

# Position paper of the Italian association of medical oncology on health disparities among transgender and gender-diverse people: the Assisi recommendations



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## Summary

Transgender and gender-diverse individuals experience substantial health disparities across the cancer care continuum. Despite well recognized unique healthcare needs, there are barriers in accessing cancer prevention and treatment services, influenced by disadvantages in key social-economic determinants of health which result in worse clinical outcomes, as compared to the general population. The Italian Association of Medical Oncology (AIOM) acknowledges the critical relevance of this issue. The “Assisi Recommendations” here summarize the outcomes of the “AIOM Oncology Ethics Day” dedicated to gender differences in oncology and cancer care of transgender and gender-diverse people. The recommendations generated during a 2-day multidisciplinary discussion address the various aspects of cancer care experience of transgender and gender-diverse people. The promotion of research in this field, through the generation of new evidence and the collection of prospective data, has been identified as a priority action to mitigate these disparities. By acknowledging the challenges of cancer care in transgender and gender-diverse people and recognizing the need for dedicated policy and clinical recommendations, AIOM demonstrates its commitment to improving the health and well-being of all patients with cancer, regardless of their gender identity or any other personal or social circumstances, as part of health-for-all societal vision.

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## Introduction

Cancer is a major public health concern worldwide, affecting individuals of all ages, genders, ethnicities, and regardless geographical borders. It has become increasingly clear that gender identity may influence cancer risk and clinical outcomes.<sup>1,2</sup> Transgender and gender-diverse individuals—those whose gender identity does not align with society’s expectations based on their sex assigned at birth (Table 1)—represent approximately 0.5–4.5% of the general population.<sup>3</sup> They often experience multiple barriers to cancer prevention and screening, face major challenges in accessing and receiving timely, quality cancer care, and are largely under-represented in clinical trials.<sup>4</sup> Disparities in the access to best cancer care commonly result in delayed diagnoses, poor adherence to screening programs, and worse clinical outcomes when compared to general population.<sup>5,6</sup>

In recent years, the Italian Association of Medical Oncology (AIOM) has increasingly recognized the importance to address the challenges of cancer care in lesbian, gay, bisexual, transgender, queer, intersex and asexual (LGBTQIA+) communities in Italy within its broader scope of reducing cancer disparities and improving outcomes for all patients, with no distinction. A key priority has been set for transgender and gender-diverse people.

AIOM has developed tailored projects to improve knowledge of cancer care in transgender and gender-diverse individuals, increase awareness amongst health providers, and formulate actionable plans for improvement. From this perspective, the 10th edition of the annual conference on ethics in cancer care called “AIOM Oncology Ethics Days”, held in Assisi in September 2022, has been dedicated to the topic of “sex and gender identity across the cancer care continuum”.

Representatives of AIOM and Fondazione AIOM met with Italian experts from different fields, including institutional and governmental stakeholders, professionals involved in the care of patients with cancer, LGBTQIA + activists, patients, and their representatives. This was a unique opportunity for comprehensive and cross-disciplinary discussions concerning the implementation of a gender-sensitive approach to cancer care. The areas discussed encompass gender identity data collection, inclusion of transgender and gender-diverse patients in clinical trials, establishment of inclusive settings, cancer screening, alignment between gender-affirming care and cancer treatments, psychological aspects of cancer care, the need for more training for healthcare professionals, modifiable risk factors, social and economic factors driving marginalization, and cooperation with LGBTQIA + associations. This event marked the concluding step of a more extensive project that began with the release of a scoping narrative review summarizing the existing knowledge regarding cancer care in transgender and gender-diverse individuals<sup>7</sup> and a survey-based study which presented a snapshot of the experiences, viewpoints, and inclinations of healthcare professionals (HCPs) and the transgender community in Italy.<sup>8</sup> Building on the foundation laid by these preceding endeavours, the stakeholders engaged in discussions leading to the recommendations here presented, designed to facilitate substantial change.

While there are clinical oncology guidelines available from other societies such as the American Society of Clinical Oncology (ASCO) for the broader LGBTQIA + community that can be adaptable to other contexts and countries,<sup>9</sup> there is a lack of specific guidance for transgender and gender-diverse individuals. For these reasons, AIOM has committed to fill such a substantial gap with the development of ten

Sex assigned at birth	The determination of an infant’s sex at the time of birth by examining the external genitalia.
Gender identity	The inner, individual perception of themselves as male, female, non-binary, another gender identity or having no gender.
Gender expression	The ways in which an individual expresses their gender within their social and cultural context, including aspects such as clothing, speech, behavior and more. A person’s gender expression does not necessarily match with their gender identity.
Transgender	People whose gender identity and/or gender expression does not align with society’s expectations based on their sex assigned at birth.
Cisgender	People whose gender identity aligns with society’s expectations based on their sex assigned at birth.
Gender diverse	Umbrella term used to refer to individuals whose gender identity and/or gender expression deviates from societal expectations or norms. It includes terms such as non-binary, genderfluid, genderqueer, gender neutral, agender, X-gender and many others.
Gender incongruence	A diagnostic term found in the International Classification of Diseases (ICD) 11th Revision, referring to an individual’s persistent and pronounced sense of incongruity between their gender identity and sex assigned at birth.
Gender dysphoria	A clinically significant sense of distress due to a perceived misalignment between sex assigned at birth and gender identity. It is also a diagnostic term found in the Diagnostic and Statistical Manual of Mental Disorders, 5th version. Not all transgender and gender-diverse individuals experience gender dysphoria.

**Table 1: Definitions.**

recommendations for equitable and inclusive cancer care for transgender and gender-diverse people.

## Materials and methods

### Conference structure

The 10th edition of the “AIOM Oncology Ethics Days” has been dedicated to the topic “sex and gender identity across the cancer care continuum”. It was held in Assisi on 23rd and 24th of September 2022, and it consisted in a 2-day multidisciplinary conference.

- Participants: representatives of AIOM and Fondazione AIOM, institutional and governmental stakeholders, HCPs involved in the care of patients with cancer (medical oncologists, surgeons, general practitioners, psycho-oncologists, nurses), jurists, philosophers, theologians, journalists, LGBTQIA + communities such as the Italian association of LGBTQIA + medical care providers (AMIGAY), and the Association for transgender culture and ethics (ACET), patients and their representatives, and representatives of other scientific societies.
- Topics: based on the data presented in our previous narrative review<sup>7</sup> and national surveys,<sup>8</sup> ten macro-areas were identified and further explored during the discussions that took place over the course of the two working days. The topics covered included: gender identity data collection, clinical trial inclusion, creation of inclusive environments, screening, coordination between gender affirming care and cancer treatments, psychological dimensions of cancer care, HCPs training, primary prevention education for transgender and gender-diverse youth, the social-economic drivers of marginalization, collaboration with LGBTQIA + associations.
- Workflow: the initial session of the congress involved didactic presentations and open discussion led by experts who shared findings from relevant literature, by transgender and gender-diverse patient who shared their personal experiences, and by LGBTQIA + activists who highlighted the current state of transgender and gender-diverse people rights within the context of the Italian national health system. The second part of the event featured a round table discussion, involving 19 panelists. Its main objective was to outline and consolidate the ten key recommendations that emerged from the event.
- Panel selection: the panel consisted of 19 members. All were experts in transgender health-related issues: medical oncologists, including members of the AIOM board, LGBTQIA + activists, representatives from the transgender community, a psychologist, and a statistician.
- Round table discussion: at the end of the first session, a list of 10 key issues and considerations for a gender-sensitive approach to cancer care was agreed

upon. The 19 stakeholders were assigned the responsibility of elaborating on each key issue and formulating a single recommendation for each issue. Following this preparatory phase, the panel unanimously ratified the 10 recommendations.

- Post-conference work: to solidify and elaborate upon the recommendations within this position paper, we further scanned the literature to find any additional publication that emerged in the interim, as described below.

## Recommendations

The proposed recommendations and actions are summarized in [Table 2](#).

### Recommendation 1: promote sexual orientation and gender identity (SOGI) data collection

Estimation of risk levels and factors, and cancer outcomes among transgender and gender-diverse individuals require availability of quality data about sexual orientation, gender identity, gender affirmation, anatomy, and hormone status of our patients as part of cancer registry and other data collections.<sup>10,11</sup> Whereas the collection of sex-related information is common in cisgender patients, for example the menopausal or reproductive status of cisgender women, these elements are commonly overlooked and often assumed in transgender and gender-diverse people, mostly in individuals who are non-binary—a term used to describe people whose gender identity extends beyond the categories of male and female—that represent a significant and growing proportion of gender-diverse population. Assumptions and prejudices underlie misinformed data and hamper the estimation of the real extent of disparities across the cancer care continuum.<sup>12,13</sup> Despite actual data showing that most patients are willing to disclose their SOGI with HCPs<sup>14,15</sup> and despite the existing recommendations by national organizations,<sup>9</sup> many HCPs still do not collect these data because of structural barriers such as lack of leadership support as well as lack of detailed protocols for data collection and specific training.<sup>16</sup> Collecting this type of information poses a challenge from a bureaucratic standpoint due to the absence of any standardized and validated model for an inclusive personal data collection. Many researchers have already tackled this issue and have suggested that a two-step process would likely be the best way forward: an initial question regarding sex assigned at birth, followed by a second question regarding gender identity.<sup>17–19</sup> A further challenge once collected SOGI data, would be recording them on the clinical records. Institutional mandates at the national, regional, or even individual centre level are necessary to modify the fields of the electronic medical records. Furthermore, both the healthcare and administrative staff who interact with the users should be trained to collect and record such data.

Recommendations	Actions
1. Promote SOGI data collection.	Choose a model for an inclusive collection of SOGI data. Advocate for a policy-change in data collection at your institution. Train all workforce interacting with patients on SOGI data collection.
2. Promote inclusion of transgender and gender diverse patients in cancer clinical trials.	Avoid presumptive language when drafting clinical protocols.  Allow GAHT among concomitant medications, unless interactions with experimental drugs and/or procedures are scientifically documented. Do not exclude HIV + patients under treatment and with a clinically acceptable CD4 lymphocyte count to participate unless interactions between antiretroviral drugs and experimental drugs and/or procedures are scientifically documented.
3. Create safe and welcoming environments for transgender and gender diverse cancer patients.	Allow transgender and gender diverse patients to register with alias name and chosen gender to healthcare registries.  Respect gender identity: use gender-sensitive language, ask for transgender and gender diverse patients' preferred pronouns. Avoid gender-labelled oncological services (e.g., female-only case studies in posters and/or other informative material in waiting rooms and clinics for gynecological cancers care). In the case of in-patient clinics offering shared rooms, transgender and gender diverse patients should be assigned to shared rooms based on their gender preference. Implement gender-neutral restrooms. Display symbols such as rainbow flag or transgender flag on official websites of hospitals.
4. Improve cancer screening guidelines referred to transgender and gender diverse individuals.	Counsel and refer patients for oncological screening programs based on their anatomy and actual risk factors, not based on sex assigned at birth alone.
5. Provide education and training to oncology HCPs about transgender and gender diverse people's health issues.	Promote education on gender-sensitive healthcare and approaches.  Organize didactic events on T transgender and gender diverse people's health topics at your institution.
6. Provide information to transgender and gender diverse people, especially youth, about modifiable cancer risk factors and other risk-increasing conditions.	Promote awareness campaigns targeted towards young LGBTQIA + individuals about quitting smoking, reducing alcohol consumption, the importance of physical activity, and healthy nutrition, and prevention and screening for sexually transmitted infections. Promote the use of pre-exposure prophylaxis (PrEP) prior to engaging in high-risk sexual activities. Promote HBV and HPV vaccinations.
7. Coordinate gender affirming care and cancer care on a case-by-case basis.	Consider a close collaboration with endocrinologists, surgeons, psychologists, and other relevant health professionals before outlining a treatment strategy. Do not interrupt GAHT unless strictly clinically needed or as requested by patients. Always share treatment decisions with your patients.
8. Provide psychological support during the whole cancer care continuum.	Collaborate with the psychological service of your health center since the patient's initial assessment.  Screen, identify early and manage possible signs of exacerbation or occurrence of gender dysphoria during the cancer care continuum. Inquire about the support network of transgender and gender diverse patients to foster local collaborations.
9. Address social determinants of health.	Work to minimize financial barriers by connecting patients with available resources such as local support organizations. Implement culturally, appropriate, and acceptable communication. Advocate for a real empowerment of transgender community: offer guidance to transgender and gender diverse patients on how they can assert their rights to receive a proper care.
10. Collaborate with LGBTQIA + organizations.	Contact representatives of LGBTQIA + organizations in your area and collaborate with them for new research projects. Make sure that transgender community's voices are always heard and incorporated within the research and care process.

**Table 2: Recommendations and actions.**

Quality, robust, reliable and gender-sensitive data collection is instrumental to improve transgender and gender-diverse people care.

### **Recommendation 2: promote inclusion of transgender and gender-diverse patients in cancer clinical trials**

The collection of these variables would also enable clinicians to examine the differences in treatment outcomes based on SOGI within clinical trials.<sup>20</sup> However, transgender and gender-diverse people are not often

included in cancer clinical trials because of several barriers such as social-economic marginalization, which may hinder access to the main research cancer centers, previous experiences of discrimination in healthcare settings, and clinical trial protocol language and inclusion/exclusion criteria that may implicitly exclude transgender and gender-diverse individuals.<sup>4</sup> Such exclusion does not only limit our understanding of the unique challenges that transgender and gender-diverse people may face when it comes to cancer prevention, diagnosis, and treatment, but also perpetuates health

disparities and inequalities in these individuals, as they may not have access to the latest treatments and therapies.<sup>21</sup>

To address this issue, pharmaceutical companies and clinical researchers should avoid presumptive language such as “women with ovarian cancer” or “men with prostate cancer” when drafting protocols and instead use inclusive language such as “individuals with ovarian/prostate cancer”. Furthermore, the use of gender affirming hormone therapy (GAHT) should be allowed by clinical trial protocols unless interactions with experimental drugs and/or procedures are scientifically documented. Another barrier to address is the exclusions of patients living with HIV and/or with a known history of HIV infection, as already enlightened by several researchers in the last years.<sup>22–24</sup> Such exclusion has been and is still somewhat systematic, and not evidence-based. Since transgender and gender-diverse individuals are burdened by a higher rate of HIV infection compared to the general population<sup>25</sup> due to intersectionality with lower-income, marginalization, and barriers to healthcare, having HIV positive status among exclusion criteria can disproportionately affect transgender and gender-diverse patients’ opportunity to participate in clinical trials.

### **Recommendation 3: create safe, welcoming, and inclusive environments for transgender and gender-diverse people**

The Assisi Recommendations enforce the importance of creating a gender-sensitive and diversity-oriented healthcare milieu. Based on the patients’ reports and lived experience, it emerged the importance on “how” transgender and gender-diverse patients are addressed. It is crucial to ask patients about their preferred name, pronouns, and adjectives to be used correctly and consistently, even in medical and administrative records, to create a sense of comfort and safety during clinical encounters and establish and maintain the therapeutic liaison.<sup>26</sup> It should be noted that patients’ correct names may differ from what is legally recognized, and HCPs should never assume. Self-determined gender is a cornerstone of a person’s identity, as recognized by the United Nations (UN), specifically the UN High Commissioner for Human Rights and included in the normative documents of the World Health Organization.<sup>27</sup> A significant step towards fostering inclusivity and affirming the autonomy of transgender and gender-diverse individuals is to allow them the option of registering with an alias name and self-identified gender in hospital health records. Providing this opportunity would enable transgender and gender-diverse individuals to maintain their sense of self, would avoid forced “outing”, and would facilitate accurate and respectful communication throughout the cancer care journey. A possible, initial solution amidst the status quo of transgender

and gender-diverse people rights in Italy is illustrated by the establishment of a “Registry for Alias names”, to recognize a gender-concordant name and a self-determined gender for individuals who have not yet completed the legal procedure of gender affirmation. In healthcare, the implementation of such a registry would catalyze the harmonization of a major source of discrimination and distress of patients. Furthermore, such a change would empower transgender and gender-diverse patients to navigate their healthcare experiences with dignity, reduce episodes of discrimination and violence, and promote their overall well-being.

Creating a structurally inclusive environment that promotes safety and acceptance is crucial within oncology practices. This can be achieved through the implementation of gender-neutral settings of care, avoiding gender-labelled oncological services as well as adopting gender-affirming rooming policies. In the case of in-patient centers that offer shared rooms, transgender and gender-diverse patients should be assigned to shared rooms based on their gender self-identification. In instances where a cisgender roommate raises objections, it is important for facility policies and procedures to clearly state that the roommate with objections should be relocated, rather than the transgender patient.<sup>12</sup>

Such a shift in the paradigm would greatly benefit from Alias Registries, even better improved if nationwide policies would allow self-determination of the gender, as opposed to the status quo of the legislation that mandates specific interventions, often castration, to yield the legal recognition of the gender status.

### **Recommendation 4: improve cancer screening guidelines and practices referred to transgender and gender-diverse individuals**

Due to the limited availability of data concerning the health status and cancer outcomes among transgender and gender-diverse individuals, in the absence of extensive prospective studies, guidelines regarding cancer screening for this population can only be derived from existing evidence in the cisgender population, and largely based on assumptions, as also elucidated in the last version of Standards of care for the health of transgender and gender-diverse people.<sup>28</sup> With regards to breast cancer, the World Profession Association of Transgender Health and the Endocrine Society recommends to adhere to local screening guidelines originally designed for cisgender women when providing care for transgender and gender-diverse individuals who underwent GAHT with estrogens and/or transgender, gender-diverse and/or non-binary individuals assigned female at birth who did not undergo mastectomy.<sup>28,29</sup> In the literature there is no consensus about how to screen transgender and gender-diverse individuals assigned female at birth who had mastectomy, with indications

spanning from annual chest examination to annual screening mammography.<sup>30–32</sup>

All individuals with a cervix should follow the same local guidelines developed for cisgender women. A significant number of transgender, gender-diverse individuals and/or non-binary assigned female at birth might choose not to undergo Papanicolaou test due to feelings of discomfort, fear of discrimination and stigma by HCPs, and occurrence or recrudescence of gender dysphoria.<sup>33,34</sup>

Prostatectomy is not commonly included among the gender-affirming surgical interventions. Transgender and gender-diverse individuals with a prostate should follow the local screening guidelines for prostate cancer. An important difference to consider is that serum level of prostate specific antigen (PSA) > 1 ng/mL in transgender and gender-diverse individuals who undergo GAHT with antiandrogens should be regarded as exceeding the normal level.<sup>35</sup> However, it should be emphasized that AIOM does not recommend population screening for prostate cancer.<sup>36</sup>

Transgender and gender-diverse individuals seem to be less likely to adhere to cancer screening programs because of structural barriers.<sup>8,37</sup> For example, during the meeting, we learnt that in Italy, citizens in the national healthcare system receive a letter of invitation to participate to population-based screenings based on the gender assigned at birth, or re-assigned. This means that individuals who undergo gender affirmation and get the legal gender recognition are then excluded by risk-appropriate screening programs because invitations are only based on the gender, assuming the population is only cis-gender. As such, transgender men are not invited to cervical and breast cancer screenings anymore, regardless of the organ-defined risk, and vice versa, for prostate cancer prevention in transgender women. AIOM emphasizes the importance to base screening programs on risk-definitions and never assume gender-restricted definitions. Cancer risk is primarily defined by the presence of specific organs, for which there is demonstration that prevention with dedicated interventions results in lower cancer mortality. Accordingly, screening of organs for cancer has nothing to do with gender, including when it is about organs that undergo sexual dimorphism in the early organogenesis. Screening programs must be designed in inclusive and gender-sensitive approaches, to ensure no one is left behind.

#### **Recommendation 5: provide education and training to oncology HCPs about transgender and gender-diverse people's health issues**

Several cross-sectional studies and surveys, conducted in Europe, United States, and Australia have demonstrated how most oncologists recognize their limited knowledge regarding the unique needs of transgender and gender-diverse individuals in oncology, especially in

terms of primary and secondary prevention.<sup>8,13,38–42</sup> It has also been highlighted that oncologists do not feel adequately equipped and confident to provide optimal care for transgender patients. Across all these studies, most respondents expressed the desire for this topic to be better addressed in medical schools, residency programs, and professional training. In our recent survey-based study, we highlighted a common lack of knowledge about transgender health-related issues among Italian oncology HCPs.<sup>8</sup> Furthermore, 72% of respondents expressed the need of receiving specific training that addresses the distinctive healthcare needs of transgender and gender-diverse patients, while 56% advocated for the incorporation of such training as a compulsory component within their educational journey. Notably, a mere 19% reported a sense of competence in furnishing assistance to transgender and gender-diverse patients.

In recent years, multiple examples of training and continuing education courses, delivered both online and in-person, have been proposed and have demonstrated clear effectiveness thereby reinforcing their role in bridging the knowledge gap and improving the quality of care for this marginalized patient demographic.<sup>43–48</sup> Critical skills to achieve encompass adjusting language to ensure inclusivity, eradicating presumptions regarding sexual orientation and gender identity, and maintaining a heightened awareness of potential instances of microaggressions, whether overt or indirect.<sup>46</sup> Significantly, these efforts contribute to an elevated level of comfort experienced by the patients.

#### **Recommendation 6: provide comprehensive education to transgender and gender-diverse people, especially youth, about modifiable cancer risk factors**

Among transgender and gender-diverse individuals there are alarming rates of tobacco consumption and alcohol use, higher compared to general population according to most studies.<sup>7</sup> This trend is particularly evident in transgender and gender-diverse youth. The California Healthy Kids Survey found a statistically significant higher prevalence of monthly alcohol consumption among transgender and gender-diverse students of middle- and high-schools compared to cisgender peers (Adjusted Odds Ratio (OR) 1.49, 95% Confidence Interval (CI) = 1.33–1.66)<sup>49</sup>; moreover, transgender and gender-diverse students were more than twice as likely to be active smokers compared to non-transgender peers (AOR 2.48, 95% CI = 2.11–2.93). The California Student Survey 2013–2015 showed that transgender and gender-diverse students had higher odds of heavy episodic drinking compared to non-transgender youth (AOR 2.33, 95% CI = 1.63–3.34) and higher odds of cigarette use in the past 30 days compared to cisgender students (AOR 1.79, 95% CI = 1.22–2.65).<sup>50</sup> Similarly, a survey conducted in a

large Midwestern University in the US reported a higher rate of tobacco consumption in transgender and gender-diverse students compared to cisgender peers (AOR 2.82, 95% CI = 1.26–6.31).<sup>51</sup>

With regards to sexually transmitted infections, transgender and gender-diverse people accounted for 2% of new HIV diagnosis in 2020 in US, with the highest proportion (28%) of diagnoses in transgender and gender-diverse individuals observed among transgender women aged 25–29 years, followed closely by transgender women aged 20–24 years (21%).<sup>52</sup> The prevalence of HIV infection is significantly higher in transgender and gender-diverse individuals compared to general population.<sup>25</sup> In this sense, promoting safe sexual practices encouraging the consistent use of condoms and pre-exposure prophylaxis (PrEP) as preventive measures against HIV infection is paramount as well as providing accurate information on the effectiveness and accessibility of these preventive methods to ensure informed decision-making and safeguard sexual health. Moreover, despite the absence of definitive data regarding the incidence of human papillomavirus (HPV) and viral hepatitis among transgender and gender-diverse individuals, it remains essential to advocate for the vaccination against HPV and hepatitis B virus (HBV), in accordance with the recommendations for the general population.<sup>7</sup>

#### **Recommendation 7: provide psychological support during the whole cancer care continuum**

Transgender and gender-diverse individuals with cancer may require significant psychological support due to a variety of factors. Many transgender and gender-diverse individuals have already experienced significant emotional and psychological distress due to familial and societal stigma and discrimination related to their gender identity, at the time of the first contact with a cancer care provider.<sup>53</sup> A cancer diagnosis can further compound these feelings of anxiety, depression, minority stress, and isolation, especially if the individual perceives the cancer diagnosis as a result of their gender identity when there might be an assumption, broadly speculative, of a causative role of the gender-affirmation treatments, notably the hormonal therapy. Transgender and gender-diverse people are exposed to a higher burden of discrimination and blaming, potentially amplifying their susceptibility to engage in harmful behaviors such as increased tobacco, alcohol, or substance use, as well as worsening existing eating disorders and elevating the risk of suicide.<sup>54</sup> These risks are already heightened among individuals who have endured stigma and discrimination since childhood, further emphasizing the urgent need to address the intersectionality of gender identity and cancer-related health outcomes, in the context of social-economic health determinants.

Furthermore, cancer treatment and its side effects can exacerbate existing feelings of dysphoria or distress related to gender identity.<sup>55</sup> For instance, sometimes, GAHT may need to be paused or discontinued during cancer treatment, which can have a significant impact on an individual's sense of self and gender identity, with the occurrence and/or re-emergence and/or intensification of gender dysphoria or other mental symptoms. Additionally, some cancer treatments may cause physical changes that can be distressing for transgender and gender-diverse individuals, such as mastectomy for transgender women or hysterectomy for transgender men.<sup>56–58</sup>

Less explored are the specific alterations in sexuality and intimate partner relationships resulting from cancer treatments, including, and not limited when genital or anal surgeries or radiation therapy are undertaken.<sup>59</sup> Further research is needed to comprehensively understand the impact of such procedures on individuals' sexual well-being and their dynamics within romantic partnerships. Examining these aspects can provide valuable insights for healthcare professionals in tailoring high-quality comprehensive supportive care.

Transgender and gender-diverse individuals may face unique challenges related to their social support networks. Many have strained relationships with family members and may not have established support networks,<sup>60</sup> which can make coping with a cancer diagnosis even more challenging. Due to these unique challenges and considerations, transgender and gender-diverse individuals with cancer may require significant psychological support throughout the cancer care continuum. This support can include access to mental health services, support groups, specific social assistance, and other resources to help them cope with the emotional and psychological impact of cancer and its treatment.

#### **Recommendation 8: coordinate gender-affirming care and cancer care on a case-by-case basis**

Gender-affirming care plays a crucial role in the well-being of transgender and gender-diverse individuals. Regarding its relationship with cancer care, the matter is twofold: on one side, concerns about the potential increased risk of cancer associated with GAHT<sup>61</sup>; on the other, the concerns on how to optimally coordinate gender-affirming care and cancer treatments in transgender and gender-diverse patients who have received a cancer diagnosis.

The available data regarding the relationship between GAHT and cancer risk in this population are limited and there is not sufficient evidence to suggest any definitive link.<sup>62</sup> Many of the assumptions of a causative link with cancer are largely speculative and not evidence based. Although some studies have indicated a potential increase in breast cancer risk among transgender women receiving estrogen therapy, the risk does not appear to reach the levels observed in cisgender

women.<sup>63</sup> Further research is necessary to fully understand the underlying mechanisms and establish a conclusive relationship. Additionally, prolonged use of cyproterone acetate, has been associated with a possible correlation with meningiomas and prolactinomas.<sup>64</sup> On the other hand, GAHT with antiandrogens in transgender women seems to provide protective effects against prostate cancer.<sup>65,66</sup> Moreover, certain gender-affirming surgical procedures, such as mastectomy and hysterectomy in transgender men, have clear oncological benefits.

With regards to the complex interplay between gender-affirming care and cancer treatment, the medical treatment may need to be individualized to meet both medical goals and gender affirmation.<sup>67</sup> For example, it is notable that in some cases surgery for breast cancer or gynecological cancers are the same interventions undertaken by some transgender and gender-diverse individuals for gender affirmation. This overlap may exert influence on the process of decision-making for surgical oncology as well as for gender-affirming care. By analyzing the transgender and gender-diverse patients' interviews from the "Cancer's margin project", Brown et al. described some cases of transgender breast cancer survivors assigned females at birth who chose bilateral mastectomy without reconstruction and who were satisfied with their treatment choice.<sup>68</sup> Other studies, examining the same interviews, underlined how gender affirming care is often uncoordinated with cancer treatments resulting in disorienting cancer care experiences for transgender and gender-diverse patients.<sup>69,70</sup> Furthermore, assessment of breast and ovarian cancer risk prior to gender-affirming surgery in individuals assigned female at birth should be performed in order to identify those who may be at high risk for breast/ovarian cancer and may benefit from risk-reducing mastectomies and/or oophorectomy.<sup>71</sup>

Cancer treatments may delay gender affirming medical therapies or surgical interventions and this must be clearly discussed with the patient at first visit.<sup>72</sup> In a recent retrospective study, Burns and colleagues reported that only 13.5% of transgender and gender-diverse cancer survivors in Dana-Farber Cancer Institute and Brigham and Women's Hospital had documented discussions with HCPs about the possible interactions between GAHT and cancer therapy.<sup>26</sup>

However, the option of discontinuing GAHT in transgender and gender-diverse cancer patients must be approached with utmost caution and only when there is a scientifically sound rationale to do so, and it is agreed by patients. All decisions, in such a delicate interplay, must be shared decisions. For a successful integration of gender-affirming care and cancer management, a comprehensive, multidimensional, multidisciplinary, and holistic approach is crucial. This could entail the coordination of various services, including endocrinology, surgery, oncology, and psychology.

## **Recommendation 9: address social determinants of health**

Transgender and gender-diverse people are at increased risk of experiencing discrimination and social-economical marginalization. Stigma and discrimination perpetrated by individuals or groups in different environments of society lead to unemployment or underemployment that, in turn, are drivers of poverty. Therefore, transgender and gender-diverse individuals may encounter several barriers in accessing housing, basic goods, and services and, consequently, may be forced to involve in risky situations and behaviors.<sup>73</sup>

Addressing social determinants of health, such as poverty, housing insecurity, and lack of insurance, can help reduce barriers to healthcare. Obviously, social determinants of health can be addressed only through a multi- and trans-disciplinary approach. However, HCPs can take small but impactful and concrete actions such as working to minimize financial barriers by connecting patients with available resources, including local support organizations. At the same time, it is paramount to advocate for a real empowerment of transgender community by equipping them with the knowledge and tools to assert their rights and secure appropriate healthcare.

## **Recommendation 10: collaborate with LGBTQIA + organizations**

HCPs should play a pivotal role in by fostering collaborative relationships with LGBTQIA + organizations to embark on fresh and impactful research initiatives. By forging these relationships, HCPs can tap into a well-spring of invaluable insights, perspectives and feedbacks from representatives of the LGBTQIA + community, contributing to the ongoing refinement and evolution of institutional practices.<sup>12</sup> As the healthcare landscape continues to evolve, it is paramount that the voices of the LGBTQIA + community are not only heard but actively integrated into every facet of policymaking. However, since transgender and gender-diverse individuals might face exclusion and marginalization even within the broad LGBTQIA + movement, it is essential to ensure that the local transgender community is fully represented and involved during the policy-change process, adhering to the principle of "not for me without me". This principle recognizes that decisions that directly impact the transgender community must be made in partnership with them, acknowledging their expertise and lived experiences as invaluable contributors to the shaping of policies that truly meet their needs.

By establishing an ongoing dialogue and meaningful engagement with local LGBTQIA + associations, HCPs can help pave the way for more inclusive, equitable, and effective healthcare systems.

## **Conclusions**

Multiple stakeholders can have a critical role in addressing the challenges of cancer care in vulnerable



### Search strategy and selection criteria

We conducted a comprehensive search of PubMed, Cochrane Library, and EMBASE databases for relevant publications from their inception until June 30, 2023. The search was limited to articles published in English. The search terms used in PubMed and Cochrane Library included (cancer or carcinoma) and (transgender or transexual or "gender minority" or "gender non-conforming" or "gender diverse" or nonbinary or transmen or transwomen or genderqueer or LGBT\*). We included various types of publications such as original research studies, review articles, letters to the editor, editorials, cohort studies, cross-sectional studies, and surveys published until June 2023. We examined the secondary references of relevant papers to identify additional articles not captured by the electronic search, thus enhancing the research outputs through snowballing. We also incorporated grey literature into our research, including registry and survey-based epidemiological statistics or reports and normative guidance and other documents of the United Nations; however, this search was not systematic, as common with grey literature. We excluded papers that approached the LGBTQIA + population as a collective entity without providing segregated data for transgender and gender-diverse individuals. Following the assessment of titles and abstracts, the two lead authors (AGL, RC) excluded duplicate entries and records that did not align with our research objectives. In cases of discrepancies, a third reviewer (DT) served as a tiebreaker. Subsequently, the full texts of the screened records were evaluated, and pertinent information was extracted into an Excel spreadsheet. We analyzed the extracted records to identify key concepts of the most relevant and original works included in the final reference list. [Supplementary Fig. S1](#) provides the PRISMA diagram illustrating our literature search process.

people to ensure the best health and outcomes for all. By recognizing the unique needs of transgender and gender-diverse individuals and working to eliminate barriers to care, AIOM has engaged with the broader civil society and LGBTQIA + communities to promote better care in the transgender and gender-diverse population. Multi-level interventions, holistic approach, and trans-disciplinary collaboration are critical to improve equitable cancer care, to result in better outcomes. There is no more excuse to avoid a patient-centred approach that considers a patient's gender and sexual identity. We believe that this is necessary and feasible through improved medical education and training on transgender health issues, promoting inclusive healthcare policies and practices, and advocating for interventions to facilitate access to healthcare for transgender and gender-diverse individuals.

As next steps AIOM is committed in the development of a multi-stakeholder and multi-disciplinary guidance with the aim of addressing the management of GAHT, surgical treatment, and other aspects of cancer care of transgender and gender-diverse patients. By better understanding the unique cancer risks and healthcare needs of this population and implementing policies that promote inclusive and equitable cancer care, AIOM reaffirms its important role in promoting equitable and inclusive cancer care for all.

### Contributors

All authors had full access and verified the underlying data reported in the manuscript and accept responsibility to submit for publication.

Dr Leone and Dr Casolino served as co-first authors.

Dr Pietrantonio and Dr Cinieri served as co-senior authors.

Concept and design: Dr Leone, Dr Casolino, Dr Trapani, Dr Pietrantonio, Dr Cinieri.

Methodology: All authors.

Acquisition and interpretation of data: All authors.

Drafting of the manuscript: All authors.

Supervision: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

### Data sharing statement

No new data were generated or analyzed in this manuscript.

### Declaration of interests

ML acted in a consulting/advisory role for Roche, Novartis, Lilly, Pfizer, Merck Sharp and Dohme (MSD), Seagen, Gilead, Exact Sciences, AstraZeneca and received speakers' honoraria from Takeda, Ipsen, Roche, Lilly, Novartis, Pfizer, Sandoz, Libbs, Knight, Daiichi Sankyo, received a travel grant from Gilead and Daiichi Sankyo, and a research grant (to the institution) from Gilead, all outside the submitted work.

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FM received honoraria from Servier, Lilly, Pierre-Fabre; research grant from Incyte.

MDM received honoraria from Pfizer, Takeda, AstraZeneca, Janssen, Eisai, Novartis, Roche, Astellas Pharma, MSD, Lilly, Merck, Amgen; research grants from Tesaro and GlaxoSmithKline; acted in a consulting/advisory role for AstraZeneca, Pfizer, Takeda, Janssen, Eisai, Novartis, Roche, MSD, Amgen.

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RBe received honoraria and/or research grant from: BI, EISAI, MSD, Amgen, Roche, Pfizer, Astra Zeneca, Lilly, GSK, BMS, Otsuka, Seagen.

GDB received honoraria and/or research grants from Roche, MSD, Tahio, Servier, Celgene, Ipsen, Sanofi; acted in consultory/advisory role for Roche, Lilly, Eisai, Incyte; has served as speaker for Servier, Clovis Oncology, Ipsen, Lilly, Merck Serono, Amgen, Novartis, BMS.

MM declares ELMA is a for-profit agency.

The other authors declare no conflict of interest to disclose.

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## Appendix A. Supplementary data

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