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Deciphering the sex gap in global life expectancy: the impact of female-specific cancers 1990–2019

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Abstract

Background: Females live longer than males, which results in a sex gap in life expectancy. This study examines the contribution of female cancers to this differential by world region and country 1990-2019 with special focus to the 15-69 age group.

Methods: Cause-specific mortality data for 30 cancers, including four female-specific cancers from 238 countries and territories was retrieved from the Global Burden of Disease Study 2019. Using life table techniques and demographic decomposition analysis, we estimated the contribution of cancer deaths to the sex gap in life expectancy by age and calendar period.

Results: At ages 15-69, females had a higher life expectancy than males in 2019. Countries with the largest sex gaps or the largest female advantage in life expectancy were in Eastern Europe and Northern Asia, Latin America and Southern Africa. In contrast, countries with the smallest sex gaps were mainly located in Northern Africa, Northern America, and Northern Europe. The contribution of female-specific cancers to sex gaps in life expectancy were largely negative, ranging from -0.15 years in the Western Pacific to -0.26 years in the Eastern Mediterranean Region, implying that the disproportionately higher premature cancer mortality among females contributed to a reduction in the female life expectancy advantage.

Conclusion: Female-specific cancers are important determinants of sex gaps in life expectancy. Their negative impact on life expectancy at working and reproductive age groups has far-reaching consequences for society. Increasing the availability and access to prevention, screening, timely diagnosis, and effective treatment can reduce this gap.

Keywords: cancer, life expectancy, sex disparity, breast cancer, cervical cancer

Background

Females live on average longer than males, which results in a sex gap in life expectancy that favours females. This sex gap has been linked to multiple determinants that explain higher mortality from various diseases including cancer in males compared with females. Previous studies have mainly focused on the determinants of (higher) mortality among males, for instance by assessing broad groups of diseases,^{1–3} lifestyles with marked gender components such as smoking,^{4–6} or biological reasons such as hormonal factors.^{7,8}

Based strictly in biological factors, adult males should experience only a slightly higher mortality than females that would translate in around one year of life expectancy difference.⁷ However, in the majority of high and middle-income countries, sex-gaps in life expectancy are well above this level, being higher than 10 years in countries like Armenia, Russia and Belarus.⁹ Therefore, reducing these life expectancy differences has been seen as a desirable aim in such settings.^{10,11} On the other hand, many countries with low income levels have shown very low sex-gaps as in Nigeria, Togo and Tokelau, where differences are lower than two years.⁹ These smaller sex gaps in life expectancy in countries of the African region have been associated with greater gender inequality,^{12–14} though others argued that it could be hiding overall poor health in females compared to males.

Only a few empirical studies have focused on female-specific determinants and causes of death to explain the sex gap in life expectancy. Such analyses will allow assessment of the role of risk behaviour such as smoking, which is highly related to lung cancer¹⁵ and the role of health care system which is highly related to outcomes and deaths for females-specific cancers.¹⁶ Moreover, female-specific cancers show a distinct age pattern that affects a relatively younger population,¹⁷ which may have an important impact on life expectancy and wider societal consequences. The few studies measuring the role of female-specific cancers in the sex gap in life expectancy estimated that these cancers contributed to decreasing the gap by 0.4 to 0.7 years in specific regions such as China, South Korea and Sweden.^{18–21} However, a comprehensive assessment of the role of female-specific cancers – compared to other cancers – to the sex gap on life expectancy in a global scale is still largely missing.

Our aim is to assess the role of all cancers and female-specific cancers on the sex gaps in life expectancy at birth and between 15 and 69 years across world regions and countries.

Methods

Data sources

We retrieved data from the Global Burden of Diseases Study (GBD) 2019 by 5-year age group, sex, cancer-specific cause of death and all-cause mortality rates for 204 countries and territories worldwide, and for the six WHO regions (African, Eastern Mediterranean, European, the Americas, South-East Asia and Western Pacific) over the period 1990–2019.^{22–25} Cancer mortality causes were grouped into four female-specific cancers (breast, cervical, ovary and corpus uterine), five major cancers (colorectal, liver, stomach, lung, and prostate); and a remaining group for other cancers (see Supplementary Table 1 for International Classification of Diseases codes). For the sake of simplicity, we included male breast cancer within breast cancer, although defined it as female-specific: females represent the great majority of breast cancer deaths (97.4% of all breast cancer deaths”).

Analyses

We estimated the life expectancies at birth and the truncated life expectancies between ages 15 and 69 using conventional life table methods.²⁶ The age group 15–69 was chosen based on the definition of premature mortality from the United Nations Sustainable Development Goals,²⁷ and in this paper we refer to it as “working” and “reproductive ages” due to the large contribution of this group to the formal and informal working economy, which includes family care and home-work activities. Sex gaps in life expectancies at birth and between the ages of 15 and 69 were decomposed into age- and cause-specific components for each country-year population. This was done using the standard demographic decomposition method developed by Andreev et al.²⁸ In brief, we first decomposed the differences in life expectancy between females and males into the contribution of each age-specific group. Second, we disentangled the contribution of causes of death within each age group using the cause-specific share of the sex gap in all-cause mortality. Finally, we aggregated the results for all ages and the 15–69 age group to provide estimates for both age groups. See Supplementary Material for further detail.

Sex gaps in life expectancies were calculated by subtracting males’ to females’ life expectancies; and the contribution of specific causes to sex gaps in life expectancy is shown in Figures 1, 2, and 4. These figures should be interpreted as follows: positive values (e.g. 0.5 years) indicate that females experience lower mortality and higher life expectancy (by 0.5 years/6 months) compared with males. Negative values (e.g. -0.5

years) imply the opposite, i.e. females have higher mortality and a shorter life expectancy compared with males.

Sensitivity analyses

We performed a secondary, in-depth analysis using recorded or registered data from the countries for which such data are available (<https://gco.iarc.fr/overtime/en>). We selected 12 countries for which we have cancer registry data for the years 2000 and 2019, representative of different world regions and of the WHO regions we used in the paper: Argentina, Australia, Canada, Costa Rica, Ecuador, Georgia, Israel, Japan, Kyrgyzstan, Poland, Singapore, South Africa, Spain and Uruguay. We replicated the analysis using these data and compared the results with our main results (Supplementary Figure 1).

Results

Sex gaps in life expectancy and the contribution of cancer in 2019: Age-profiles

Life expectancy at birth for females in 2019 was higher compared with males in all world regions (Figure 1), ranging from 2.6 years in the Eastern Mediterranean region to 6.4 years in the European region. Total cancers contributed positively to the sex gaps in life expectancy, i.e. the relatively higher cancer-specific mortality of males contributed to widening the female life expectancy advantage. Specifically, the total cancer contribution to life expectancy difference in males compared with females ranged from 0.1 years in the African and the Eastern Mediterranean Regions to 1.8 years in the Western Pacific Region. In Europe and Western Pacific Regions, cancer explained about 25% of the sex gap in life expectancy (1.5 out of 6.4 years and 1.8 out of 6.3 years, respectively). At working and reproductive age groups – particularly up to age 50 years – however, the cancer contribution was smaller or even negative, meaning in the latter case that females had higher cancer mortality compared with males (Western Pacific Region is the exception). This implies that cancers at these ages contributed to a reduction in the sex gap in life expectancy, narrowing of the female life expectancy advantage.

<Figure 1 here>

Most cancer types contribute to widening the sex gap in life expectancy (i.e. higher mortality in males compared with females) (Figure 2). For example, lung cancer widens the sex gap in life expectancy, ranging from 0.1 years in the African Region to 0.7 years in the European Region. As expected, however, female-specific cancers' contribution to the sex gap in life expectancy displayed negative values (narrowing the sex gap), ranging from -0.4 years in the Western Pacific Region to -0.7 in the Region of the Americas. In all regions except Europe and the Western Pacific, the contribution of female-specific cancers cancelled out the male's life expectancy disadvantage from lung cancer. Out of all four female-specific cancers, breast cancer was the highest contributor in all regions except in Africa, where cervical cancer was as prominent as breast cancer. Remarkably, the impact of female-specific cancers on the sex gap in life expectancy was relatively higher during working and reproductive ages.

<Figure 2 here>

Sex gaps in life expectancy, the contribution of cancer to the sex gap in life expectancy (15–69 ages) and the contribution of female-specific cancers to sex gaps in life expectancy (15–69 ages)

Similar to life expectancy and its difference by sex at birth, sex gaps in life expectancy between the ages of 15 and 69 were positive in almost all countries (i.e. females have higher life expectancy and lower mortality compared with males – See Figure 3a). Countries with the largest sex gaps or with the largest female advantage in life expectancy were located in Eastern Europe and Northern Asia, Latin America and Southern Africa (e.g., 5.4 years in Ukraine, 4.0 years in Mongolia, 2.6 years in Venezuela and Brazil and 3.0 years in Namibia). In contrast, countries with the smallest sex gaps were mainly located in Northern Africa, Northern America, and Northern Europe (e.g., 0.5 years in Morocco, 0.8 years in Canada and 0.6 years in Norway).

Total cancer mortality contribution to the sex gap in life expectancy between ages 15 and 69 was positive in most European countries (0.38 years in Ukraine), and East Asia (0.28 years in China), i.e., widening the life expectancy difference between males and females (Figure 3b). In contrast, total cancer mortality contributed to a reduction on the sex gap in life expectancy in most central and south American countries (e.g., -0.29 years in Bolivia), in African countries (e.g., 0.18 years in Zimbabwe), and in most west and south-east Asian countries (e.g., -0.18 years in Indonesia).

The contribution of female-specific cancers to the sex gap in life expectancy between ages 15 and 69 was highest in Africa and the Eastern Mediterranean Region (e.g., -0.45 years in Pakistan; -0.37 years in Eritrea) (Figure 3c). In contrast, the contribution of

female-specific cancers in this age-group was lowest in the European and Western Pacific Regions (e.g., -0.13 years in Switzerland and China).

<Figure 3 here>

Contribution of cancer to the sex gap in life expectancy (ages 15–69) over time (1990–2019)

In all regions and across all analyzed years, female-specific cancers contributed to the narrowing of the sex gap in life expectancy between ages 15 and 69 of at least 0.15 years (-8.6%) in the Western Pacific Region in 2019 and up to 0.26 years (-22.8%) in the Eastern Mediterranean Region in 2019 (Figure 4). Over the period 1990–2019, the sex gap in life expectancy between ages 15 and 69 increased in Africa, South-East Asia and the Western Pacific Region, decreased in Europe and the Americas Region, and stagnated in the Eastern Mediterranean Region. In Europe and in the Americas Regions, in which female-specific cancer mortality was the highest in 1990, the female-specific cancer contribution to sex gap in life expectancy declined. This decline was mainly driven by a reduction in breast cancer mortality. In the other regions, in which female-specific cancer mortality in 1990 was lower, the female-specific cancer contribution to the sex gap in life expectancy increased over time. For example, in the Eastern Mediterranean Region female-specific cancers contribution to the sex gap in life expectancy increased from -0.18 years to -0.26 years, causing a decrease in female life expectancy advantage, which is driven by increasing mortality from breast and ovarian cancer. Interestingly, in 2019 the contribution of cervical cancer to the sex gap in life expectancy between ages 15 and 69 ranged from -0.12 years in the African Region to -0.04 years in the European Region, meaning that it contributed to the narrowing of the sex gap in life expectancy. Cervical cancer's contribution to the sex gap in life expectancy has remained relatively stable across all world regions over the last three decades, albeit at different levels (e.g. in 2019, -0.12 years in the African Region or -0.04 years in European Region).

The contribution of non-female-specific cancers to the sex gap in life expectancy decreased over time in both Europe and the Americas Regions. For example, lung cancer mortality contributions in Europe declined from 0.22 years in 1990 to 0.09 years in 2019, and in the Americas from 0.08 years to 0.02 years. In other words, the female life expectancy advantage is partially reduced due to changing mortality trends in lung cancer by sex, i.e. declining in males and increasing in females. In other world regions, non-female-specific cancers have contributed to increasing or stagnating the difference in life expectancy between females and males. Detailed results on the contribution of

each specific cancer on sex gaps in life expectancy by countries, regions and over time are presented in Supplementary Material (page 4).

<Figure 4 here>

Sensitivity analyses

The contribution of female-specific cancers to the sex gaps in life expectancy between ages 15 and 69 for the selected 12 countries using both GBD and register data suggest that the differences in the contribution of female-specific cancer mortality to the sex gap in life expectancy when using GBD vs register data are minimal (mean 0.006 years, $sd=0.02$ years) (Supplementary Figure 1).

Discussion

This is the first study to assess the importance of cancers focusing on the impact of female-specific cancers on the sex gap in life expectancy by adopting a regional and global perspective over the period 1990–2019. Not surprisingly, mortality from cancer explains a notable part of this sex gap in life expectancy, e.g. ~25% in the European and Western Pacific Regions (1.52 out of 6.42 years and 1.77 out of 6.33 years, respectively). The contribution of female-specific cancer to the sex gap in life expectancy was striking at younger, reproductive and productive ages –causing a female disadvantage in life expectancy-. In the Eastern Mediterranean Region, female-specific cancers contribute -0.26 years to the sex gap in life expectancy, a sizeable amount given that the overall sex gap is 1.10 years. In fact, this contribution equals or outnumbers the contribution of the most common cause of cancer deaths, i.e., lung cancer. Nonetheless, we found marked regional differences in the contribution of female-specific cancers to the sex gap in life expectancy between ages 15 and 69, which was highest in the Eastern Mediterranean Region and lowest in Western Pacific Region. Examining the impact of cancers on the sex gap in life expectancy not only serves as an equity indicator but also represents a meaningful and easy to understand metric for assessing health disparities.

In most Regions, females had higher life expectancy at working and reproductive ages, but also higher cancer mortality compared with males. The marked impact of cancer in these working and reproductive years has far-reaching consequences for society. For example, women are the main contributor to the healthcare workforce and an important contributor to the care sector. Additionally, premature deaths from cancer have important consequences in terms of family dynamics and child well-being. A recent study has estimated that premature deaths from cancer caused over a million new maternal

orphans in 2020.²⁹ Studies quantifying premature mortality in women are needed to encourage public health and social policy makers to adequately tackle sex inequalities in health and mortality.

In 2019, the contribution of female-specific cancer to the sex gap in life expectancy between ages 15 and 69 ranged between -0.15 and -0.26 years in WHO Regions. Although it is in the reverse direction, this contribution to the sex gap in life expectancy is similar or higher to that of lung cancer in all WHO Regions and periods. Using lung cancer mortality as a benchmark is particularly useful because it is the leading cause of cancer deaths worldwide.³⁰ Preventative action against lung cancer's most important cause (tobacco smoking) has been highly effective among males, and has successfully reduced smoking-related cancers in many countries.^{31,32} On the other hand, smoking and lung cancer rates have increased in females,³³ so the contribution of lung cancer to the sex gap in life expectancy will probably remain stable in many countries.¹⁵

While the contribution of lung cancer to the sex gap in life expectancy will likely remain stable in the future, over the last three decades the mortality from female-specific cancers such as breast and ovarian cancer has increased in Africa, Eastern Mediterranean, South-East Asia and Western Pacific Regions, while stagnating or declining in the other Regions. Similarly, cervical cancer mortality continues to rise in Africa. The availability of prevention and early detection programmes, as well as timely access to cancer diagnosis centres and treatment for these female-specific cancers, remain difficult in low- and middle-income countries with constrained health systems. Additionally, the role of women in many cultures further hinders timely access to healthcare services throughout the cancer continuum. As a consequence, the impact of female-specific cancers has increased over time in most WHO regions. Cancer control policies have mainly focused on amenable factors such as smoking, while the prioritisation of tackling female-specific determinants is almost non-existent and urgently needed.

Breast and cervical cancers are the two highest causes of premature deaths for women, even higher than maternal mortality in all countries.³⁴ Breast cancer is the largest contributor to female-specific cancer mortality in most countries due to the prevalence of breast cancer risk factors such as obesity, alcohol consumption, physical inactivity and reproductive factors, which include having fewer children and delaying motherhood. In most high-income countries, the breast cancer mortality rate has decreased by approximately 40% since 1990.³⁵ These countries typically diagnose at least 60% of their breast cancer cases at early stages, at which point treatment is more effective and

affordable.³⁶ This is not the case for the majority of low- and middle-income countries, where incidence and mortality are on the rise.³⁷ While breast cancer screening through mammography is not feasible for most resource-constrained settings, strengthening healthcare systems for earlier diagnosis and treatment has also been shown to improve breast cancer survival.¹⁶ The Global Breast Cancer Initiative from WHO and the Women's Health Initiative have contributed to increasing the awareness of female-specific cancers.³⁵ Tackling the so-called by the WHO "best-buys" –the set of cost-effective and evidence-based interventions that have been identified as the most effective ways to prevent and control non-communicable diseases- would contribute to reducing non-communicable diseases, including general cancers and female-specific cancers.³⁸

Cervical cancer is the second leading female-specific cancer in terms of mortality. It has the same female-specific cancer mortality as breast cancer in the African Region. In many high-income countries, cervical cancer control has been successful because of access to effective screening programs coupled with efficient management of both pre-cancerous lesions and cancer cases. This is in stark contrast with the extremely high rate of cervical cancer in low- and middle-income countries, where lower access to human papillomavirus (HPV) vaccination and quality screening programs remain substantial. In the future, increased HPV vaccination and screening are expected to reduce the elevated cervical cancer incidence and mortality in these countries.³⁹ In fact, access to HPV vaccines has been unequal across the Regions and we are still far from the targeted 90% vaccination rate of adolescent girls by 2030⁴⁰, but the recent change from a two-dose vaccination to a one-dose protocol might accelerate the progress to cervical cancer mortality reduction.⁴¹ The impact of HPV vaccination on cervical cancer deaths would be greatest in the African region, followed by South-East Asia region and the Americas. Future decline in cervical cancer mortality in Africa and South-East Asia may increase the sex-gaps in life expectancy due to the currently low sex-gaps in life expectancy because of high female excess mortality due to poorer access to healthcare, which also suggests that the sex-gaps will be more similar to those observed in Western countries.

Over the last three decades, the sex gap in life expectancy during working and reproductive ages has increased in Africa, South-East Asia and Western Pacific Regions, while they have decreased or stagnated in Europe, the Americas and in the Eastern Mediterranean regions. In the first group of regions the contribution of female-specific cancers has remained stable or increased, whereas it has declined in Europe and the Americas, mainly due to the improvement in the management and treatment of

breast cancer.³⁴ In Africa, cervical cancer mortality levels remain high, whereas in all regions except Europe and North America, female-specific cancers have not declined over the analysed timespan. While successes in cancer control have reduced mortality among females,⁴² female-specific cancers are also associated with risks such as hormonal and reproductive hazards, which are more difficult to ward off. Continued public health efforts should increase prevention, particularly in regions where the risk of female-specific cancers is higher. This applies to almost all regions of the world except high-income countries for breast cancer, and more specifically Middle and Southern Africa, South-East Asia and Latin America for cervical cancer.

Some limitations should be considered when interpreting the results. The data used was from the Global Burden of Disease 2019 Study.²²⁻²⁵ While these data have been broadly used and validated in various epidemiological studies, they depend on existing national data and their quality, therefore differ across countries. Although the country-specific results should be interpreted with caution, our results align with those from similar studies performed using national mortality statistics as a source: China, South Korea and Sweden.¹⁸⁻²¹ Additionally, we carried out sensitivity analyses using data for selected countries (at least one for each WHO region) for which national register data was available. The differences between estimates calculated based on GBD data compared to those based on register data are minimal (Supplementary Figure 1). Finally, while informative, our estimates for countries with missing mortality register data should be interpreted with caution.

In conclusion, female-specific cancers are significant contributors to the gender disparity in life expectancy, but their impact varies across different Regions and periods. To address the high mortality rates from breast and cervical cancer in Africa, South-East Asia, Eastern Mediterranean, and Western Pacific regions, there is an urgent need to improve access to prevention, early detection and effective treatment programmes. This would not only reduce mortality rates but also contribute towards achieving the UN Sustainable Goals on good health, gender equality and reduced inequalities. In Europe and North American regions, where female-specific cancer mortality rates have decreased at a slower rate than other cancers affecting men, innovative strategies are necessary to target the determinants of female-specific cancers and further reduce their declining trend. Addressing systemic factors that delay progress towards reducing mortality rates from female-specific cancers remains a critical global public health challenge.

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Data availability

The datasets used in this were retrieved from publicly available source, namely the Global Burden of Diseases Study (GBD) 2019 and can be accessed from the GBD Results Tool (Institute of Health Metrics and Evaluation) using the following link: <http://ghdx.healthdata.org/gbd-results-tool>.

We retrieved data from the Global Burden of Diseases Study (GBD) 2019 by 5-year age group, sex, cancer-specific cause of death and all-cause mortality rates for 204 countries and territories worldwide, and for the six WHO regions (African, Eastern Mediterranean, European, the Americas, South-East Asia and Western Pacific) over the period 1990–2019.²² Cancer mortality causes were grouped into four female-specific cancers (breast, cervical, ovary and corpus uterine), five major cancers (colorectal, liver, stomach, lung, and prostate); and a remaining group for other cancers (see Supplementary Table 1 for International Classification of Diseases codes).

Author contributors

STL, ER, RR and IS conceptualised and designed the study. STL analysed and ER contributed to data analysis. STL produced results and created the figures. STL, ER, RR and IS interpreted the data and drafted the manuscript. AA, JM and KUS aided in

interpreting the data and drafting the manuscript. All authors aided in interpreting the results, critically reviewed the manuscript and approved the final manuscript.

Conflict of interest

The authors declare no competing interests.

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Figures

Figure 1. Sex gap in life expectancy at birth (females – males, in years), and the contribution of all cancers to the sex gap in life expectancy in 2019 according to age group and world region.

Note: Positive sex gap values indicate that females have higher life expectancy compared with males, and negative values imply the opposite. Positive contribution of a disease suggests that it contributes towards a widening of the sex gap while negative contribution suggests the opposite e.g., a narrowing.

Figure 2. Contributions of cause-specific cancer mortality to the sex differences in life expectancy at birth in 2019 by age group and world region.

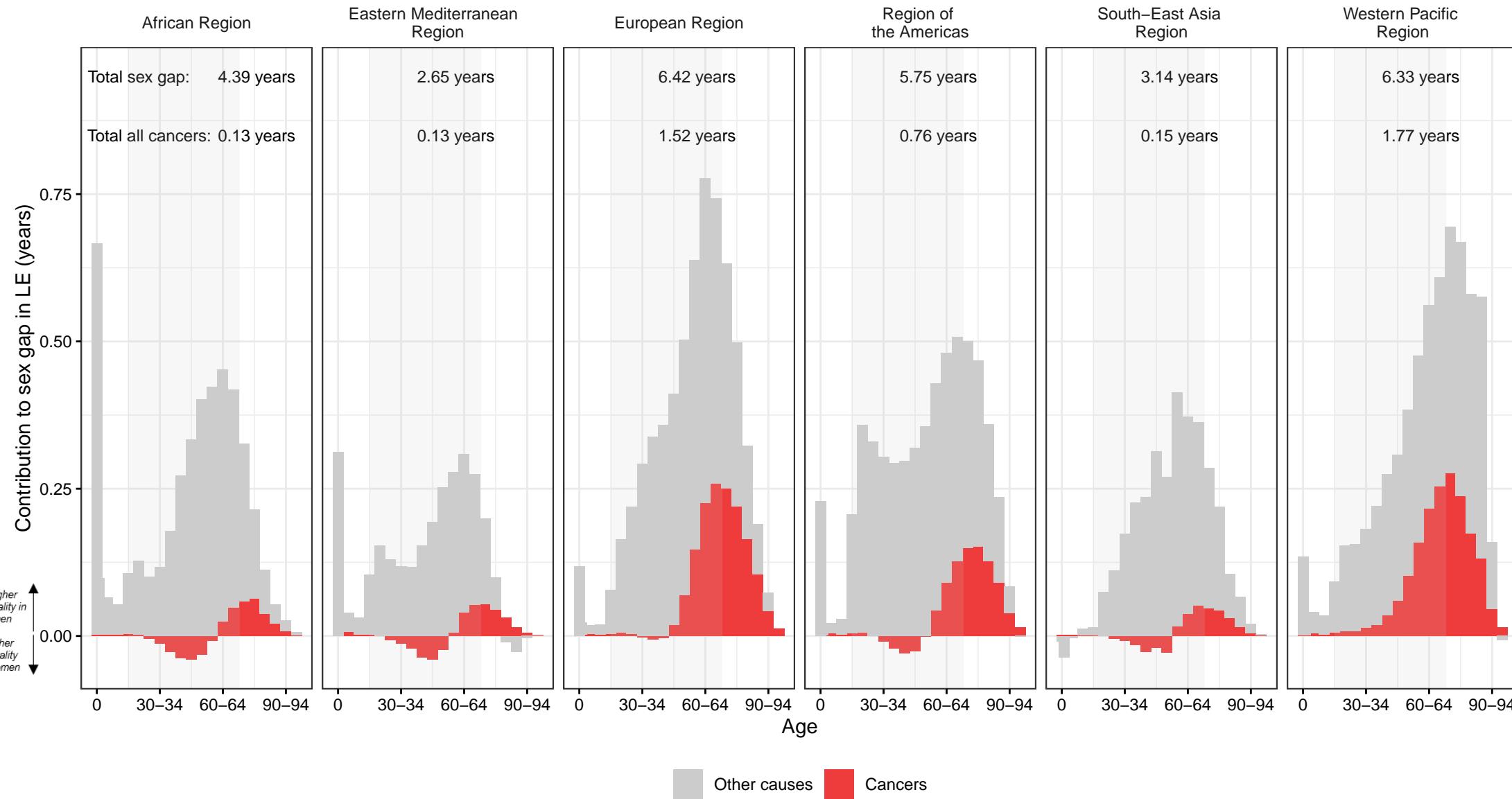
Note: Positive contributions suggest that a disease contributes towards a widening of the sex gap and increasing the female advantage, while negative contribution suggests the opposite e.g., a narrowing of the gap.

Figure 3. World maps for ages 15 to 69 (2019); A) Sex gaps in life expectancy (females – males), B) the contribution of all cancers to the sex gap in life expectancy, and C) the contribution of female-specific cancers to sex gaps in life expectancy.

Note: Positive sex gap values indicate that females have higher life expectancy compared with males, and negative values imply the opposite. Positive contributions suggest that a disease contributes towards a widening of the sex gap and increasing the female advantage, while negative contribution suggests the opposite e.g., a narrowing of the gap.

Figure 4. The contribution of cancer-specific mortality to the sex gap in life expectancy between ages 15 and 69 (in years) in 1990, 2005 and 2019 according to world region.

Note: Positive contributions suggest that a disease contributes towards a widening of the sex gap and increasing the female advantage, while negative contribution suggests the opposite e.g., a narrowing of the gap.



Contribution to sex gap in LE (years)

African Region

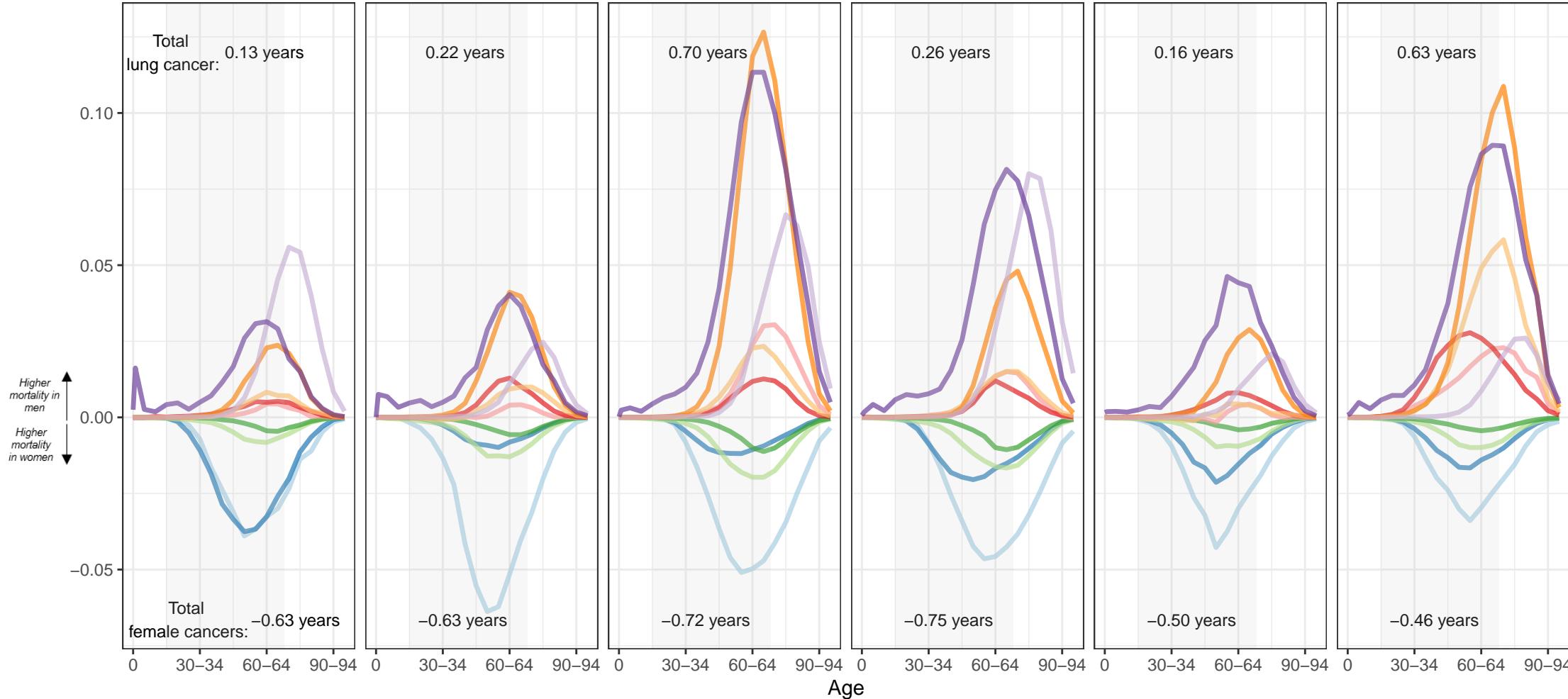
Eastern Mediterranean Region

European Region

Region of
the Americas

South-East Asia
Region

Western Pacific
Region



Breast cancer Ovarian cancer Colon and rectum cancer Stomach cancer Prostate cancer

Cervical cancer Uterine cancer Liver cancer Lung cancer Other cancers

