

CONQUERING CANCER: MISSION IMPOSSIBLE... UNLESS A GENDER DIMENSION IS TAKEN INTO ACCOUNT

What gender dimension means and why it is important for cancer R&I

A gender dimension in the context of Horizon Europe missions refers to the **integration of sex/gender analysis methods in the research content**. It aims to stimulate excellence in science and technology by “fixing the knowledge”. “Sex” and “gender” are two distinct terms that should not be used interchangeably.

“**Sex**” refers to the biological characteristics of beings, whether female, male, or intersex. This involves different levels of expression: genes, gametes, morphology (primary and secondary sex characteristics).

“**Gender**” refers to socio-cultural processes that shape behaviours, preferences, values, products, technologies, knowledges, and how individuals and groups interact with their environment. Importantly, the two terms interact with and influence each other. A sex and gender perspective in health and cancer R&I is crucial as it focuses on people’s circumstances in relation to their economic, social, cultural and working environments. Analysing **factors intersecting with sex and gender** is key to avoid overlooking or overemphasising sex or gender differences (e.g. age, comor-

bidity, disabilities, environment, ethnicity, geography, religion, sexual orientation, socioeconomic status, etc.).

As Gendered Innovations¹ presents it: **“[s]ex and gender can influence all stages of research or development processes, from strategic considerations for establishing priorities and building theory to more routine tasks of formulating questions, designing methodologies, and interpreting data. Many pitfalls can be avoided—and new ideas or opportunities identified—by designing sex and gender analysis into research from the start. Sex and gender anal-**

1 | Gendered Innovations (a collaboration between Stanford University and the European Commission): <https://genderedinnovations.stanford.edu/methods-sex-and-gender-analysis.html>

This initiative provides with a wide range of terms explanation, methods, checklists and case studies in science, health & medicine, engineering and environment with regards to the integration of a gender dimension in research and innovation. We highly recommend consulting the Health & Medicine Checklist to incorporate sex and gender analyses: http://genderedinnovations.stanford.edu/methods/health_med_checklist.html

ysis work alongside other methodologies in a field to provide yet further “controls” (or filters for bias) providing critical rigor in science, medicine, and engineering research, policy, and practice”.

An emphasis has been made on the significant inequities “in access to and quality of cancer prevention, screening, early detection, treatment, care and survivorship support among Member States and among different social groups and demographic groups” (p. 17, recommendation 9), mentioning age and **gender**. That is why **the integration of sex/gender analysis methods as a 14th cross-cutting recommendation** in all the Mission’s areas is necessary. Below we discuss differences in the incidence and mortality, development, diagnosis and responses to therapy as well as the quality of life and survivorship.

Examples of how sex and gender interact in relation to cancer

Incidence and mortality²: women and men not only differ in the fact that they have sex-specific cancers such as uterine cancers or prostate cancers but the incidence and mortality of various non-sex specific cancers are associated with these differences:

- Colorectal cancer: “women developed right-sided malignancy while men manifested more on the left side (Kim et al., 2015). Right-sided colon cancer is associated with a higher severity compared with left-sided disease (Kim et al., 2015). The cause of disparity in location might be due to differences in estrogen level between men and women.”
- Breast cancer: 99% of breast cancers are

found in females. This leaves 1% of males and transgender men and women whose research needs must be addressed too, as their incidence and characteristics may differ from cisgender people³.

- Melanoma mortality: “Men had a 34% higher risk of death compared with women (Crocetti et al., 2015)”.
- Genetic and molecular sex differences with the example of the bladder cancer: “Men show a higher incidence of bladder cancer than women (Siegel et al., 2016)[...] It was reported that the His213 allele genotype *SULT1A1* significantly decreased the risk of bladder cancer exclusively in women (Zheng et al., 2003)”.
- Sex hormones: estrogen seems to have a protective role in cancers such as colon cancer or leukaemia. However, “[e]strogen is linked closely to a higher rate of thyroid cancer development in women (Lee et al., 2005; Dorak and Karpuzoglu, 2012)”.

Efficacy and toxicity of treatments⁴: 5-FU, Paclitaxel, Doxorubicin, Cisplatin, Bevacizumab, Rituximab anti-cancer agents all present sex differences in efficacy and toxicity. This is linked to the fact that research involving animal model and clinical trials has been almost only male-oriented.

Gendered lifestyles:

- Colorectal cancer⁵: diet, physical activity (PA) and obesity are three factors that play a role in the incidence of colorectal cancer. There are gender-specific responses to these as women tend to have better diets, drink less alcohol and report less physical activity than men.

2 | Kim, H. I., Lim, H., & Moon, A. (2018) Sex Differences in Cancer: Epidemiology, Genetics and Therapy. *Biomolecules & therapeutics*, 26(4), 335–342.

3 | de Blok, C.J.M. et al. (2019) Breast cancer risk in transgender people receiving hormone treatment: nationwide cohort study in the Netherlands. *BMJ*, 365: l1652.

4 | Kim, H. I., Lim, H., & Moon, A. (2018) *Ibid*.

Moreover, obesity, and especially weight gain in the waist and abdominal area has a stronger negative impact for men than for women.

- Smoking and lung cancer⁶: Cancer rates in women increased after they started smoking in larger numbers. Once smoking and cancer were linked, the overall smoking rate decreased, revealing that non-smoking women were more at risk at developing lung cancer than men (20% of death cases for women vs less than 15% for men).

Quality of life and gender: women and men can at times experience cancer and treatments in different ways, leading to a different quality of life (QOL).

- Cancer pain and QOL⁷: among women, QOL was significantly predicted by pain intensity and by depression, whereas among men, depression was the only symptom found to predict QOL.
- Colorectal patients' QOL⁸: gender differences were shown in illness symptoms and chemotherapy treatment effects where women reported body image, abdominal pain and dry mouth as the symptoms affecting their QOL while men reported fecal incontinency, sexual impotency and sexual arousal.

Survivorship: gender norms and social expectations of masculinity and femininity

shape how individuals experience illness and perform the roles of patient and survivor.

- Lymphoma survivors⁹: women tend to report greater personal posttraumatic growth and positive outcomes of cancer on their lives while men tend to deny growth and positive outcomes to maintain masculinity, preventing them from experiencing the benefits of growing from difficult experiences.
- Women continue to be primary caregivers and are affected by their relatives' cancer experience.

Recommendations on how to integrate a gender dimension in Framework conditions for Missions, Mission Work Programmes, project portfolios and evaluation

- Include sex and gender analysis in animal studies and clinical trials as a default requirement and if sex and gender are not relevant, an explanation must be provided why not. Sex and gender must be included in the entire research cycle from research design, methodology, to data interpretation and communication. It should be noted that populations understudy can vary depending on the cancer researched whether it is sex-specific or mixed-sex.
- Include the integration of sex and gender in the research proposal as part of the evaluation process.

5 | Conti, Lucia, Manuela Del Cornò, and Sandra Gessani (2020) Revisiting the Impact of Lifestyle on Colorectal Cancer Risk in a Gender Perspective. *Critical Reviews in Oncology/Hematology*, 145: 102834.

6 | Chloe Bird, video "Sex & Gender Influences on Health & Disease". Available at National Institutes of Health Health website.

7 | Pud, Dorit (2011) Gender Differences in Predicting Quality of Life in Cancer Patients with Pain. *European Journal of Oncology Nursing: The Official Journal of European Oncology Nursing Society*, 15(5): 486–91.

8 | Trinquinato, Isadora et al. (2017) Gender Differences in the Perception of Quality of Life of Patients with Colorectal Cancer. *Investigación y Educación en Enfermería*, 35(3): 320–29.

9 | Powroznik, Karen, Irena Stepanikova, and Karen Cook (2018) Growth from Trauma: Gender Differences in the Experience of Cancer and Long-Term Survivorship. *Gender, Women's Health Care Concerns and Other Social Factors in Health and Health Care (Research in the Sociology of Health Care)*, 36: 17–36.

- Include gender scholars in the relevant research domain in the research team.
- Include gender experts among Mission project evaluators and ensure gender balance among evaluators.
- Strive for gender balance in research teams.
- Include in Work Programmes research projects that address knowledge gaps in cancer research (e.g. by focusing on only women or men, or trans women and men, or intersex individuals, etc.). Projects filling the data gaps should receive equal attention as studies that have a gender-balanced sample.
- Include gender indicators in Mission monitoring and evaluation and among key performing indicators.
- Using new technologies such as AI and machine learning to improve data gathering, interpretation, and medical protocol/ treatment decisions was mentioned in several recommendations (e.g. 4, 6, 12). This will be beneficial to the whole society only if the dataset is free from gender bias¹⁰.
- Fund research that focuses on a gender analysis of quality of life of cancer patients, survivors and their carers while recognising that women are primary carers worldwide.

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