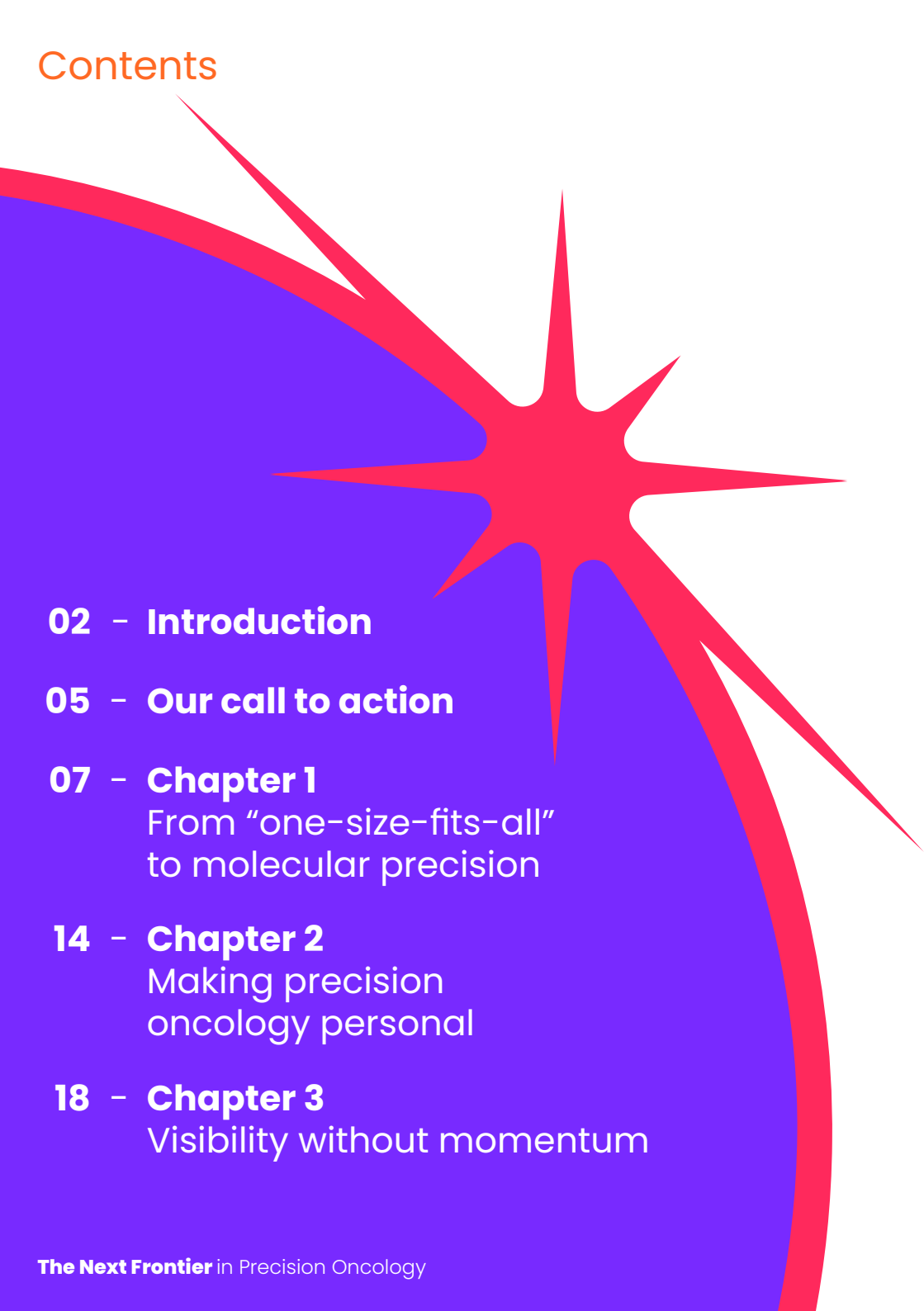


# The Next Frontier in Precision Oncology

Why sex and gender must be  
recognised as the foundations  
of Precision Oncology

- 
- 02 – Introduction**
  - 05 – Our call to action**
  - 07 – Chapter 1**  
From “one-size-fits-all”  
to molecular precision
  - 14 – Chapter 2**  
Making precision  
oncology personal
  - 18 – Chapter 3**  
Visibility without momentum


# Precision medicine in oncology:

## Progress, promise – and no “sex factor”

Over the past two decades, oncology has undergone a profound transformation. Once dominated by broadly cytotoxic treatments that indiscriminately targeted rapidly dividing cells, cancer care is now all about precision medicine. Clinicians now classify tumours by molecular and genomic characteristics, match patients to targeted therapies, and increasingly harness the immune system to fight disease. These advances have extended survival, reduced unnecessary toxicity for some patients, and, in a subset of cancers, made long-term remission possible even in advanced disease.

### Yet progress has created a paradox.

Precision oncology is becoming more accurate at targeting tumours and rare molecular alterations, yet two of the most fundamental drivers of variation between patients: sex and gender, remain overlooked. Sex and gender are key determinants of cancer risk and outcome and should be considered as such. Nevertheless, these two variables are not consistently embedded across research, development, regulation, treatment or care. The result is avoidable evidence gaps that affect safety, effectiveness and outcomes.



This topic was recently explored at **The Next Frontier in Precision Oncology**, an event convened by Madano in partnership with Healthcare Communications Association and Women in Pharma, bringing together leading experts to examine the implications for research, care and policy.



### **Dr Berna Özdemir**

MD PhD Senior Medical Oncology Consultant, University Hospital Bern; Founding Member, ESMO Gender Medicine Taskforce



### **Linda Geddes**

Award winning science journalist



### **Merel Hennink**

Cancer Patients Europe (CPE) and Lung Cancer Europe (LuCE) Board Member

**One message emerged clearly:** realising the full promise of precision oncology requires the oncology ecosystem to unite around sex and gender as foundational drivers of cancer risk, treatment and outcomes.

# The Next Frontier in Precision Oncology:

Our call to action

We call for coordinated action from stakeholders across the oncology ecosystem to:

## 1. Raise awareness and drive accountability

- ✦ Ensure all stakeholders – from clinicians to policymakers – recognise sex and gender as determinants of cancer risk and outcomes.

## 2. Embed sex as a standard biological variable

- ✦ Integrate sex into clinical trial design from the outset.
- ✦ Report outcomes and safety data by sex.
- ✦ Ensure dosing reflects differences in body composition and age.
- ✦ Involve patients early in shaping research priorities.
- ✦ Reflect sex-based considerations in clinical guidelines and education.

## 3. Address gender as a determinant of access and outcomes

- ✦ Implement gender-responsive strategies to improve equitable access to early detection and diagnosis.
- ✦ Build health systems that deliver respectful, high-quality care for all.
- ✦ Integrate sex and gender across the full continuum – from research and development, to regulation, treatment and patient care.

# From “one-size-fits-all” to molecular precision

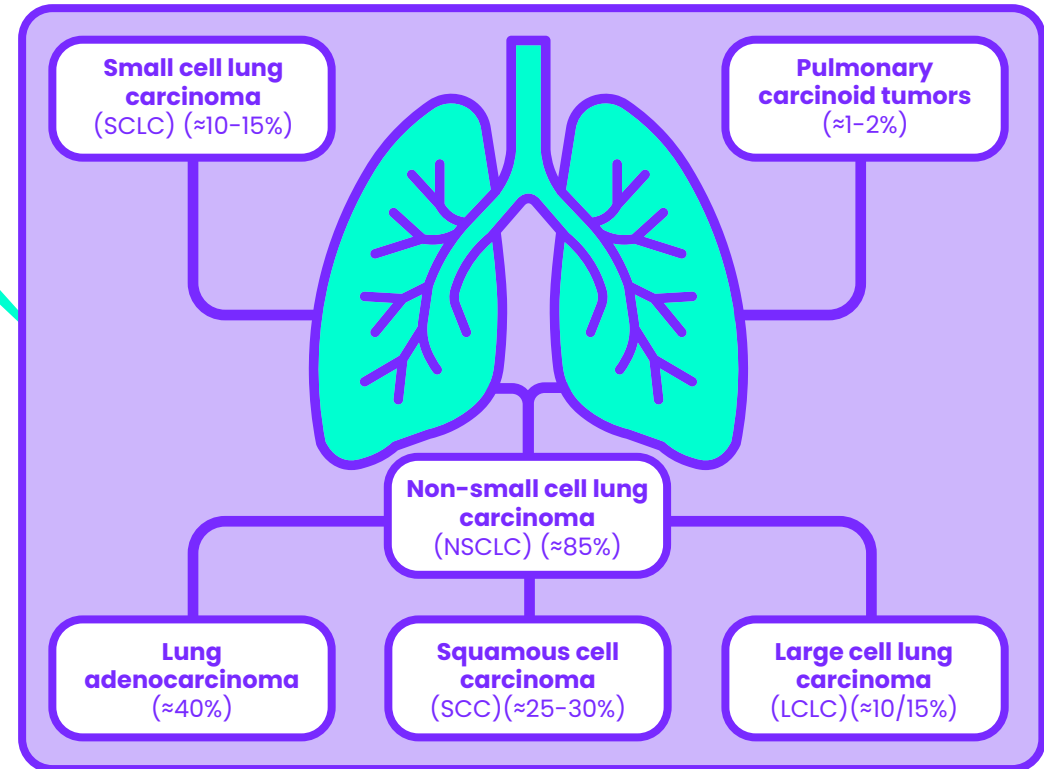
Historically, cancer treatment was blunt by design. Surgery, radiotherapy and chemotherapy were developed on the premise that rapidly dividing cancer cells could be selectively damaged. While effective in some contexts, these approaches were inherently non-specific and frequently associated with significant toxicity.

The genomic revolution transformed oncology by showing that cancer is not a single disease, but a group of related conditions driven by distinct genetic mutations. A major breakthrough has been the identification of driver mutations – key genetic changes that fuel cancer growth – enabling more targeted, personalised treatments that can be less toxic than traditional chemotherapy.

Targeted therapies, often oral, began to replace or supplement chemotherapy. The emergence of immunotherapies in the early 2010s marked another inflection point, offering durable responses – and in some cases cures – for a subset of patients with metastatic disease.

Lung cancer illustrates this evolution. Once classified into two broad categories (small-cell and non-small-cell), it is now subdivided into multiple molecularly defined subtypes.

Figure 1. Classification of Lung Cancers.<sup>1</sup>



**Dr Berna Özdemir**, MD PhD Senior Medical Oncology Consultant at University Hospital Bern and Founding Member of the ESMO Gender Medicine Taskforce, highlighted that patients whose tumours harbour alterations such as EGFR mutations or ALK rearrangements can receive targeted therapies that outperform standard chemotherapy, with patients living longer than those receiving non-specific cytotoxic treatment when matched to the correct targeted therapy.

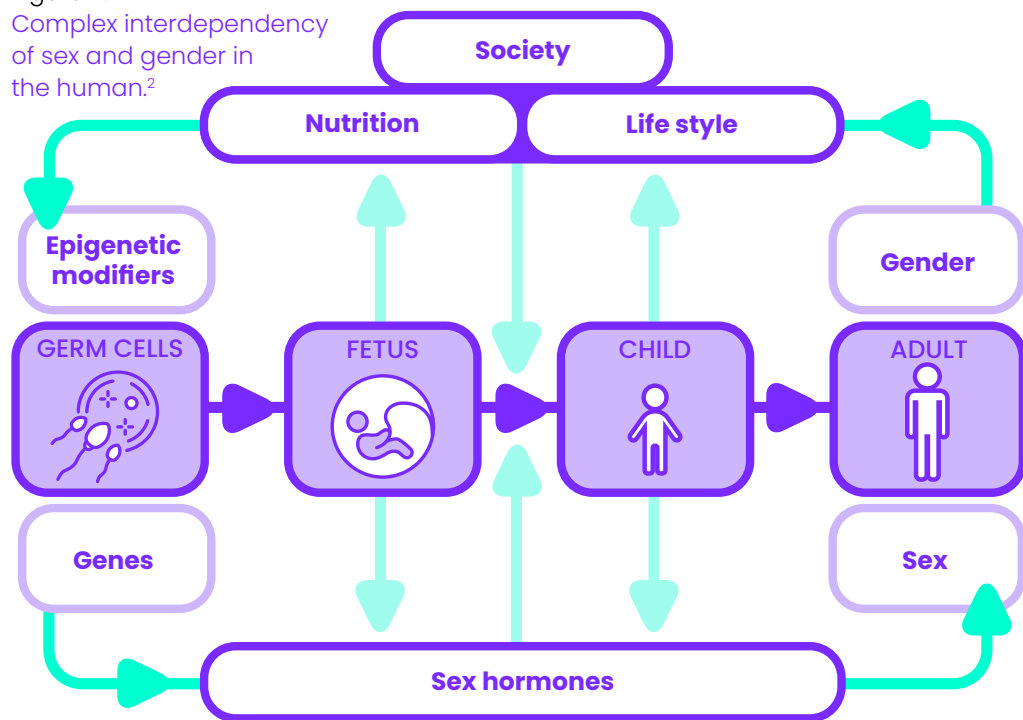
# Precision — for whom?

Despite these advances, access to precision oncology remains inequitable. Availability of molecular testing, specialist expertise and novel

therapies continues to vary widely by geography, socioeconomic status and health system capacity.

Less visible — and far less systematically addressed — is how sex and gender shape cancer risk, treatment response, toxicity and outcomes.

Figure 2. Complex interdependency of sex and gender in the human.<sup>2</sup>



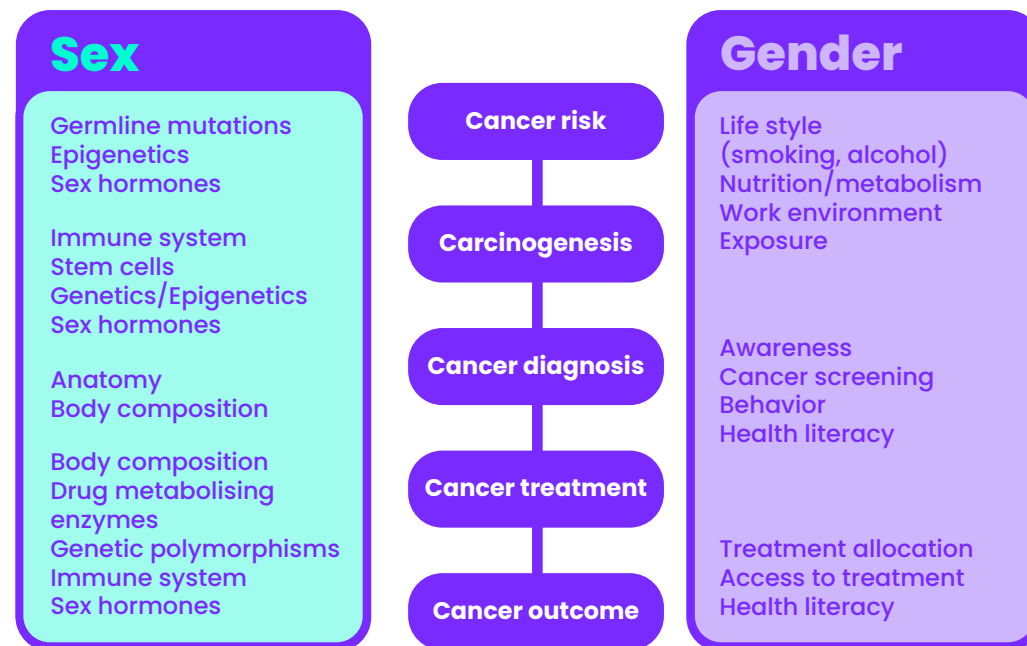
## Dr Berna Özdemir explained that:

Sex refers to biological attributes, including chromosomes, hormones and anatomy.

While distinct, sex and gender influence each other. They are intertwined in ways that influence biology, behaviours, access to care and lived experience.

Gender is a social construct encompassing roles, behaviours, identities and norms that vary across cultures and over time.

Figure 3 Cancer as a prime example of sex and gender differences.



In oncology, sex and gender matter — yet neither is consistently integrated into precision medicine frameworks.

## What the data already tell us — and what we still ignore

✦ **Cancer risk and mortality:** Across almost all cancer types and regions, male sex is associated with higher risk of developing cancer and higher risk of dying from it. This pattern has been observed consistently since cancer registries were established in the 1970s. Thyroid cancer is a notable exception, with higher incidence in women.<sup>3</sup>

✦ **Treatment toxicity:** When it comes to cancer treatment, sex-based differences in toxicity have been observed, with female patients experiencing higher rates of severe adverse effects across treatment types. These toxicities include life-threatening infections, bleeding, thrombosis and organ damage, often leading to dose reductions, treatment interruptions or premature discontinuation — even in curative settings.<sup>4</sup>

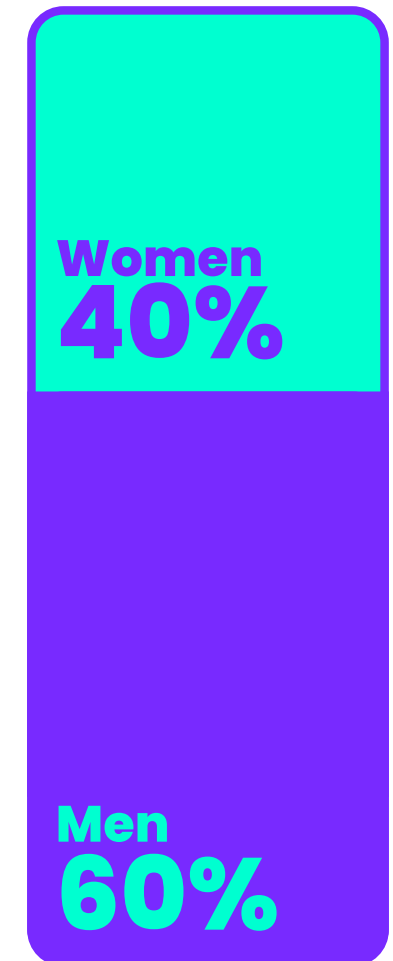
✦ **Knowledge and agency:** Sex and gender differences extend beyond biology. According to a Lancet Commission titled Women, power, and cancer, women living with cancer experience gender bias alongside other forms of discrimination — including those linked to age, race, ethnicity, socioeconomic status, sexual orientation and gender identity — which can leave them structurally disadvantaged. These overlapping factors can limit women’s ability to reduce preventable cancer risks and create barriers to timely diagnosis and prompt, high-quality care.<sup>5</sup>

# Structural bias built into precision medicine

Despite this evidence, sex and gender are rarely treated as a core biological variables in oncology research and drug development. Bias is introduced early and amplified at every stage:

- ✦ **Preclinical research:** Cancer drugs are predominantly tested in male animals, based on the flawed assumption that females introduce excessive variability due to their hormonal cycle (called estrus in mice).<sup>6</sup>
- ✦ **Dose selection:** The “standard” reference patient is a 70-kg, white, male. Differences linked to sex, body composition, ethnicity or age are rarely explored systematically.<sup>7,8</sup>
- ✦ **Clinical trials:** Women remain under-represented. Over the past 20 years, enrollment typically sits at around 60% men and 40% women.<sup>9</sup>
- ✦ **Reporting:** Toxicity is rarely reported by sex. Because it is seldom a primary endpoint, sex-disaggregated safety data often remain unpublished or inaccessible.<sup>9</sup>

Figure 4: Proportion of men and women typically enrolled in clinical trials.



# When imprecision compromises patient care

These gaps create real-world risks for patients. Post-hoc analyses of approved drugs can suggest differential benefit — or potential harm — by sex. Yet, because trials are not powered to detect these differences, clinicians are left without clear guidance. **Dr Berna Özdemir** described the resulting ethical tension clearly:

**“I cannot withhold the treatment because it’s an approved treatment — that would be unethical. But if the treatment is detrimental, then I’m putting my patient at risk.”**

## Making precision oncology personal:

### Why sex and gender matter to patients

Precision medicine promises the right treatment for the right patient at the right time. For people living with cancer, that promise is often only partially realised. Treatments may be precisely matched to tumour biology, but they are far less tailored to the individual receiving them.

As Merel Hennink, Board Member at Cancer Patients Europe (CPE) and Lung Cancer Europe (LuCE), explained during the event:

**“For me, [I thought] precision medicine meant I would get a treatment made for me as a person. But that’s not what it is.”**

Patients experience treatment through side effects that disrupt daily life and long-term tolerability, and uncertainty when evidence is incomplete. These realities become sharper in rare, gene-driven cancers where the data are limited from the start:

**“At first I thought being rare meant I was special. But special also means less research.”**

Merel also explained that within patient communities, sex-specific effects are often observed before they are studied:

**“Men on the medication had a complete drop in testosterone — that was discovered. Women had very similar symptoms, but for us it wasn’t investigated.”**

For patients, this is the point where “precision” stops being reassuring and starts feeling incomplete — particularly when therapies are taken for years. Patients consistently call for care and research that reflects the whole person, not only the tumour:

**“We are not subjects. We are human beings.”**

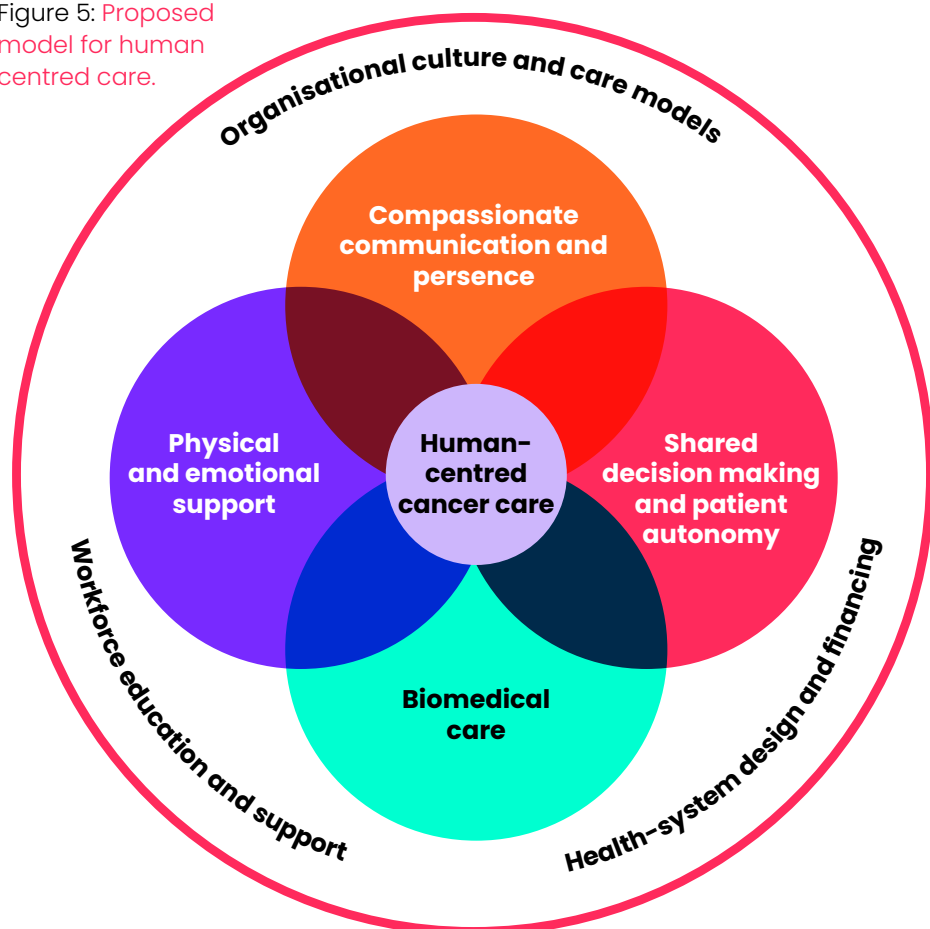
And they are clear about what would improve the system:

**“Patients need to be involved from the start — in the research question and all the way through.”**

Precision medicine that does not consider sex and gender is not fully precise. It may target the tumour, but it does not consistently serve the person. As highlighted by the Lancet Oncology Commission titled *The human crisis in cancer care*<sup>10</sup>, a truly effective precision

oncology approach must move beyond tumour biology alone to reflect the full biological and social reality of people living with cancer.

Figure 5: Proposed model for human centred care.



**Visibility without momentum:**  
Media coverage and the stakeholders driving change

Despite clear clinical relevance, sex and gender remain marginal topics within public and media discourse on precision oncology. According to social media analysis conducted by Madano's Insights Practice, a stark imbalance between the scale of precision oncology as a topic and the limited attention given to sex and gender exists within the conversation.

## Sex and gender: hiding in plain sight

In the last 12 months, precision oncology generated more than **74,000 news and social media posts**. In contrast, **only around 6,000 posts addressed sex and gender in oncology**.

For every 50 news articles or social posts about precision oncology there was just one on sex and gender.

(1.6k)

Sex and gender

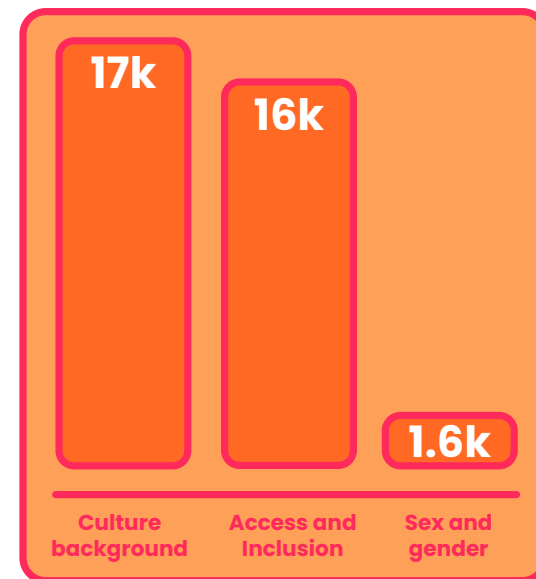
(74k)

Precision Oncology

This is not simply because equity topics are less visible. Other equity-related themes — such as cultural background, access and inclusion — receive nearly ten times more coverage than sex and gender.

Sex and gender in oncology is 10x less likely to be discussed than other equal topics.

Frequency of topics discussed in social & new media in relation to oncology



## A conversation defined by frustration, not clarity

Where the issue is discussed, the dominant sentiment is confusion, followed by disappointment and disapproval. Findings reflect growing frustration that well-established biological differences are still not systematically incorporated into research, development, regulation, treatment and care, even as patient experience continues to outpace the evidence base.

# Signs of progress— but no sustained narrative

## **There are early signals of momentum.**

Influential media voices have begun to spotlight sex and gender gaps. Regulators, professional bodies and political institutions have begun to take action. Patient advocacy organisations remain the most consistent drivers of attention and credibility.

However, activity remains fragmented and episodic. Without sustained, coordinated narratives and accountability, attention spikes and then dissipates.

**“Gender bias in medical research: how women are still overlooked.”**

The Week

**“Women are still under-represented in medical research. Here’s where the gender gap is most pronounced.”**

Time

**“Male bias in medical trials risk women’s lives. But at least the data gap is finally being addressed.”**

The Guardian

# Pharmaceutical company pledges: commitment without specificity

Pharmaceutical companies increasingly acknowledge diversity and inclusion as core principles in research and development. Analysis conducted by Madano, based on a structured review of publicly available **“diversity in trials”** statements and pledges from ten global

pharmaceutical companies (AbbVie, AstraZeneca, Bristol Myers Squibb, Eli Lilly, GSK, MSD, Novartis, Pfizer, Roche, Sanofi), shows broad recognition that trials should better reflect the populations they aim to serve.

This recognition, however, is rarely translated into specific, operational commitments. As Max Taylor, Senior Research Director at Madano, noted:

**“We’re seeing quite a lot of general commitments to making sure that clinical trials are representative, but not specific commitments related to sex- and gender-based reporting.”**

Few pledges reference sex-disaggregated analysis, sex-specific safety reporting or tailored dosing strategies. Time-bound targets and measurable outcomes are notably absent.

**No companies stand out as leaders or laggards** – suggesting the issue is not lack of awareness, but lack of expectation. Without clearer standards and guidelines from professional bodies, regulators, payers and policymakers, many commitments risk remaining aspirational rather than driving meaningful change.

# Who is driving change

## Driving momentum:

- ✦ Patient advocacy groups
- ✦ Some regulators and professional bodies
- ✦ Policy actors, particularly at EU level

# References

- 1 Rina, et al. The Genetic Analysis and Clinical Therapy in Lung Cancer: Current Advances and Future Directions. *Cancers*. 2024; 16(16):2882. <https://doi.org/10.3390/cancers16162882>
- 2 Regitz-Zagrosek. Sex and gender differences in health. *EMBO Rep* 13, 596–603 (2012). <https://doi.org/10.1038/embor.2012.87>
- 3 Clocchiatti, et al. Sexual dimorphism in cancer. *Nat Rev Cancer* 16, 330–339 (2016). <https://doi.org/10.1038/nrc.2016.30>
- 4 Unger, et al. Sex Differences in Risk of Severe Adverse Events in Patients Receiving Immunotherapy, Targeted Therapy, or Chemotherapy in Cancer Clinical Trials. *J Clin Oncol*. 2022 May 1;40(13):1474–1486. doi: 10.1200/JCO.21.02377. Epub 2022 Feb 4. PMID: 35119908; PMCID: PMC9061143.
- 5 Ginsburg, et al. Women, power, and cancer: a Lancet Commission. *The Lancet*, Volume 402, Issue 10417, 2113 – 2166
- 6 Karp, et al. The Sex Inclusive Research Framework to address sex bias in preclinical research proposals. *Nat Commun* 16, 3763 (2025). <https://doi.org/10.1038/s41467-025-58560-5>
- 7 Özdemir, et al. Sex and Gender Differences in Anticancer Treatment Toxicity: A Call for Revisiting Drug Dosing in Oncology. *Endocrinology*. 2022 Jun 1;163(6):bqac058. doi: 10.1210/endo/bqac058. PMID: 35560216; PMCID: PMC9113364.
- 8 Delahousse, et al. Sex differences in the pharmacokinetics of anticancer drugs: a systematic review. *ESMO Open*. 2024 Dec;9(12):104002. doi: 10.1016/j.esmoop.2024.104002. Epub 2024 Dec 10. PMID: 39662226; PMCID: PMC11697095.
- 9 Jenei, et al. The Inclusion of Women in Global Oncology Drug Trials Over the Past 20 Years. *JAMA Oncol*. 2021;7(10):1569–1570. doi:10.1001/jamaoncol.2021.3686
- 10 Rodin, et al. The human crisis in cancer: a Lancet Oncology Commission. *The Lancet Oncology*, Volume 26, Issue 12, e628 – e670



**Madano** is a communications consultancy committed to building a better world through intelligent and creative communications.

We help our healthcare clients bring products, services and propositions to life, turning complex concepts into simple and compelling messages.'

As you'd expect, we're strong on the science, with specialist knowledge in a range of therapeutic areas, including oncology, rare diseases, gene therapy and neuroscience. But we also provide creative flair and strategic thinking, delivering programmes built on unique ideas, insights and evidence.

If you would like to discuss how we can work together to advance this agenda, or learn more about our expertise in oncology, **please get in touch** via [info@madano.com](mailto:info@madano.com).



**madano**  
Shaping the future