Milano 23 Giugno 2023

VII CONVEGNO NAZIONALE DELLA RETE ONCOLOGICA SIFACT

Oncologia di genere

Rosalba Miceli, Biostatistician,
S.S. Biostatistics for Clinical Research

Sistema Socio Sanitario

Fondazione IRCCS
Istituto Nazionale dei Tumori

Regione Lombardia

rosalba.miceli@istitutotumori.mi.it

Disclosure

- I have no financial or non-financial interests or relationships with a profit health care company, neither currently nor over the last 3 years.

- I have no actual or potential conflict of interest in relation to this presentation.

Sex or gender identity?

"Something" that is assigned at birth based on chromosomal makeup

A social construction related to behaviors and characteristics based on labels of masculinity and femininity

How people perceive and describe themselves

Biological aspects of an individual determined by its anatomy, given by chromosomes, hormones, and their interactions

Sex or gender identity?

"Something" that is assigned at birth based on chromosomal makeup

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How people perceive and describe themselves

Biological aspects of an individual determined by its anatomy, given by chromosomes, hormones, and their interactions.

- Sex
- Gender identity

Sex

- Traditional division of individuals into females and males.
  - Biological and anatomical aspects.
  - Differential organization of chromosomes, reproductive organs, and sex steroid levels.
  - Historically, sex has been assumed to be binary and static.
    - Masculine and feminine characteristics have been taught as complete opposites and associated to sex.
    - In reality they share many similarities.

Albert K, doi: 10.1016/j.patter.2022.100534

Sex in medical research

- Historically, medical research studies have excluded female patients, or have included underrepresentation of them, following the concept that the "norm" was constituted by the male body.
  - Main reason: due to variations in female hormones, women were more difficult to study.

Sex in medical research (cont.)

- Consequences:
  - Research data collected from males, and research results, were generalized to females.
  - Individuals who did not conform to the "norm" could be misdiagnosed, missed treatment opportunities, received incorrect doses of medications, or even "wrong" medications.
- For many years medical practice (EBM and Guidelines) was based on evidence obtained from clinical trials conducted almost exclusively on one sex, mainly male.
- This has contributed negatively to the progress of knowledge and has reduced the possibility of generalizing the results of medical studies to the entire population.

Brady E, doi: 10.1038/s41467-021-24265-8.

Sex in medical research (cont.)

But, over the years:

- Preclinical and clinical studies have demonstrated that sex-based differences exist at the genetic, cellular, biochemical, and physiological levels.
- Medical research has highlighted:
  - Strong correlation between sex and incidence, prevalence, symptoms, age of onset and severity of certain pathologies.
    - Certain diseases present differently in men and women, and men and women experience illness differently (cardiovascular disease, lung cancer, depression and Alzheimer's disease).
  - Some treatments have different effects or adverse reactions on women and men.

Sex role in cancer studies

Risk factor

Prognostic factor

Predictive factor

Sex as risk factor

Sex has a role in etiology and development of cancer

- Associated with the risk of developing a specific tumor for healthy subject.
- There are sex-specific tumors (uterus, ovary, prostate).
- Examples of cancers having high male-to-female ratio: colorectal cancers; lung and bronchus; non-Hodgkin lymphoma; Kaposi sarcoma.

Sex as prognostic factor

Outcome is different in untreated patients or in homogeneously treated in F and M patients

VOLUME 23 · NUMBER 4 · FEBRUARY 1 2005

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Influence of Sex on Toxicity and Treatment Outcome in Small-Cell Lung Cancer

Simron Singh, Wendy Parulekar, Nevin Murray, Ronald Feld, William K. Evans, Dongsheng Tu, and Frances A. Shepherd

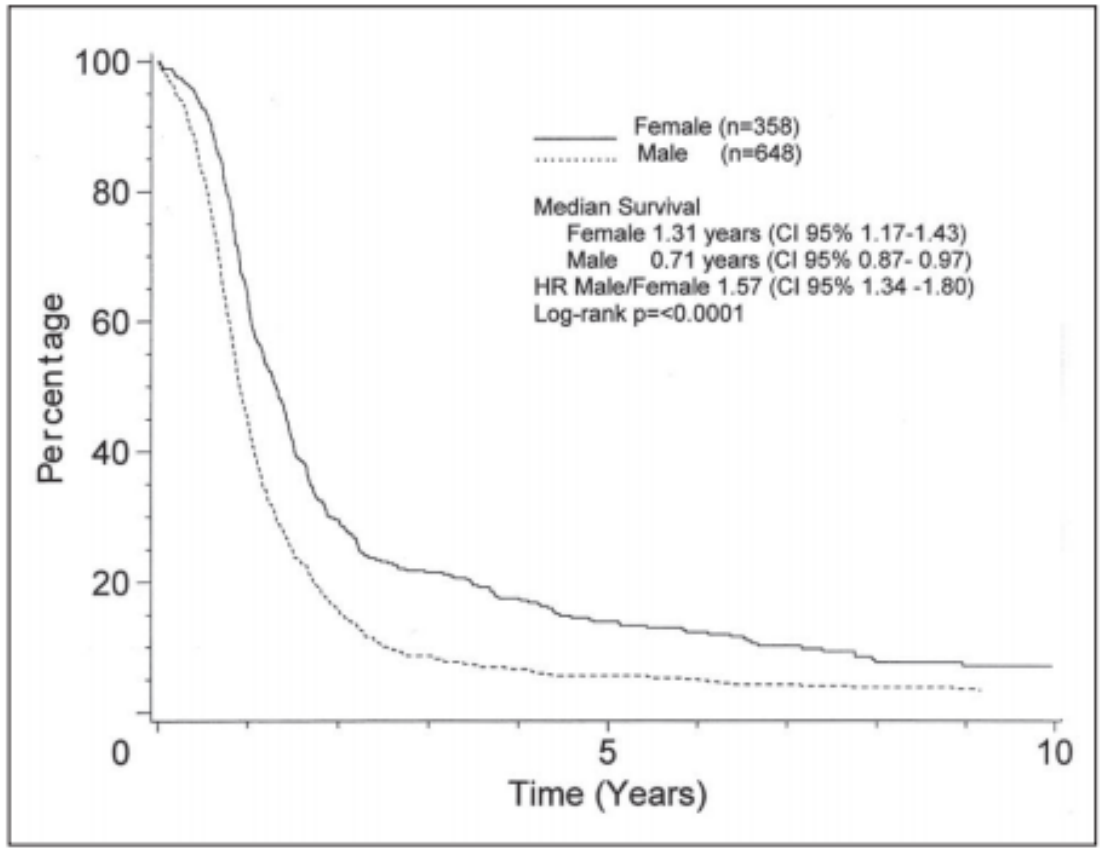


Fig 1. A comparison of survival for male and female patients. HR, hazard ratio.

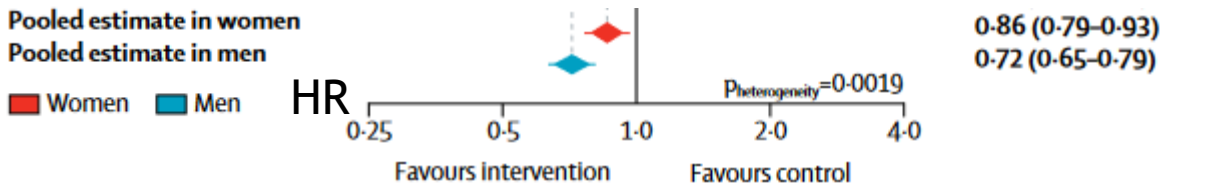
Sex as predictive factor

Differential treatment outcome according to sex

Cancer immunotherapy efficacy and patients' sex: a systematic review and meta-analysis

Fabio Conforti, Laura Pala, Vincenzo Bagnardi, Tommaso De Pas, Marco Martinetti, Giuseppe Viale, Richard D Gelber, Aron Goldhirsch

Lancet Oncol 2018; 19: 737–46



- Different tumors (melanoma, small-cell/non–small-cell lung, mesothelioma, head and neck, renal cell, urothelial, stomach).
- Pooled analysis: Treated vs untreated patients showed higher survival (lower death HR) independently of sex.
- The effect was more marked in M, and the difference F-M was statistically significant.

Nevertheless, **patient's sex is not taken into account in clinical decision making**.

Why taking into account sex in medical research?

- The results of medical studies are more reliable if women and men are equally included, and
- **Ignore sex differences challenges the quality and integrity of science and medicine**.

- Efforts have been made by professional and governmental organizations to increase women representation in clinical trials over the past 30 years.
- **Women are now routinely included in clinical trials** ("Why Women's Health Can't Wait", Brigham and Women's Hospital, 2014).

https://www.brighamandwomens.org/assets/bwh/womens-health/pdfs/connorsreportfinal.pdf (2014)

Why taking into account sex in medical research? (cont.)

Sex bias still exists:

- In about 20,000 North American clinical studies published from 2000 to 2020 (oncology, neurology, immunology and nephrology) there was a low representativeness of women.

- The number of RCTs aimed at obtaining results stratified by sex is still low
- Or results of stratified analyses are poorly used to adapt prevention, detection and treatment strategies for the benefit of women and men.

- In COVID-19 studies (ClinicalTrials.gov, Jan 2020-Jan 2021), 21.2% mentioned "sex" as recruitment factor, 5.4% took into account sex in the study design, 4% included sex as explanatory variable.

Steinberg JR, 2021, doi: 10.1001/jamanetworkopen.2021.13749.
Sugimoto CR, et al. 2019, doi: 10.1016/S0140-6736(18)32995-7
Brady E. 2021, doi: 10.1038/s41467-021-24265-8

Gender

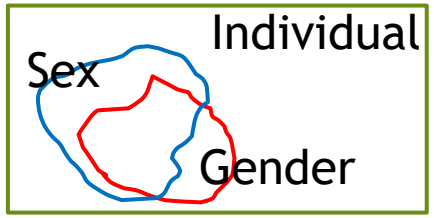
- In common feeling sex and gender represent the same concept.

- However, gender is a social construct and typically refers to:
  - Persons' gender identity (how they see themselves or experience their own gender).
  - How a person is perceived by others, or experiences differential treatment in relation to their perceived gender.
    - Includes norms, roles, expectations, stereotypes, associated with being a woman, man, girl or boy, as well as relationships with each other.
  - Between individuals differences characterized by relational, psycho-social, emotional, and behavioural aspects.

- **Gender varies from society to society and its definition can change over time**.

Sex and gender

- Sex and gender are not opposing but interdependent dimensions: biological characters ⟺ gender identity.



  - Hormones affect persons continuously, from birth throughout entire life, but they alone, or together with chromosomes, are not able to determine gender behavior.
  - On the other hand, gender determinants can have impacts on the body
    ➔ sex cannot be considered as separate from gender.

- **Sex and gender are not binary and static over time, nor necessarily aligned.**
  - The sex-gender relationship varies according to geographical areas, historical periods and cultures.

Sex and gender (cont.)

- Sex, gender and their interaction influence health outcomes.

- Example COVID-19 pandemic:

  - Men experienced more severe outcomes (hospitalizations, deaths) than women;
  - Women presented higher "long-COVID" risk.

  - Men's increased SARS-COV2 risk was also linked to their lower rates of handwashing, higher rates of smoking and alcohol misuse, higher frequency of comorbidities as compared to women.

  - SARS-CoV-2 infection had higher impact on some subgroups (children, health operators, pregnant women), and on women as caregivers.

https://www.who.int/news-room/questions-and-answers/item/gender-and-health

Gender in medical research

- Gender-related determinants are almost never investigated.

- Gender norms and roles, and **gender intersections with other individual characteristics**

could contribute to differentiate health behaviors, disease susceptibility, or how it is experienced.

Gender in medical research
Intersectionality

- This concept was born in 1989 (Prof. Crenshaw) to describe the challenges that individuals could experience caused by intersecting characteristics, including sex and gender.

- "Intersectional analysis" was intended as a tool for policy development to
  - Reveal the minority subgroups generated by intersecting multiple identities, to be of help and not leave behind.
  - Highlight discriminations and disadvantage occurring as a consequence of intersection of sex and gender and the combination of other identities.

Glob Health Action 2015, 8: 30292 - http://dx.doi.org/10.3402/gha.v8.30292

https://eige.europa.eu/thesaurus/terms/1263

Gender in medical research
Intersectionality (cont.)

- The society could consider "outside the normal" some minority subgroups, and create "antibodies" against them:
  - Differentials in power relations (e.g. politics, religion)
  - **Discriminations, stigmatizations,** disadvantages (e.g. barriers to equal participation in the workforce, especially for women's)
  - **Barriers to access (or unequal distribution of) resources, healthcare services, and treatments.**
- **The above challenges contribute to inequality between individuals and, ultimately, could influence health/disease/mortality**.

- **Understanding intersectionality is essential to:**
  - Design more effective programmes and policies to improve health.
  - **Clarify the relationship between sex/gender inequalities and health inequalities**.

Merone, 2022 doi: 10.1089/whr.2021.0083

https://www.who.int/news-room/questions-and-answers/item/gender-and-health

Gender Equality Index 2021. Health. European Institute for Gender Equality.

https://www.bccic.ca/why-is-intersectionality-important-to-achieve-gender-equality/

Health inequality

- There is a growing recognition of:
  - existence of large and unacceptable inequalities in health among population groups, related in particular to sex, gender and intersectional characteristics.
  - need to understand the inequality causes.

- Healthcare professional have an ethical and professional obligation to offer the **best care to every patient regardless of sex, gender identity or, in general, minority membership** and, therefore, to eliminate health disparities.

- **What about research?**

Malmusi 2014, Doi:dx.doi.org/10.3402/gha.v7.23189

CONSORT-Equity 2017 extension and elaboration for better reporting of health equity in randomised trials

Vivian A Welch,[1,2] Ole F Norheim,[3,4] Janet Jull,[5] Richard Cookson,[6] Halvor Sommerfelt,[3,7] Peter Tugwell,[8] CONSORT-Equity and Boston Equity Symposium

- Extension to the CONSORT (Consolidated Standards of Reporting Trials) statement
- Developed by a multidisciplinary team for <u>better design and reporting of RCTs where health equity is relevant,</u> i.e.
  - evaluating an intervention focused on people experiencing social disadvantage and/or
  - exploring the difference in the effect of the intervention between two groups experiencing different levels of social disadvantage.

https://www.equator-network.org/reporting-guidelines/consort-equity/

CONSORT-equity (cont.)

Randomisation		
Sequence generation:		
8a	Method used to generate the random allocation sequence	
8b	Type of randomisation; details of any restriction (such as blocking and block size)	Report whether randomisation was stratified on PROGRESS-Plus characteristic(s)
Allocation concealment mechanism:		
9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation:		
10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding:		
11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
11b	If relevant, description of the similarity of interventions	
Statistical methods:		
12a	Statistical methods used to compare groups for primary and secondary outcomes	
12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Report details of additional analyses focused on health equity, including whether analyses to estimate heterogeneity of effects between population subgroups were done on an additive or multiplicative scale, and whether pre-specified.
Ethical concerns		
New item		Report details of ethical clearance and informed consent
Results		
Participant flow (a diagram is strongly recommended):		
13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Describe for each group, numbers of participants who were assigned, received and who were analysed across relevant PROGRESS-Plus characteristics

CONSORT-equity (cont.)

PROGRESS-Plus

PROGRESS-Plus is an acronym used to identify characteristics that stratify health opportunities and outcomes.

- **PROGRESS** refers to:
  - Place of residence
  - Race/ethnicity/culture/language
  - Occupation
  - Gender/sex
  - Religion
  - Education
  - Socioeconomic status
  - Social capital

- **Plus** refers to:

  1) personal characteristics associated with discrimination (e.g. age, disability)
  2) features of relationships (e.g. smoking parents, excluded from school
  3) time-dependent relationships (e.g. leaving the hospital, respite care, other instances where a person may be temporarily at a disadvantage)

Intersectionality characteristics

https://methods.cochrane.org/equity/projects/evidence-equity/progress-plus

Research and health inequalities related to sex and gender

In US:

Since the early 2000s funding agencies such as the National Institutes of Health (NIH) in the United States have required:

- Inclusion of women and minority groups in funded clinical research.
- Clinical trials be designed to provide information about differences by sex/gender, race, and/or ethnicity.
- Recently expanded: using ‘‘sex as a dependent variable’’ for earlier stage biological research.

https://eige.europa.eu/gender-mainstreaming/toolkits/gear/what-gender-equality-plan-gep

Research and health inequalities related to sex and gender (cont.)

In EU:

- Funding agencies are expecting researchers to consider inequalities, and in particular those related to sex/gender, in their projects (e.g. GenderNet).

- With the introduction of Horizon Europe, **Gender Equality Plans (GEPs)** are requested by the EC for participation in research programmes.

  - GEP: strategic instrument establishing priorities, objectives (and timelines), and specific measures to improve gender equality within organisations and in the field of research and innovation.

https://eige.europa.eu/gender-mainstreaming/toolkits/gear/what-gender-equality-plan-gep

In Italy:

- Primo passo In Italia verso una medicina "inclusiva":

legge 3/2018 "*Delega al Governo in materia di sperimentazione clinica di medicinali nonché disposizioni per il riordino delle professioni sanitarie e per la dirigenza sanitaria del Ministero della Salute*".

- Art. 3 "Applicazione e la diffusione della medicina di genere nel Servizio sanitario nazionale" richiede la predisposizione di «un **Piano volto alla diffusione della medicina di genere mediante divulgazione, formazione e indicazione di pratiche sanitarie che nella ricerca, nella prevenzione, nella diagnosi e nella cura tengano conto delle differenze derivanti dal genere, al fine di garantire la qualità e l'appropriatezza delle prestazioni erogate dal Servizio sanitario nazionale in modo omogeneo sul territorio nazionale**».

- Piano approvato il 13 giugno 2019.

http://www.salute.gov.it/imgs/C_17_pubblicazioni_2860_allegato.pdf

Medicina di genere

- La medicina di genere, o medicina genere-specifica, è definita da OMS come lo studio dell'influenza delle differenze biologiche (definite dal sesso) e socio-economiche e culturali (definite dal genere) sullo stato di salute e di malattia degli individui.

- **L'implementazione di un "approccio di genere" potrebbe consentire di eliminare le disuguaglianze e identificare terapie “personalizzate” in base al genere.**

Piano per la medicina di genere

- Prodotto congiuntamente dal Ministero della Salute e dal Centro di riferimento per la Medicina di Genere dell'ISS, con la collaborazione di un Tavolo tecnico-scientifico di esperti regionali sul tema e dei referenti per la medicina di genere della rete degli IRCCS, nonché AIFA e dell'AGENAS.

- Riporta obiettivi strategici, attori coinvolti e azioni previste per l'applicazione di un approccio di genere in sanità.

- Aree d'intervento previste dalla legge 3/2018:
  - percorsi clinici di prevenzione, diagnosi, cura e riabilitazione
  - formazione
  - comunicazione
  - ricerca e innovazione

https://www.epicentro.iss.it/medicina-di-genere/aggiornamenti

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  - percorsi clinici di prevenzione, diagnosi, cura e riabilitazione
  - formazione
  - comunicazione
  - **ricerca e innovazione:**
    - ***promozione e sostegno della ricerca (biomedica, farmacologica e psico-sociale) basata sulle differenze di genere***

https://www.epicentro.iss.it/medicina-di-genere/aggiornamenti

Sex and gender in medical research: examples

Sex and gender in medical research

- Some journals are considering "sex" offending and replace all instances of “sex” with “gender”.
- Up to 2010 in electronic health record systems sex marker is binary
  ➔ difficult to record experiences of transgender patients.

- Suggested approach (Clayton 2016):

Table. Suggested Approach for Reporting Demographic Characteristics of Study Participants and Outcome by Sex and Gender (N = 59)

Demographic Characteristics	
Total No.	59
Age range, y	18-90
Sex, No.[a]	
Male participant	27
Female participant	32
Gender, No.[b]	
Men	26
Women	33
Outcome, No. (%)[c]	50 (85)
Males	20 (40)
Females	30 (60)
Outcome, No. (%)[d]	
Male	20 (74)
Female	30 (94)

Sex assigned at birth

Current gender identity

Both still binary!

doi: 10.1016/j.patter.2022.100534

Clayton et al., 2016. doi:10.1001/jama.2016.16405

2646 - Sex differences in burden of adverse events in patients receiving immunotherapy

R. Miceli 1, H. Eriksson 2, A.J. Eustace 3, G. Lo Russo 1, S. Alfieri 1, M. Moksnes Bjaanæs 4, F. Pietrantonio 1, L. De Cecco 1, A. Prelaj 1, C. Proto 1, Johan Franzen 2, Deirdre McDonnell 5, Jose Javier Berenguer Pina 5, Teresa Beninato 1, Laura Mazzeo 1, Patrizia Giannatempo 1, E. Verzoni 1, J. Crown 5 , A. Helland 6

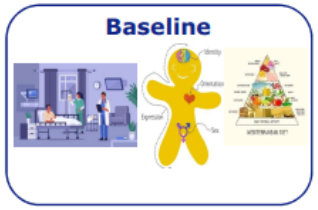
1 Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 2 Karolinska Institutet, Theme Cancer. Karolinska University Hospital-Solna, Solna, Sweden; 3 Dublin City University, Dublin, Ireland; 4 Oslo University Hospital, Oslo, Norway; 5 St Vincent's University Hospital, Dublin, Ireland; 6 Radium Hospital/Oncology, University of Oslo, Institute of Clinical medicine, Oslo, Norway

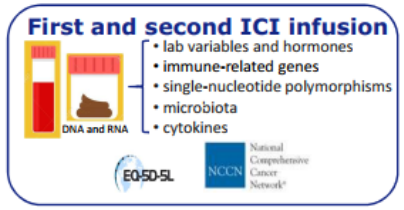
Background/Methods:

- The increasing use of Immune checkpoint inhibitors (ICIs) is associated with unique immune-related adverse events (irAEs) that can require treatment discontinuation.
- Responses are limited to patient subsets, and sex-driven differences in immune responses are proposed as potential factors contributing to disease outcome and response to ICI.
- Despite the thorough collection of irAEs data in registrational studies, sex differentiation is infrequently published.
- irAEs inequalities between female (F) and male (M) patients could also be linked to intersectional gender dimensions (psycho-social and behavioral determinants, exposure to lifestyle), and no studies have been conducted to study such association.

Methods:

- Cancer patients receiving ICIs were recruited and followed –up in a prospective observational study to find irAEs determinants.
- Collected data:
  - irAEs, treatment response, recurrence and survival.





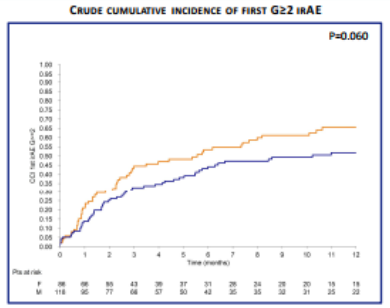
Women receiving ICIs experience a higher irAE burden and require close monitoring to avoid ICI interruption. Also, measuring irAEs cumulative load (burden) provides insights into differences between women and men patients.

G-DEFINER Project
Sponsored by: European Union's Horizon 2020 research and innovation programme under grant agreement No 741874
PI: rosalba.miceli@istitutotumori.mi.it

SCAN ME

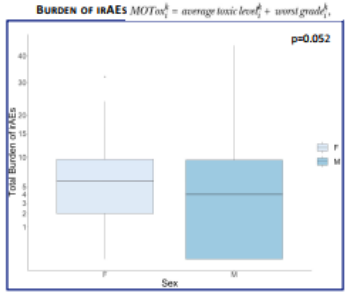
N. (%) of patients	n. irAEs	F (N=86) n. patients	n. irAEs	M (N=118) n. patients	p value
Number of irAEs per patient					0.5325
No events	--	14/86 (16.3%)	--	32/118 (27.1%)	
1 irAE	--	22/86 (25.6%)	--	25/118 (21.2%)	
2 irAEs	--	16/86 (18.6%)	--	21/118 (17.8%)	
3 irAEs	--	14/86 (16.3%)	--	14/118 (11.9%)	
4 irAEs	--	9/86 (10.5%)	--	14/118 (11.9%)	
≥5 irAEs	--	11/86 (12.8%)	--	12/118 (10.2%)	
Any grade adverse event	208	72/86 (83.7%)	246	86/118 (72.9%)	0.089
Grade 1	109	55/86 (64.0%)	145	64/118 (54.2%)	0.106
Grade 2	67	44/86 (51.2%)	73	50/118 (42.4%)	0.255
Grade 3	27	21/86 (24.4%)	23	21/118 (17.8%)	0.294
Grade 4	5	5/86 (5.8%)	3	2/118 (1.7%)	0.135
Grade 5	0	0/86 (0.0%)	2	2/118 (1.7%)	0.51
First irAE G≥2	208	72/86 (83.7%)	246	86/118 (72.9%)	0.060*
First irAE G≥3	109	55/86 (64.0%)	145	64/118 (54.2%)	0.115*
System Organ Class					
Systemic	25	20/86 (23.3%)	20	19/118 (16.1%)	0.212
Dermatologic	35	21/86 (24.4%)	43	29/118 (24.6%)	1
Rheumatic	10	8/86 (9.3%)	23	16/118 (13.6%)	0.387
Gastrointestinal	35	24/86 (27.9%)	49	28/118 (23.7%)	0.519
Opthalmic	2	1/86 (1.2%)	2	2/118 (1.7%)	1
Neurologic	4	2/86 (2.3%)	4	2/118 (1.7%)	1
Cardiac	3	3/86 (3.5%)	4	4/118 (3.4%)	1
Endocrine	46	32/86 (37.2%)	42	26/118 (22.0%)	0.019
Renal	2	2/86 (2.3%)	8	7/118 (5.9%)	0.308
Hepatic	22	17/86 (19.8%)	20	11/118 (9.3%)	0.04
Respiratory	20	12/86 (14.0%)	22	16/118 (13.6%)	1
Hematologic	4	4/86 (4.7%)	9	8/118 (6.8%)	0.765

* from cumulative incidence curves comparison.



Multivariable Fine and Gray model (applying the "sex balancing weights" and with adjustment for cancer type, ICI type, and ICI setting): p=0.078

- ICI interruption was more frequent in F patients (48.8% vs 28.0%, p=0.004), and 27.9% of F vs 11.8% of M interrupted ICI due to irAE occurrence.
- 83.7% of F developed any grade irAE vs 72.9% of M (p=0.089).
- F patients presented a higher frequency of any kind of event except for rheumatic, renal, respiratory and hematologic, that were more frequent in M.
- 12-m cumulative incidence of first G≥2 irAE was 65.6% in F vs 51.8% in M (p=0.060).
- Also, irAE burden (taking into account irAEs number and grade) was higher in F than M (median=6 vs 4, p=0.052).



Multivariable quantile regression analysis: p=0.050

Future Directions for Research:

- Design prospective clinical studies to evaluate the effectiveness of interventions directed to reduce health inequalities (irAEs, therapy/interventions efficacy) between women and man patients.
- Implement personalized approaches to disease prevention and treatment, taking into account disease and individual characteristics, like psycho-socio-economical features and quality of life.

These research findings could provide policy makers with information useful to implement gender specific guidelines into the administration of ICI therapy.

Clinicaltrials.gov: NCT04435964. ENCePP: EUPAS31282

GENDER·NET Plus
Promoting gender equality in H2020 and the ERA

DOI: 10.1200/JCO.2023.41.16_suppl.2646

Key features significantly different between F and M populations

N. (%) of patients	Overall 204	F 86	M 118	P
Personal sense of being				
Woman	82 (40.2)	82 (95.3)	0 (0.0)	--
Man	116 (56.9)	2 (2.3)	114 (96.6)	
Not reported	6 (2.9)	2 (2.3)	4 (3.4)	
Marital status				**0.005**
Couple	123 (60.3)	**43 (50.0)**	**80 (67.8)**	
Not couple	57 (27.9)	30 (34.9)	27 (22.9)	
Divorced/Separated	18 (8.8)	8 (9.3)	10 (8.5)	
Never married	18 (8.8)	6 (7.0)	12 (10.2)	
Widowed	21 (10.3)	**16 (18.6)**	**5 (4.2)**	
Not reported	24 (11.8)	13 (15.1)	11 (9.3)	
Living arrangement				0.156
Alone	42 (20.6)	**22 (25.6)**	**20 (16.9)**	
Not alone	140 (68.6)	53 (61.6)	87 (73.7)	
Children	11 (5.4)	7 (8.1)	4 (3.4)	
Other	3 (1.5)	1 (1.2)	2 (1.7)	
Parents	3 (1.5)	1 (1.2)	2 (1.7)	
Parents+sibl	1 (0.5)	1 (1.2)	0 (0.0)	
Partner	90 (44.1)	**29 (33.7)**	**61 (51.7)**	
Partner+children	32 (15.7)	14 (16.3)	18 (15.3)	
Not reported	22 (10.8)	11 (12.8)	11 (9.3)	
Income				0.220
≤2000	18 (8.8)	9 (10.5)	9 (7.6)	
>2000, ≤3000	50 (24.5)	21 (24.4)	29 (24.6)	
>3000, ≤5000	37 (18.1)	14 (16.3)	23 (19.5)	
>5000	53 (26.0)	**17 (19.8)**	**36 (30.5)**	
Not reported	46 (22.5)	25 (29.1)	21 (17.8)	
BMI				**0.009**
Underweight	10 (5.2)	**9 (11.5)**	**1 (0.9)**	
Healthy Weight	86 (44.8)	32 (41.0)	54 (47.4)	
Overweight	72 (37.5)	**26 (33.3)**	**46 (40.4)**	
Obesity	24 (12.5)	11 (14.1)	13 (11.4)	
W/H not reported	12	8	5	
Mediterranean diet score				0.052
Mean (SD)	5.95 (2.08)	6.31 (2.12)	5.69 (2.01)	
Not reported	30 (14.7)	13 (15.1)	17 (14.4)	
Physical activity				0.218
Inactive	19 (9.3)	9 (10.5)	10 (8.5)	
Very low int.	76 (37.3)	**35 (40.7)**	**41 (34.7)**	
Low int.	57 (27.9)	20 (23.3)	37 (31.4)	
Moderate int.	30 (14.7)	14 (16.3)	16 (13.6)	
High int.	6 (2.9)	0 (0.0)	6 (5.1)	
Not reported	16 (7.8)	8 (9.3)	8 (6.8)	

Expected correlation between living arrangement and marital status

N. (%) of patients	Overall 204	Not couple 57	Couple 123	Not reported 24	p
Living arrangement					<0.001
Alone	42 (20.6)	37 (64.9)	0 (0.0)	5 (20.8)	
Children|parents|other	18 (8.8)	14 (24.6)	1 (0.8)	3 (12.5)	
Partner+-children	122 (59.8)	1 (1.8)	**119 (96.7)**	2 (8.3)	
Not reported	22 (10.8)	5 (8.8)	3 (2.4)	14 (58.3)	

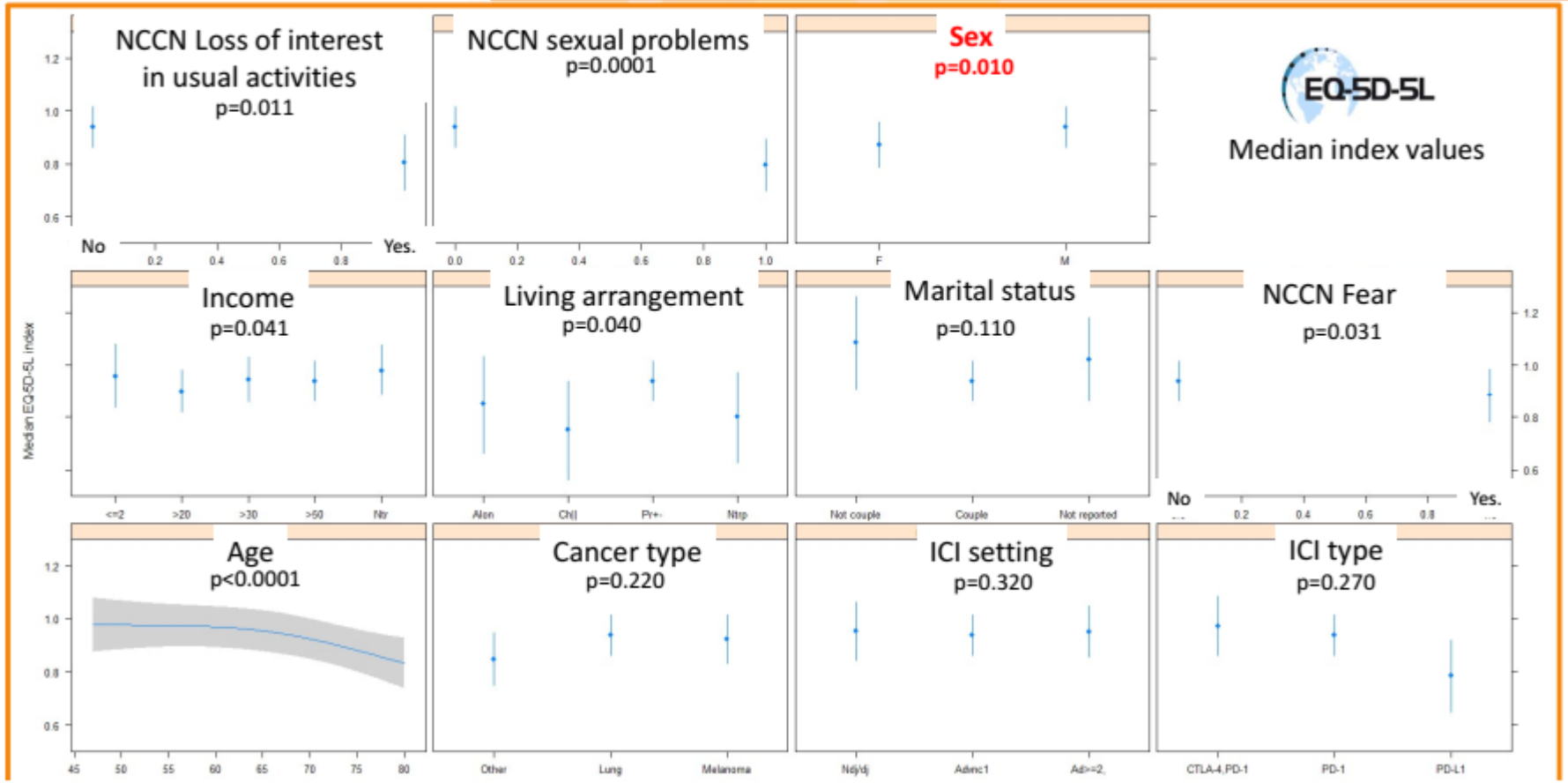
Key QoL features significantly different between F and M populations

Dimensions: health today, Self care (washing/dressing), Usual activities, Pain/discomfort, Anxiety/depression

Dimensions: Distress thermometer; Problems: Practical, Family, Emotional, Spiritual/religious, Physical.

	Overall	F	M	p
N. (%) of patients	**179**	**75**	**104**	
NCCN emotional problems:				
Fear	36 (20.1)	22 (29.3)	14 (13.5)	0.015
Loss of interest in usual activities	33 (18.4)	21 (28.0)	12 (11.5)	0.009
Sexual	20 (11.2)	1 (1.3)	19 (18.3)	0.001
Genitourinary diseases	10 (4.9)	0 (0.0)	10 (8.5)	0.006
EQ-5D-5L				
Anxiety/depression (mean (SD))	1.82 (0.87)	2.00 (0.90)	1.69 (0.83)	0.019
Pain/discomfort (mean (SD))	1.94 (0.99)	2.15 (1.14)	1.80 (0.85)	0.020

Sex is independently associated with EQ-5D-5L QoL index at multivariable analysis



OncoGender
PROMOTING INCLUSION IN ONCOLOGY

The Project, led by the Fondazione IRCCS Istituto Nazionale dei Tumori di Milano (INT) and the Associazione Italiana di Oncologia Medica (AIOM), involves researchers from different scientific Institutions:

Name	Surname	Institution
Patrizia	**Amantini**	ELMA RESEARCH S.r.l., Milano
Rossana	**Berardi**	Università Politecnica delle Marche, Azienda Ospedaliero-Universitaria Ospedali Riuniti di Ancona, Ancona
Matteo	**Lambertini**	U.O. Clinica di Oncologia Medica, IRCCS Ospedale Policlinico San Martino, Genova; Department of Internal Medicine and Medical Sciences (DiMI), School of Medicine, University of Genova, Genova, Italy
Alberto Giovanni	**Leone**	Fondazione IRCCS Istituto Nazionale dei Tumori di Milano
Silvia	**Marsoni**	Precision Oncology, IFOM-The FIRC Institute of Molecular Oncology, Milano
Massimo	**Massagrande**	ELMA RESEARCH S.r.l., Milano
Rosalba	**Miceli**	Fondazione IRCCS Istituto Nazionale dei Tumori di Milano
Federica	**Morano**	Fondazione IRCCS Istituto Nazionale dei Tumori di Milano
Filippo	**Pietrantonio**	Fondazione IRCCS Istituto Nazionale dei Tumori di Milano
Elena	**Ripamonti**	ELMA RESEARCH S.r.l., Milano
Dario	**Trapani**	European Institute of Oncology, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Milan, Italy; Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts
Francesca	**Zenesini**	ELMA RESEARCH S.r.l., Milano

- Transgender and gender-diverse individuals (TGD) face challenges, including barriers to health care access and inequities in treatment, that may influence their cancer risk and outcomes.

- **A review was conducted focusing on primary and secondary prevention and epidemiology of cancer, barriers to health care services, and health care practitioners' knowledge about specific issues pertaining to TGD individuals.**

doi:10.1001/jamaoncol.2022.7173

Findings:

- Transgender and gender-diverse people:
  - had high **prevalence** of tobacco and alcohol use and high rates of infection with HPV and HIV.
  - were less likely to adhere to **cancer screening programs** and had a higher incidence of HIV- and HPV-associated cancers.
- **Social and economic determinants** seemed to drive these disparities in risk factors and outcomes.
- **Barriers** met by TGD persons in accessing oncology services:
  - discrimination and discomfort caused by gender-labeled services,
  - stigma, lack of cultural sensitivity of health care operators.
- **Lack of knowledge** about gender minorities' health needs among health care practitioners.

Barriers to health care access and inequities in treatment may influence TGD cancer risk and outcomes

doi:10.1001/jamaoncol.2022.7173

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

OncoGender PROMOTING INCLUSION IN ONCOLOGY

ORIGINAL RESEARCH

Cancer care in transgender and gender-diverse persons: results from two national surveys among providers and health service users by the Italian Association of Medical Oncology

A. G. Leone[1†], R. Miceli[2†], D. Trapani[3,4], M. Massagrande[5], F. Morano[1], S. Marsoni[6], N. La Verde[7], R. Berardi[8], R. Casolino[9], M. Lambertini[10,11], D. Dalu[7], M. Di Maio[12], G. D. Beretta[13], F. Perrone[14], S. Cinieri[15] & F. Pietrantonio[1*]

DOI: 10.1016/j.esmoop.2023.101578

Questionnaire for oncology professionals

Aims: to gain insights into knowledge on gender and TGD issues, and into professionals' attitudes and experience in treatment and follow-up of TGD cancer patients.

Questions:

- Personal characteristics and other information on professional role.
- Knowledge about TGD people health issues.
- Attitudes and professional experiences with TGD cancer patients.
- Specific training needs.
- Suggestions for improving cancer health services for TGD people.

DOI: 10.1016/j.esmoop.2023.101578

Rosalba Miceli , Fondazione IRCCS Istituto Nazionale dei Tumori, Milano

Questionnaire for TGD people

Aims: to gain insights into TGD health needs and gender-related barriers to using health care services.

Questions:

- Personal characteristics and social context; presence of chronic diseases, including cancer.
- Discrimination, harassment and violence experiences due to their sexual orientation and gender identity, with particular reference to health care services.
- Global evaluation of health care services and suggestions for improving health care services.
- Channels used to collect health-related information.

DOI: 10.1016/j.esmoop.2023.101578

Rosalba Miceli , Fondazione IRCCS Istituto Nazionale dei Tumori, Milano

Oncology professionals communication and treatment attitudes towards gender identity

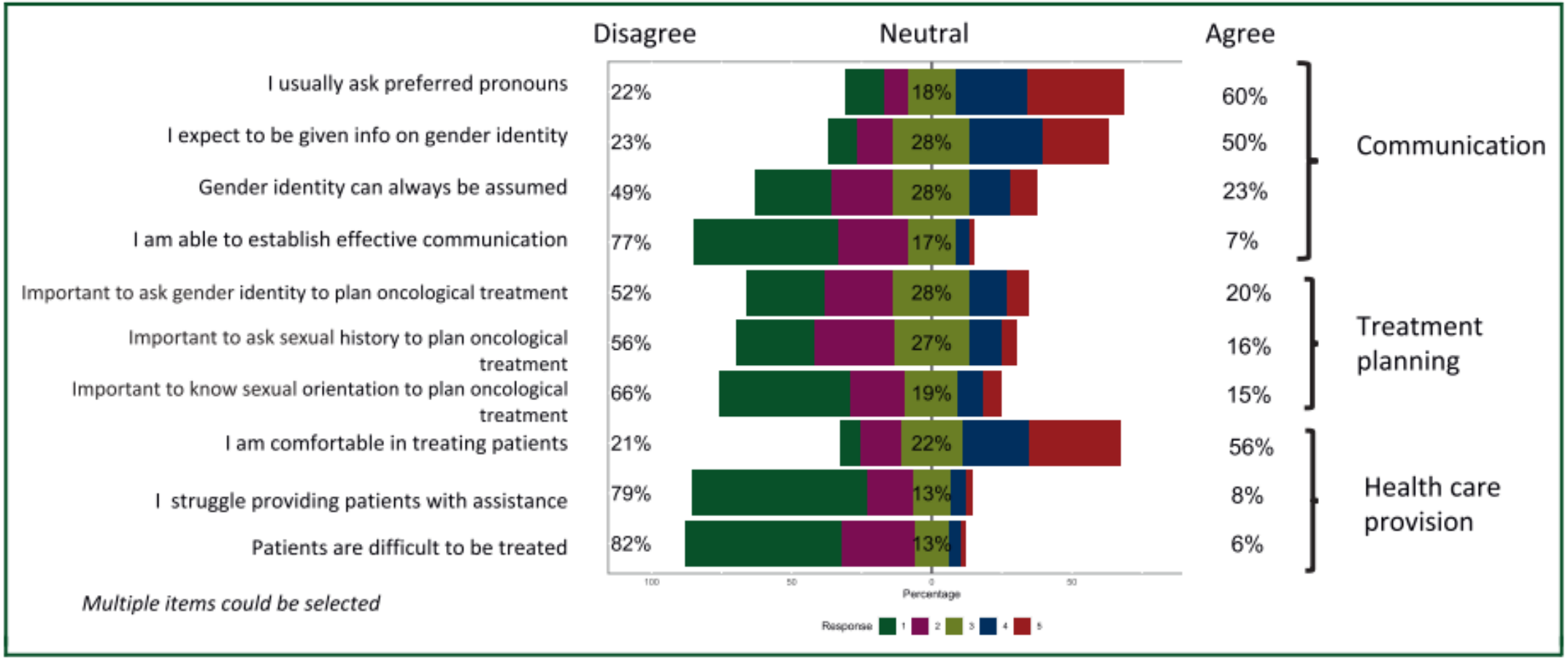


Figure 3. OHP attitudes toward TGD patients.
OHP, oncology health care providers; TGD, transgender and gender-diverse.

DOI: 10.1016/j.esmoop.2023.101578

Forms of discrimination by oncology professionals reported by TGD patients

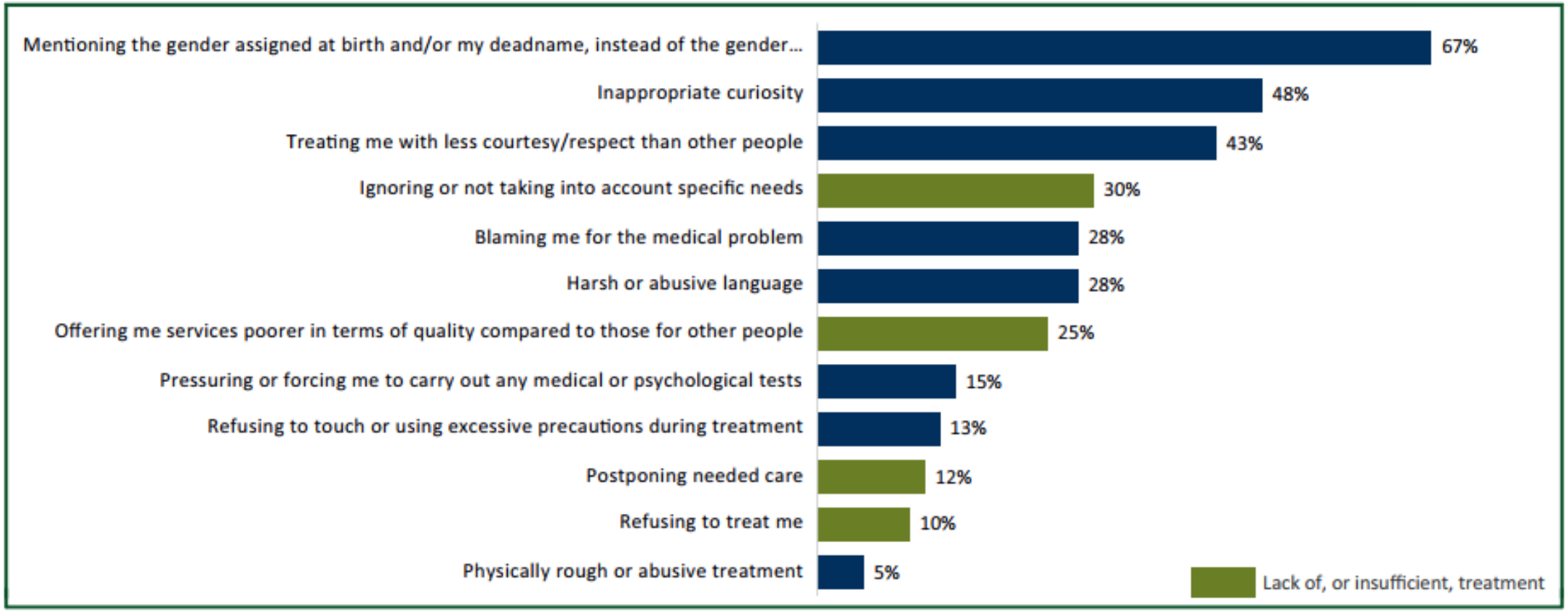
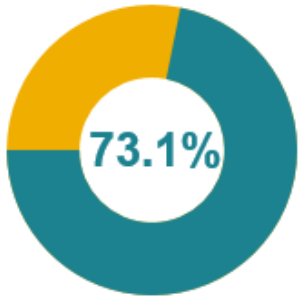


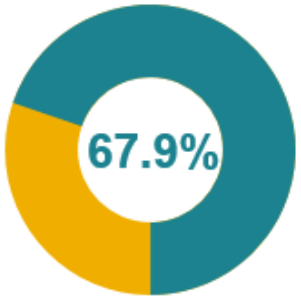
Figure 5. Forms of discrimination by health care providers reported by TGD respondents as patients.
TGD, transgender and gender-diverse.

DOI: 10.1016/j.esmoop.2023.101578

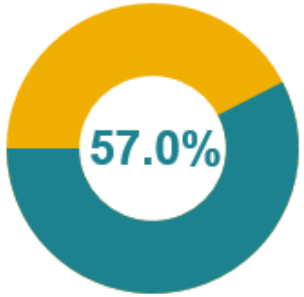
Possible consequences of discriminatory or negative attitudes from some health care professionals for TGD persons



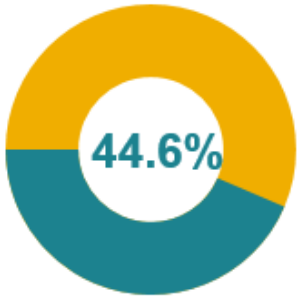
Patients don't participate to cancer screening or prevention programs



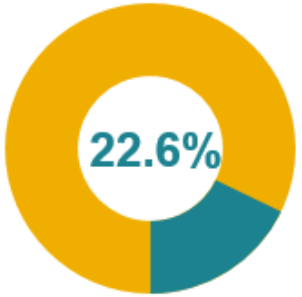
Patients address their oncologic problems to healthcare services with sensible delay



Patients don't trust health care professionals



Patients don't address their oncologic problems to healthcare services



Patients don't receive appropriate oncologic treatments

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Oncologia
La salute declinata su sesso e identità di genere
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FONDAZIONE AIOM

Position paper of the Italian Association of Medical Oncology on health disparities among transgender and gender-diverse persons: the ASSISI Statements

Alberto Giovanni Leone, Raffaella Casolino, Dario Trapani, Rosalba Miceli, Massimo Massagrande, Federica Morano, Nicla La Verde, Davide Dalu, Rossana Berardi, Silvia Marsoni, Matteo Lambertini, Bianca Iula, Eva Carieri, Manlio Converti, Massimo Di Maio, Giordano Domenico Beretta, Francesco Perrone, Saverio Cinieri, Filippo Pietrantonio

Submitted on European Journal of Cancer

- Promote SOGI data collection and inclusion of TGD patients in cancer clinical trials
- Use inclusive language and respect gender identity
- Create safe and welcoming environments for TGD cancer patients
- Improve cancer screening guidelines referred to TGD individuals
- Provide education and training to oncology HCPs about TGD health issues
- Provide information to TGD persons, especially youth, about modifiable cancer risk factors
- Coordinate gender affirming care and cancer care on a case by case basis
- Provide psychological support during the whole cancer care continuum
- Address social determinants of health
- Collaborate with LGBTQIA+ organizations

Conclusions: inclusion of sex and gender in clinical research

- Both in observational studies and in clinical trials, accurate and adequate planning is needed to collect variables related to biological attributes, gender identities and behaviors of women and men, intersectional characteristics (e.g. PROGRESS-Plus).

- In the absence of planning it is very difficult to extrapolate ex post the results obtained from the analysis of aggregated data.

- Pay attention to sex/gender in all phases of research: study design, processing of the data collected, interpretation of the results, communication of research results.

- General principles to be followed in planning and data processing phases of clinical trials: Tannenbaum et al., McGregor et al.,], SAGER guidelines.

Tannenbaum,. 2016, Doi 10.1186/s12874-016-0247-7.
McGregor 2016, doi: 10.1186/s13293-016-0099-1.
Heidari, SAGE, 2016 doi: 10.1186/s41073-016-0007-6


GENDER·NET Plus
Promoting gender equality in H2020 and the ERA
Italian Ministry of Health,
Swedish Research Council,
Irish Research Council,
Research Council of Norway
The audience
for attention
European Union's Horizon 2020
research and innovation
programme, grant agreement
No 741874
THANK YOU

Any questions