in clinical trials. Without this, assessing responsiveness to treatment by SGM subpopulations (e.g., straight transgender women, cisgender bisexual men) and applying trial results accordingly is not possible. For example, if such data are not collected for a prostate cancer trial, an oncologist may have difficulty applying results to a transgender person receiving estrogen therapy. Clinicians and institutions without structured patterns of collecting such data may also make decisions about whom to query on the basis of assumptions they make regarding their patients.

Comprehensive Data Collection

Requisite data to understand cancer incidence, treatment efficacy, and outcomes among SGM people would include information on sexual orientation, gender identity (including whether someone is transgender or not), intersex status, anatomy, and hormone concentrations. The two latter data elements would allow researchers to understand the relationships between these factors and cancer risk, biology, and outcomes. Also of clinical importance, we recommend querying patients about name and pronouns, which are vitally important to use correctly and consistently, including in documentation, to create safety in clinical encounters and establish and maintain rapport.[58] Of note, patients' correct names may be different from what is legally recognized.

Most organizations in the United States currently recommend a two-step question that queries gender identity and sex assigned at birth because it has been found to improve identification of transgender people over a one-step question.[59–62] Some patients who are transgender have concerns over questions regarding sex assigned at birth because they force transgender people to adhere to categorizations that do not apply to them.[63,64] For example, a transgender woman

TABLE 3. National Academies of Sciences, Engineering, and Medicine Sample Questions

Subject	Responses
Sexual Orientation	Which of the following best represents how you think of yourself? [Select ONE]: ☐ Lesbian or gay ☐ Straight, that is, not gay or lesbian ☐ Bisexual ☐ [If respondent is AIAN:] Two-spirit ☐ I use a different term: [free text] (Don't know) (Prefer not to answer)
Gender Identity	Q1: What sex were you assigned at birth on your original birth certificate? ☐ Female ☐ Male (Don't know) (Prefer not to answer) Q2: What is your current gender? [Mark only one] ☐ Female ☐ Male ☐ Transgender ☐ [If respondent is AIAN:] Two-spirit ☐ I use a different term: [free text] (Don't know) (Prefer not to answer)
Intersex	Have you ever been diagnosed by a medical doctor or other health professional with an intersex condition or a difference of sex development (DSD), or were you born with (or developed naturally in puberty) genitals, reproductive organs, or chromosomal patterns that do not fit standard definitions of male or female? ☐ Yes ☐ No (Don't know) (Prefer not to answer)

Abbreviation: AIAN, American Indian and Alaska Native.

asked about sex assigned at birth might feel compelled to answer "male," which would be inconsistent with her gender and may erode her rapport with clinicians or decrease her willingness to return to the clinic. In addition, questions about sex assigned at birth may promote assumptions about anatomy and hormone concentrations based on these designations that may be inaccurate and lead to poorer care.[43] Alternatively, patients could be asked to compare gender identity with sex assigned at birth, as in, "Is your gender identity different from your sex assigned at birth?" which allows patients to avoid answering questions directly about sex assignment. Another option is to ask patients whether they are transgender. Other scholars suggest that explaining why clinicians, researchers, or others are asking about sex assigned at birth may increase the desire of respondents to answer such questions.[65] Also of ongoing concern is the stigma and discrimination patients may face when clinicians know they are transgender. Institutional, policy, and structural changes are needed to improve safety for transgender people in clinical encounters.

In March 2022, the National Academies of Sciences, Engineering, and Medicine released a consensus report on how to collect health data regarding sexual orientation, intersex status, and gender identity in clinical, research, and administrative contexts.[50] The National Academies of Sciences, Engineering, and Medicine report reviewed a number of variations for phrasing the questions, but the unifying concept was that it should be a two-step measure that includes a question about gender identity and one about sex assigned at birth. We have included their example measures in Table 3.

In practice, most clinical environments are most easily able to use measures available in their electronic medical record (EMR). The weaknesses of the example in Table 3 include (1) concerns about sex assigned at birth questions described above; (2) although the number of people in the United States who identify as nonbinary is rising, no nonbinary response option is included in the question about gender (National Academies of Sciences, Engineering, and Medicine authors noted a paucity of tested measures that include nonbinary as a response option); (3) the terms "female" and "male" are used in these items as gender categories, but these usually refer to sex assigned at birth; and (4) the measure for gender asks respondents to choose a single category—"male," "female," "transgender," or another option. Transgender men and transgender women may have difficulty choosing one of those gender categories and furthermore may find it offensive that transgender is seen as a nonoverlapping category with the terms "female" and "male."

Efforts are afoot to accelerate testing a revised version of data collection measures, including a gender question that builds on the National Academies of Sciences, Engineering, and Medicine's recommended questions but replaces the response option "transgender" with "nonbinary." Research is also underway to develop comprehensive data collection measures related to anatomy and physiology rather than these being assumed on the basis of sex assigned at birth. Two very important takeaways from this new resource from the National Academies of Sciences, Engineering, and Medicine include that (1) patients deserve to have their identities counted and (2) the exact construct of these measures will improve over time.

Phrasing and nomenclature change over time, and thus, regardless of current recommendations, oncology clinicians must listen to and use patients' language about their experiences.[66–68] For example, the term "transsexual" was widely used in the past decade but is now considered offensive by some, and the more inclusive term "transgender" is preferred.[69,70]

Terminology may also vary throughout the United States; for example, people on the west and east coasts of the United States may be likely to use the term "queer" to describe their sexual orientation, whereas in the South the term may be considered insulting.[71] Generational variations also exist in the use of SGM terminology.[72,73] For instance, younger generations may also be more accepting of the term "queer."[72]

Acceptable terms to identify people who have anatomy that does not fit into typical binary notions of sex assignment are also debated. For example, words previously and currently used by the medical community, such as "hermaphrodite" or "disorders of sex development," are disliked by the majority of people with related experiences. In contrast, the terms "intersex" and "differences of sex development" are more widely accepted.[74]

Using terminology that reflects patients' experiences, identities, and terminology for their bodies is of utmost importance, particularly in oncology contexts because some related conditions are associated with increased risks of particular cancers.[75,76] For example, Klinefelter syndrome (47XXY) may be associated with an increased risk of lymphoma and breast cancer compared with those without Klinefelter syndrome. Androgen insensitivity syndrome is associated with increased risk of testicular cancer for patients with cryptorchidism compared with the general population.[77,78] To provide quality cancer care across the cancer care continuum and to ensure nuanced and accurate cancer research, the clinical and research communities must remain adaptable to changing terms.[79–81]

Comprehensive Data Collection in EMRs

Identifying underserved populations through data collection is a primary strategy for advancing health equity and reducing health disparities.[82,83] In 2015, the Office of the National Coordinator for Health Information Technology thus mandated that EMRs have the capacity to record, modify, and access sexual orientation and gender identity data.[82]

The Centers for Medicare and Medicaid Services included sexual orientation and gender identity data collection in their equity plan, recognizing standardized data collection as an essential first step for reducing health disparities.[84] Likewise, in 2016, the Health Resources and Services Administration added sexual orientation and gender identity data collection to the Uniform Data System reporting requirements, and federally qualified health centers are expected to record and report sexual orientation and gender identity items as part of program participation.[85] With the passage of the Patient Protection and Affordable Care Act, the Office of the National Coordinator for Health Information Technology required structured recording of sexual orientation and gender identity data in EMRs in the Health IT Certification Criteria final rule.

Despite the numerous guidelines, policies, and requirements for the collection of such data, the completeness of EMRs, including EMRs of patients with cancer, is largely unknown. Comprehensive data such as we have described is rarely included, given lack of institutionally driven mandates to complete sexual orientation, gender identity, and anatomy fields and lack of knowledge among clinicians and staff on how to review, collect, and record such data in the EMRs. While national efforts are underway to identify the best questions and how to systematically implement them, we recommend asking all patients for their name, pronouns, gender identity, sexual orientation, transgender identity and/or experience, anatomy, and exogenous hormones and other hormone-modifying therapies such as spironolactone or gonadotropin-releasing hormone agonists.

ONCOLOGIC AND HEMATOLOGIC CONSIDERATIONS FOR GENDER MINORITIES

Cancer Disparities Associated With Diminished Access to Care

Barriers to health care access[86–89] may play a substantial role in health disparities for transgender people. Hormone therapy improves quality of life for transgender people who desire it[44,90]; yet, its use is contested by some clinicians. In the following section, we review what is known regarding potential hematology and oncology disparities for transgender people and known connections, or lack thereof, between hormones and hematologic and oncologic conditions.

Hematologic Conditions

Estrogen Exogenous estrogen may be associated with an increased risk of venous thromboembolism (VTE).[91–96]

Whether or to what degree VTE risk might relate to dose, route of administration, or duration of therapy, remains unknown.

Increased VTE risk was previously noted in studies of ethinyl estradiol, a more thrombogenic estrogen.[97,98] Although ethinyl estradiol is still the main estrogen in oral birth control for cisgender women, it is no longer used for feminizing gender-affirming regimens. By contrast, conjugated equine estrogens and 17-β-estradiol appear much safer,[99] and 17-β-estradiol may be the safer of the two.[100] In studies of patients receiving 17-β-estradiol, increased VTE risk is not always noted relative to the general population.[101,102]

The impact of barriers to care and minority stress on VTE risk have not been studied.[91] Many studies report coexisting conditions that might explain an increased risk for VTE among people receiving exogenous estrogen, including smoking, HIV, malignancy, high cholesterol, coagulopathies, and hypertension.

In cisgender women, increased thrombogenicity seems associated with increased estrogen dose across oral estrogen products observed and with the addition of progestins to estrogen regimens.[103] A lower risk of VTE has been noted with the use of transdermal compared with oral estradiol.[95,99,104] Transgender women receiving oral conjugated estrogens have been observed to have elevated proinflammatory cytokine concentrations (interleukin [IL]-1, IL-6, IL-8, and tumor necrosis factor-α) along with increased white blood cell count.[92,105] Cisgender women receiving oral estrogens have been noted to have increased D-dimer, factor VIII, factor IX, and thrombin activatable fibrinolysis inhibitor. None of these have been observed with transdermal estrogens.[106] Given that many of these factors are produced in the liver, first-pass metabolism is thought to play a role in the procoagulant effects of oral but not transdermal estrogens. However, studies comparing transdermal estrogen products with oral estrogen products do not assess serum estradiol concentrations, which might be lower with transdermal products than concentrations achieved with other routes of administration. Thus, whether the lower risk observed with transdermal estrogen preparations relates to decreased dose delivered, an avoidance of first-pass proinflammatory cytokine metabolism in the liver, or some other mechanism, has not been determined.

Testosterone Exogenous testosterone treatment stimulates erythropoiesis. Data are not sufficient to associate testosterone therapy with polycythemia itself, and no increase in rates of VTE has been reported in transgender people receiving exogenous testosterone.[91,94,107–109] Also, data are not sufficient to stratify the hematocrit increase by route of testosterone administration or by testosterone formulation. However, data in cisgender men suggest that exogenous testosterone may increase the risk of thromboembolism, although data are overall mixed and likely inadequate.[110–112]

Cancer

Limited available data demonstrate that overall cancer incidence does not differ for transgender people relative to cisgender control research participants.[108,113]

Breast cancer Small, retrospective studies suggest that transgender women may have lower rates of breast cancer than cisgender women.[47,114] One of the larger studies that was conducted in the Netherlands[47] was not conclusive, being based on only 18 breast cancer diagnoses among 2,260 transgender women. An earlier study of transgender U.S. veterans reported only 3 cases of breast cancer among transgender women and 7 cases among transgender men among a total of 5,135 persons.[115] Low reported cancer rates may be due to shorter lifetime exposure to estrogen for transgender women, whose hormone exposure typically begins later in life.[116] Also, exogenous gender-affirming hormone regimens typically do not contain progestins, which are associated with increased breast cancer incidence for cisgender women.[117]

For transgender people receiving exogenous testosterone, higher concentrations of androgens might increase breast cancer risk, particularly for androgen receptor–positive cancers.[118] Alternatively, testosterone exposure may have antiproliferative effects.[119] In vitro studies have shown that some androgens (testosterone and dihydrotestosterone) can inhibit the growth of cancer cells.[119] A study of the histology of mammary tissue from transgender men who had received testosterone showed both a reduction in glandular tissue and an increase in fibrous connective tissue.[114,117]

Prostate cancer Multiple case reports exist of prostate cancer among transgender women.[120,121] However, decreased androgen concentrations in transgender women and nonbinary people receiving estrogen and/or antiandrogens might decrease the risk of prostate cancer, and decreased rates of prostate cancer have been noted in transgender people receiving exogenous estrogen compared with cisgender men.[48]

Other reproductive organ cancers Transgender men have presented with ovarian, uterine, and cervical cancers,[19] but no current evidence exists to suggest that the rates are higher than the rate in cisgender women.[108,122] Most transgender people receiving testosterone in European studies have undergone hysterectomy within 5 years of starting hormone therapy because this was previously mandated by protocol, limiting the utility of the data when considering prolonged testosterone exposure.

Hormone Treatment and Other Tumors

Case reports also exist of transgender individuals receiving estrogen who present with meningiomas,[123,124] prolactinomas,[125] and other pituitary tumors. Human pituitary cells (lactotrophs) are estrogen-sensitive; however, no studies associate prolactin rise with estrogen treatment alone.[126] By contrast, modest data exist for the development of hyperprolactinemia associated with combination estrogen and cyproterone acetate treatment.[127] Prolactin concentrations return toward baseline when cyproterone acetate is discontinued, suggesting that the progestin is the relevant stimulus for the prolactin rather than the estrogen.[127] When estrogen is combined with either spironolactone or a gonadotropin-releasing hormone agonist, prolactin concentrations are stable.[128,129] Although prolactinoma is listed as a risk of using exogenous estrogen in the Endocrine Society's 2017 treatment guideline,[96] no studies to date have shown prolactinoma development, even when estrogens are combined with cyproterone acetate.

In summary, studies to date have not shown increased rates of cancer for transgender people. As prospective data collection matures, rates of cancers relative to cisgender people will become clearer. A risk of increased cancer morbidity and mortality associated with lack of access to care and minority stress may present a far greater risk to transgender people than potential cancer risks of hormone therapy.

CREATING SAFER ONCOLOGIC ENVIRONMENTS

Barriers to Care

Sexual and gender minority people face assumptions and stigma in oncologic encounters. Sexual minority people, who can also be gender minorities, experience assumptions about partners. For example, a woman may be presumed to be heterosexual, and a clinician may ask if she has a husband.[130] People are also often presumed to be cisgender—in other words, having a gender that is the same as that commonly associated with their sex assigned at birth. Patients may also experience stigma if they correct faulty assumptions or if clinicians learn about their identities.[130] Exclusion of partners from health care experiences may be particularly traumatic in oncologic settings, given the high stakes involved in treatment or the intense grief and fear patients and partners may experience at the end of life.[42] Similarly, in these contexts, it may be especially painful for patients not to have their gender appropriately recognized. However, anti-SGM stigma from oncology clinicians has the potential to do great harms,[40] such as if patients are not provided efficacious and timely treatment. Given these possibilities, SGM people may face incredible pressure to hide their identities.

Conflation of Gender and Anatomy

Oncology language and materials often conflate gender with anatomy (Table 1).[131] For example, a transgender woman may be seen in a clinic with implicit messaging about gender—a blue color scheme or pictures of men on the walls. Similarly, she may receive educational materials that refer only to men. She may be presumed to be a man by her clinicians. She may experience use of the wrong pronouns (e.g., he/him or they/them) or her legal name rather than her correct name in that setting, a phenomenon referred to as *misgendering*.[132] Misgendering has many ill effects, including increased barriers to care and mental health sequelae (Table 1).[133–135] National oncology organizations also conflate gender identity and anatomy in cancer guidelines, and thus oncology clinicians are steeped in gendered assumptions about cancers that may translate to the ways in which they address patients.[136–138]

Conflation of gender and anatomy also may preclude participation of gender minority or intersex people in clinical trials. Clinical trials may unnecessarily use gender as an inclusion criterion, such as by restricting participation to "men with prostate cancer." Trials may also ask about sex assigned at birth during intake and, if the only options are "male" and "female," exclude some intersex participants. Sexual and gender minority and intersex people with cancer thus experience barriers to cutting-edge therapies.

Gender-Related Care During Cancer Treatment

Hormone therapies and surgeries are lifesaving interventions for gender minority people who want them, and improve quality of life.[44,45,139] As discussed earlier in this chapter, concerns have been raised about the impacts of hormone therapy on cancer risks and outcomes.[47,48] In the absence of clear data, oncologists and patients are put in a position to weigh the hypothetical risks against the benefits of gender-related interventions in the setting of oncologic treatment. Transgender people face many barriers to hormone therapy, so these conversations may serve to widen rifts between patients and oncologists.[140]

Data Accuracy and Insurance

Normal laboratory ranges are calculated on the basis of the gender or sex marker in the EMR. However, these data may be entered on the basis of insurance information, patient-reported information at the time of registration, or on the basis of other documents, and could represent sex assigned at birth, gender identity, or neither, and clinicians and patients may not have the ability to easily change this designation. Normal laboratory ranges for cisgender men and women do not necessarily extrapolate to the bodies of transgender people on or off hormone therapy.[141–143] Given this, the laboratory

values of transgender people may have inappropriate abnormal flags, and clinicians and patients will have to interpret for themselves whether these values are indeed abnormal or of clinical concern.[58] Even more concerning, some chemotherapeutic medications, including carboplatin, are dosed on the basis of creatinine clearance, which is calculated on the basis of gender or sex designation in the chart.[144] No data exist, to our knowledge, regarding the implications of these dosing decisions for transgender people.

In addition, transgender people may face barriers to insurance coverage for cancer treatment (e.g., for testicular or prostate cancer) based on the sex or gender marker entered at registration.[145,146] Insurance coverage for adolescent and young adult patients with cancer may also be under the name of a parent or guardian, creating difficulties in maintaining privacy and accurately representing a patient's gender in the EMR.

Improving Safety

Addressing barriers to care for SGM people with cancer will require multilevel interventions. Cancer organizations such as ASCO are in the process of updating guidelines to incorporate inclusive language regarding gender, such as stating *people* with ovarian cancer rather than *women* with ovarian cancer. ASCO also added language to guideline templates that emphasizes the importance of avoiding gendered language.[147,148] Cancer centers should ensure that names of clinics, waiting rooms, or other facilities are not gendered (e.g., "Center for Women's Cancers") and that all-gender bathrooms are available and accessible for patients. All institutions should ensure that nondiscrimination policies cover sexual orientation and gender identity along with other protected classes and that grievance policies are explicit and accessible for patients who have experienced discrimination.[149–151] Rooming policies should be based on gender identity rather than sex assigned at birth and should prioritize the safety of SGM people who are at greater risk of harm.

Clinical trials should avoid exclusion based on gender, history or current use of hormone therapy, or HIV status. Cancer centers should also ensure that advertising and facility optics are inclusive and welcoming, that SGM staff and clinicians are employed and cultural humility training is available, and that referrals are available to vetted, knowledgeable clinicians.

On an individual level, we recommend that all oncology clinicians introduce themselves to patients using their name and pronouns and ask for the same information from all patients, avoid gendered language regarding partners, and solicit and center the treatment priorities of patients.[41,130] The Sidebar provides a list of recommendations.

SEXUAL AND GENDER MINORITY ONCOLOGY CLINICIAN TRAINING: BEST PRACTICES AND RESOURCES

When combined with institutional and policy changes, oncology clinician–directed cultural humility trainings may be one way to improve the care received by SGM people with cancer. We use the term *cultural humility* preferentially because whereas cultural competence suggests that a clinician could gain expertise in an experience distinct from their own, cultural humility instead reflects a need for ongoing self-evaluation and critique. Also, cultural humility reflects the importance of addressing hierarchies in clinician–patient relationships and developing mutual partnerships in their stead.[152] Qualitative research with SGM people who have been diagnosed with cancer suggests that such training should address institutional and individual clinician- and staff-level factors.[40,41] We would also advocate for addressing systems-level factors—for example, training clinicians and staff regarding the importance of changing EMRs, national guidelines, insurance policies, and local and national policies that may create barriers to quality care for SGM people with cancer.

Sexual and gender minority cultural humility training for oncology clinicians is particularly timely for a number of reasons. First, an increasing number of jurisdictions and professional associations are either encouraging or mandating such training.[153,154] Second, competition among clinicians is likely motivating increased participation rates in the Human Rights Campaign Healthcare Equality Index, a national grading scale that publishes ratings of health institutions.[155] Finally, the increased national dialogue about equity and discrimination is likely driving clinicians' self-examination and a desire for change. For example, from June 2020 to June 2021, requests for trainings from the National LGBT Cancer Network, a nonprofit organization that provides education, training, and advocacy to improve the lives of SGM people who have been diagnosed with cancer, more than doubled.[156]

Efforts to meet this growing demand have emerged from several sectors. Several oncology centers, including the H. Lee Moffitt Cancer Center and Research Institute (Tampa, FL), the George Washington University Cancer Center (Washington, DC), the Barbara Ann Karmanos Cancer Institute (Detroit, MI), and the Cleveland Clinic (Cleveland, OH) conduct SGM cultural humility trainings. The Moffitt Cancer Center's Curriculum for Oncologists on LGBTQ+ Populations to Optimize Relevance and Skills (COLORS) training has been pilot tested with oncologists in Florida and is now being evaluated in a two-arm clinical trial with a random sample of oncologists nationwide.[157,158] The training is expected to relaunch for broad access in 2022.

Nonprofit organizations focused on advocacy and education also provide trainings. The National LGBT Cancer Network conducts trainings at a range of oncology venues

and has recently partnered with the Society of Gynecologic Oncology to develop the newly launched Welcoming Spaces trainings.[159] This is a series of eight online, 45-minute, oncology-focused trainings that qualify for the Human Rights Campaign's Healthcare Equality Index standards, and they offer continuing education credits for a wide variety of different health professionals. Focused instead on building the cohort of diverse cancer researchers, the Building the Next Generation of Academic Physicians research group offers in-depth workshops regarding SGM cancer care and research.[160]

Many other local LGBTQ+ organizations also conduct trainings for oncologists. For example, Fenway Health runs the National LGBTQIA+ Health Education Center and offers a wide variety of trainings.[161]

A recently published article regarding using the multicultural orientation framework for SGM trainings in oncology reviewed best practices regarding approaching training at oncology centers for maximum success.[162] For health systems looking to develop their own trainings, *A Guide to Best Practices in LGBTQI+ Cultural Competency Training*, created by multiple organizations and led by the Whitman-Walker Institute and the National LGBT Cancer Network, can accelerate that process, as can new recommendations regarding such trainings."[163,164] Table 2 provides a summary of resources.

The growth in demand for SGM-focused cultural humility trainings has driven the creation of a series of new resources providers can use to access SGM training for themselves and their office staff. With the resources listed above, oncology providers currently have free access to state-of-the-art trainings about these underserved populations. Using these trainings may decrease barriers to equitable care for SGM people at risk for and experiencing cancer. Questions have been raised about the utility of cultural humility trainings for clinicians and in some studies have been demonstrated to be less likely to predict clinician knowledge than preconceived biases.[165] Given these findings, we recommend that, alongside training for oncology providers, institutions partner with SGM people with cancer to develop measurement tools to assess the efficacy of training at specific sites; assess cancer facilities in terms of optics, clinician–patient relationships, referrals, and other aspects; and develop and test interventions to ensure the quality of care for SGM people at that institution.[166]

CONCLUSIONS

In this article, we review unmet research needs regarding SGM people with cancer and measures to address them, what is known and unknown regarding the role of hormones in hematologic and oncologic disorders, barriers to care for SGM people with cancer and mechanisms to decrease them, and resources for individual oncology clinicians and institutions to increase SGM oncology cultural humility and knowledge. Systematic comprehensive data collection will be needed to fill the gaps in knowledge regarding cancer risks, prevalence, and outcomes for SGM people with cancer so that interventions can be developed to decrease cancer disparities. In the interim, we suggest that individual oncology clinicians and oncology institutions take the steps outlined throughout this article and in the Sidebar to ensure that SGM people with cancer receive high-quality care and are included in all aspects of oncology.

Ultimately, systems changes will be needed to move away from gendered-care models to ensure SGM visibility and clinical safety and access. For example, laboratory values and chemotherapy dosing based on a sex or gender marker must be redesigned and reimagined. Insurance companies must change their algorithms for coverage so that claims are not denied for transgender people with ovarian, fallopian tube, uterine, testicular, prostate, breast, and other cancers. National oncology organizations must continue to move away from gendered language in guidelines and toward greater accuracy and inclusion. Oncology cooperative groups and individual principal investigators must move away from gendered inclusion and exclusion criteria in trials to enhance generalizability and access. Such changes are needed to ensure data accuracy, safety, and improved outcomes for all people living with cancer.

AFFILIATIONS

[1]Center for Gerontology and Healthcare Research, Department of Health Services, Policy & Practice, Brown University School of Public Health, Providence, RI
[2]Department of Public Health Sciences, University of Rochester Medical Center, Rochester, NY
[3]National LGBT Cancer Network, Providence, RI
[4]Department of Cancer Epidemiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL
[5]School of Interdisciplinary Health Programs, Western Michigan University, Kalamazoo, MI
[6]Department of Obstetrics and Gynecology, Stanford University School of Medicine, Palo Alto, CA
[7]Division of Endocrinology, Icahn School of Medicine at Mount Sinai, New York, NY
[8]Mount Sinai Center for Transgender Medicine and Surgery, New York, NY

CORRESPONDING AUTHOR

Ash B. Alpert, MD, MFA, Center for Gerontology and Healthcare Research, Department of Health Services, Policy & Practice, Brown University School of Public Health, Box G-S121-6, Providence RI 02903; Twitter: @ash_alpert; email: ash_alpert@brown.edu.

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