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Projections in Breast and Lung Cancer Mortality among Women: A Bayesian Analysis of 52 Countries Worldwide

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Abstract

Among women, lung cancer mortality rates have surpassed those for breast cancer in several countries. This reflects the breast cancer mortality declines due to access to screening and effective treatment alongside the entrance of certain countries in stages of the tobacco epidemic in which smoking becomes more prevalent in women. In this study, we project lung and breast cancer mortality until 2030 in 52 countries. Cancer mortality data were obtained from the WHO Mortality Database. Age-standardized mortality rates (ASMR), per 100,000, were calculated (direct method) for 2008 to 2014 and projected for the years 2015, 2020, 2025, and 2030 using a Bayesian log-linear Poisson model. In 52 countries studied around the world, between 2015 and 2030, the median ASMR are projected to increase for lung cancer, from 11.2 to 16.0, whereas declines are expected for breast cancer, from 16.1 to 14.7. In the same period, the ASMR will decrease in 36 countries for breast cancer and in 15 countries for lung cancer. In half of the countries analyzed, and in nearly three quarters of those classified as high-income countries, the ASMR for lung cancer has already surpassed or will surpass the breast cancer ASMR before 2030. The mortality for lung and breast cancer is higher in high-income countries than in middle-income countries; lung cancer mortality is lower in the latter because the tobacco epidemic is not yet widespread. Due to these observed characteristics of lung cancer, primary prevention should still be a key factor to decrease lung cancer mortality.

Significance: The mortality for lung and breast cancer is projected to be higher in high-income countries than in middle-income countries, where lung cancer mortality is expected to surpass breast cancer mortality before 2030. *Cancer Res; 78(15); 4436–42. ©2018 AACR.*

Introduction

Cancer is among the leading causes of morbidity and mortality worldwide, with an estimated incidence of 14 million new cases and 8.2 million cancer deaths in 2012 (1). Among women, the leading cancers worldwide in terms of mortality are breast, colorectal, lung, cervix, and stomach (2).

The incidence rate of breast cancer per 100,000 women varies widely, from 27 in Middle Africa and Eastern Asia to 92 in North America, while the variation in mortality rates is more limited and ranges from 6 in Eastern Asia to 20 in Western Africa (3). The difference between incidence and mortality rates is explained by a higher survival in most developed regions, where the 5-year relative survival rate is over 80% (4). Breast cancer mortality rates have been declining in several countries (5), which essentially reflects the trends toward improved access to cancer screening and effective treatments (5).

The incidence rate of lung cancer per 100,000 women is lower than that of breast cancer, ranging from 0.8 in Middle Africa to 33.8 in North America (3). However, lung cancer has one of the lowest 5-year net survival rates, at under 20% in developed countries (6, 7), which makes it the leading cause of cancer mortality (2). Because over 60% of lung cancer deaths in women are attributable to smoking (8), the geographical heterogeneity in the burden of lung cancer mortality results mostly from differences in the patterns of tobacco consumption across regions. Similarly, the temporal trends in lung cancer mortality rates closely follow the levels of smoking, with a lag of a few decades, as depicted in the model proposed by Lopez and colleagues (9) for the tobacco epidemic.

Previous studies (10–12) have shown that breast cancer prevention and control efforts, mostly due to secondary

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Note: Supplementary data for this article are available at Cancer Research Online (http://cancerres.aacrjournals.org/).

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prevention and improved management, have resulted in clear declines in breast cancer mortality rates. For lung cancer, men in developed countries have experienced a dramatic epidemic, which is now declining, although lung cancer is still the leading cause of cancer mortality, whereas in women the lung cancer epidemic has started generally later than in men, and rates are still rising in many developed countries (13), with lung cancer mortality projections being higher than those for breast cancer.

Thus, different patterns may be expected between countries, depending on the implementation of breast cancer screening programs and access to effective treatment and the stage of the tobacco epidemic each country is at present.

The objective of this study is to project the mortality rates of lung cancer and breast cancer in women worldwide, in order to identify international patterns of joint variation in lung and breast cancer mortality until 2030.

Materials and Methods

Data sources

Breast and female lung cancer mortality data were obtained from the World Health Organization (WHO) Mortality Database (14) for the period from 2008 to 2014. Deaths by lung cancer and breast cancer and population were grouped by country, year, and age (17 groups; from 0–4 to 75–79, and ≥80 years). Population data were also available for the projected years (2015, 2020, 2025, and 2030) and were obtained from the United Nations Population Division (15).

Countries selected

From 2008 to 2014, the WHO Mortality Database did not include data from all of the countries for all the selected years. The countries included in this study had to fulfill two conditions: (i) the population had to be over 1,000,000; (ii) at least 4 of the 7 years from the period 2008 to 2014 had to be reported in the WHO mortality database. Fifty-two out of 193 countries fulfilled these criteria: 14 from America (Argentina, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Guatemala, Mexico, Panama, Puerto Rico, the United States, Uruguay, and Venezuela), seven from Asia (Hong Kong, Israel, Japan, Kazakhstan, Kuwait, Kyrgyzstan, and Republic of Korea), 29 from Europe (Austria, Belarus, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, the Russian Federation, Serbia, Slovakia, Spain, Sweden, Switzerland, Ukraine, and the United Kingdom) and two from Oceania (Australia and New Zealand). None of the African countries accomplished the inclusion criteria. Also, for the purpose of the analysis, we classified the included countries according to the continent (America, Asia, Europe, and Oceania), the World-Bank level of income classification (high-income, upper-middle-income, lower-middle-income) and the World Bank Geographical Regions (East Asia and Pacific, Europe and Central Asia, Latin America and the Caribbean, Middle East and North Africa, North America). No data were available from countries from low-income economies, South Asia, and sub-Saharan Africa.

Statistical analysis

For each country, lung cancer and breast cancer age-standardized mortality rates (ASMR) in women (reported as per 100,000 person years) were calculated, based on the WHO world standard population (16).

A log-linear model was used to predict country-specific mortality rates. Assuming that the number of deaths for the ith age group and the tth year follows a Poisson distribution of average $\mu_{i,t}$ the following Bayesian model was suggested according to previous studies (17, 18):

$$\frac{\mu_{i,t}}{Y_{i,t}} = e^{(\alpha_i + \beta_i (t - t_o))},$$

where $Y_{i,t}$ is the population and t_0 is the reference year. Before applying the model, the number of years used to estimate the model and the number of years predicted must be taken into account. Using all the available years is not necessarily the best option to obtain the best model, as the condition of log-linearity in the model could not be met. In contrast, models created from a small number of years can meet the condition of log-linearity, but they produce estimates with poor accuracy. An acceptable balance between the two is considered to be between 5 and 10 years (19). We fit our model to the 2008 to 2014 period and used it to predict rates for the years 2015, 2020, 2025, and 2030.

A Gaussian distribution was applied as prior for all α_i and β_i so $\alpha_i \sim$ Normal $(0, \tau_\alpha)$ and $\beta_i \sim$ Normal $(0, \tau_\beta)$ with precision parameters τ_α and τ_β having flat hyperpriors $\tau_\alpha \sim$ Gamma (ψ, ϕ) and $\tau_\beta \sim$ Gamma (ψ, ϕ), where $\psi = \phi = 0.001$. The models were implemented using WINBUGS and run in *R* (20, 21). Each model was generated by a Markov Chain Monte Carlo run of three chains of 25,000 values, discarding the first 5,000 as a burn-in process and keeping every second. The chains differentiated for the initial values of τ_α and τ_β (1 in the first chain, 0.1 in the second chain, and 10 in the third chain) and an initial value of 0 for all α_i and β_i. Therefore, we obtained 30,000 samples of the model parameters, which allowed us to predict the future number of deaths by lung cancer and breast cancer in each age group. Once the predicted number of deaths is obtained, the distribution of the mortality rates can be described.

The results were reported as the median and the 95% credible interval (CI) predicted for lung cancer and breast cancer for the projected years 2015, 2020, 2025, and 2030. The number of deaths and the ASMR were reported. To summarize the results of all the countries or a group of them, the median, minimum, and maximum of the medians were reported categorized by continent, income group and World Bank group. To report the percent change in both diseases in a decade, the ratio of the median of the projected rate for 2020 and the observed rate for 2010 is calculated and represented in Fig. 1.

Ethics

All data used in this study are legally accessible to the public and appropriately protected by the law (the information was publicly aggregated data and does not contain data on individuals), so ethical approval was not required.

Results

Table 1 presents the observed and projected breast and lung cancer ASMR in women in 52 countries grouped by continent, income group, and World Bank group. Overall, the projected median ASMR is increasing for lung cancer from 11.2 in 2015 to 16.0 in 2030. Only in Oceania a decrease of the ASMR is expected, from 17.8 to 17.6. The highest rates are projected for Europe and Oceania, and the lowest for America and Asia. Overall, for breast cancer, the ASMR decreases from 16.1 to 14.7. The highest rates are

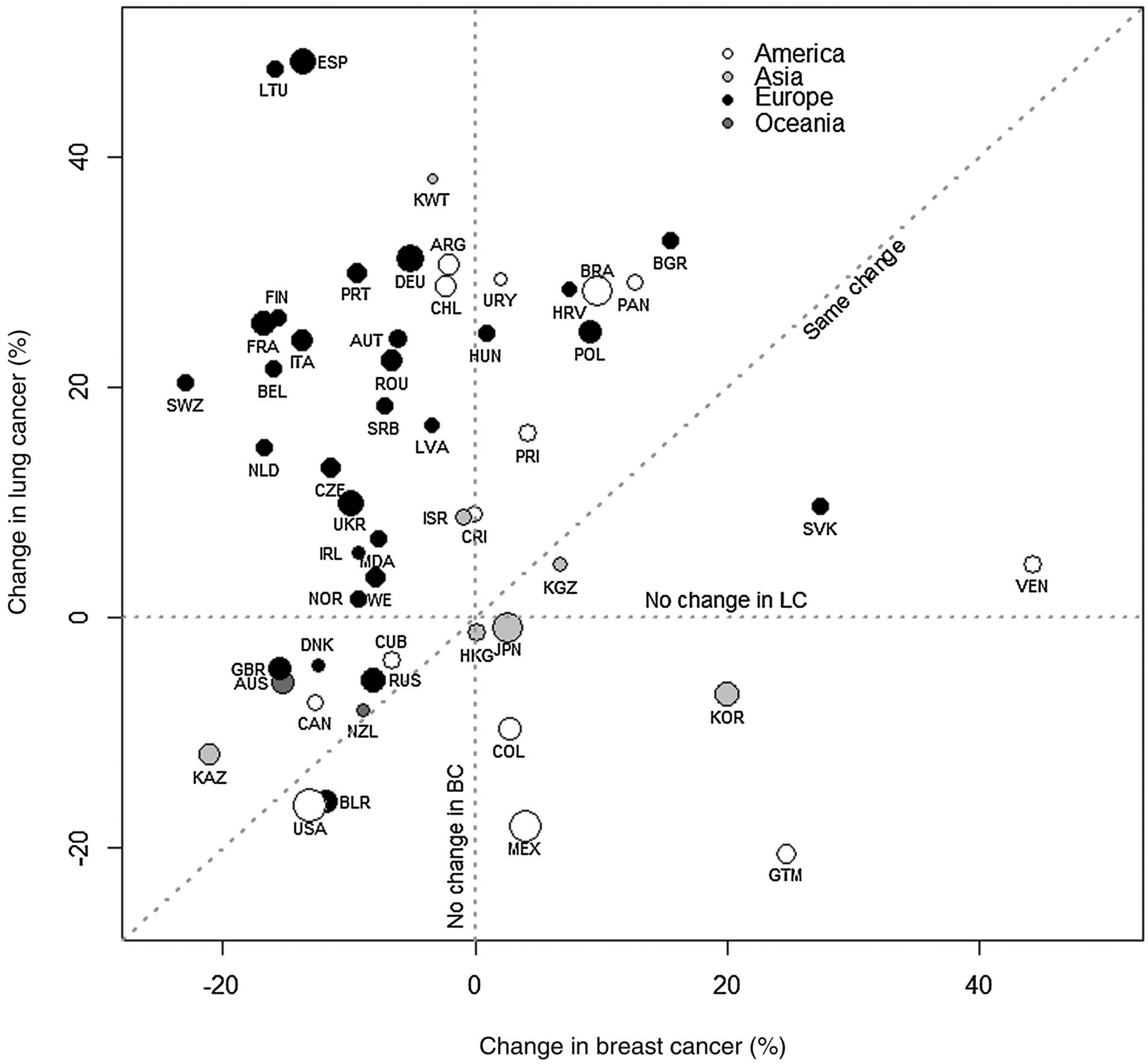

Figure 1.
Percentage of change in the lung cancer age-standardized mortality rate and breast cancer age-standardized mortality rate from 2010 (observed) to 2020 (projected). The size of the marker represents the precision of the projection (greater precision, greater size).

projected with a decreasing trend for Europe, while the lowest for Asia, although with an increasing trend. The highest ASMR for breast and lung cancer are found, if compared with the middle-income countries as a whole, in the high-income group, in which lung cancer mortality is projected to have surpassed breast cancer mortality by 2020. The highest percentage of countries with decreasing breast cancer mortality is found in the high-income group. Supplementary Tables S1–S3 show the number of deaths, the crude mortality rate, and the ASMR for the years 2010, 2015, 2020, 2025, and 2030.

As summarized in Table 2, lung cancer mortality had already surpassed breast cancer mortality by 2010 in 15 of the 52 countries. Lung cancer mortality will surpass breast cancer mortality before 2030 in other 11 countries. For the remaining 26 countries, mortality for lung cancer is not expected to surpass breast cancer mortality until 2030. Table 2 also indicates in which countries the trend increase or decrease, and when it will happen with a probability over 0.95.

Figure 1 depicts the percent variation in mortality for both cancers from 2010 to 2020. Comparing the mortality rates observed in 2010 and those projected to 2020, a decrease in the ASMR for lung cancer is expected in 16 countries. A decrease in the ASMR for breast cancer is expected in 34 countries. Supplementary Fig. S1 shows the evolution of both rates for lung and breast cancers from 2010 to 2030.

Discussion

By 2030, the lung cancer ASMR is projected to be higher than the breast cancer ASMR in women in 26 of the 52 analyzed

Table 1. Median, minimum, and maximum of the projected rates for lung cancer and breast cancer ASMR in women in 52 countries worldwide; number and percentage of countries within category where breast cancer and/or lung cancer ASMR is/are going to decrease and period when lung cancer ASMR surpassed or will surpass breast cancer ASMR

		LC				BC				Decreasing		When LC surpass BC		
	n	2015	2020	LC	2030	2015	2020	2025	2030	LC	BC	By 2010	Before 2030	Not in 2030
Overall	52	11.2 (3.3–32.5)	12.4 (3.0–37.0)	37 (71.2%)	16.0 (2.9–51.4)	16.1 (6.0–22.4)	15.1 (6.5–22.7)	14.7 (7.1–24.7)	14.7 (7.7–30.6)	16 (30.8%)	34 (65.4%)	15 (28.8%)	11 (21.2%)	26 (50.0%)
Continent														
America	14	10.0 (3.3–27.2)	11.1 (3.0–26.4)	11.9 (2.9–25.8)	13.0 (2.9–25.3)	14.2 (6.2–21.4)	14.1 (7.0–21.6)	13.9 (8.2–24.7)	14.8 (10.0–30.6)	6 (42.9%)	5 (35.7%)	3 (21.4%)	1 (7.1%)	10 (71.4%)
Asia	7	9.3 (4.9–18.2)	9.3 (5.2–18.1)	9.3 (5.0–18.3)	9.7 (5.0–18.8)	10.3 (6.0–19.5)	10.4 (6.5–19.2)	10.5 (7.1–19.0)	10.7 (7.7–19.0)	4 (57.1%)	3 (42.9%)	2 (28.6%)	0 (0.0%)	5 (71.4%)
Europe	29	15.5 (3.6–32.5)	16.6 (3.4–37.0)	17.9 (3.4–43.2)	20.8 (3.4–51.4)	17.1 (12.8–22.4)	16.7 (11.9–22.7)	15.9 (11.2–24.7)	15.4 (10.5–29.3)	4 (13.8%)	24 (82.8%)	8 (27.6%)	10 (34.5%)	11 (37.9%)
Oceania	2	17.8 (15.8–19.7)	17.5 (15.6–19.4)	17.5 (15.3–19.7)	17.6 (15.0–20.2)	16.2 (14.3–18.0)	15.3 (13.2–17.4)	14.8 (12.3–17.4)	14.7 (11.5–17.8)	2 (100.0%)	2 (100.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)
Income group														
High	33	15.6 (5.0–32.5)	16.6 (6.2–37.0)	17.9 (7.9–43.2)	19.1 (8.5–51.4)	16.0 (6.0–21.4)	15.0 (6.5–21.6)	14.1 (7.1–24.7)	13.6 (7.7–29.3)	9 (27.3%)	25 (75.8%)	14 (42.4%)	10 (30.3%)	9 (27.3%)
Upper-middle	15	9.1 (3.6–20.5)	10.1 (3.4–22.1)	11.2 (3.4–24.8)	11.8 (3.2–27.8)	16.2 (9.9–22.4)	15.8 (10.0–22.7)	15.5 (10.1–24.7)	15.8 (10.3–30.6)	6 (40.0%)	7 (46.7%)	1 (6.7%)	1 (6.7%)	13 (86.7%)
Lower-middle	4	5.1 (3.3–7.2)	5.5 (3.0–7.5)	5.9 (2.9–8.1)	6.5 (2.9–8.9)	14.0 (6.2–17.9)	13.6 (7.0–17.1)	13.5 (8.2–16.5)	13.6 (10.0–16.8)	1 (25.0%)	2 (50.0%)	0 (0.0%)	0 (0.0%)	4 (100.0%)
WORLD bank group														
East Asia and Pacific	5	15.8 (9.3–19.7)	15.6 (9.3–19.4)	15.3 (9.3–19.7)	15.0 (9.4–20.2)	9.9 (6.0–18.0)	10.1 (6.5–17.4)	10.3 (7.1–17.4)	10.7 (7.7–17.8)	0 (0.0%)	3 (60.0%)	4 (80.0%)	0 (0.0%)	1 (20.0%)
Europe and Central Asia	31	13.7 (3.6–32.5)	15.4 (3.4–37.0)	17.8 (3.4–43.2)	19.5 (3.4–51.4)	16.6 (10.3–22.4)	16.1 (10.4–22.7)	15.5 (10.5–24.7)	14.8 (10.4–29.3)	26 (83.9%)	5 (16.1%)	8 (25.8%)	10 (32.3%)	13 (41.9%)
Latin America and the Caribbean	12	8.8 (3.3–20.5)	9.3 (3.0–20.5)	9.6 (2.9–20.9)	10.1 (2.9–21.8)	13.5 (6.2–21.4)	14.1 (7.0–21.6)	14.7 (8.2–24.7)	15.3 (10.0–30.6)	9 (75.0%)	8 (66.7%)	1 (8.3%)	1 (8.3%)	10 (83.3%)
Middle East and North Africa	2	8.2 (5.0–11.4)	9.1 (6.2–12.1)	10.7 (8.4–12.9)	13.5 (13.1–14.0)	16.8 (14.1–19.5)	16.7 (14.1–19.2)	16.8 (14.6–19.0)	17.3 (15.6–19.0)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)
North America	2	25.5 (23.9–27.2)	24.2 (21.9–26.4)	23.0 (20.3–25.8)	22.1 (19.0–25.3)	15.0 (14.9–15.1)	14.1 (13.9–14.2)	13.3 (13.0–13.5)	12.7 (12.2–13.2)	0 (0.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: LC, lung cancer; BC, breast cancer.

Table 2. Classification of the countries according to the trend in lung and breast cancer age-standardized mortality rate by continent

Trend in lung cancer	Trend in breast cancer	America	Asia	Europe		Oceania
Decreasing (16 countries)	Decreasing (10 countries)	**Canada**[a] **Cuba** **United States of America**[a,b]	Kazakhstan[a]	**Denmark** **United Kingdom**[a] Belarus Russian Federation[a]		**Australia**[a] **New Zealand**
	Increasing (6 countries)	Colombia Guatemala Mexico[b]	**Hong Kong**[a] **Republic of Korea** Japan			
Increasing (36 countries)	Decreasing (24 countries)	Chile[b] Argentina[b]	Israel Kuwait	**Ireland** **The Netherlands**[a,b] Austria[b] Belgium[a,b] Czech Republic[b] Finland[b] Germany[a,b] Republic of Moldova Lithuania Portugal[b]	**Norway** **Sweden** Italy[a,b] Serbia[b] Spain[a,b] Switzerland[b] France[a,b] Latvia Romania[b] Ukraine[a]	
	Increasing (12 countries)	Brazil[a,b] Costa Rica Panamá Puerto Rico Uruguay Venezuela[a]	Kyrgyzstan	**Hungary**[b] **Poland**[b] Bulgaria[b] Croatia[b] Slovakia[a]		

NOTE: Countries where lung cancer surpassed breast cancer age-standardized mortality rate by 2010 (bold) or will surpass before 2030 (underlined).
[a]The probability of the trend (decreasing or increasing) in breast cancer is over 0.95.
[b]The probability of the trend (decreasing or increasing) in lung cancer is over 0.95.

countries, adding 11 countries to the 15 that already reported this situation by 2010. Twenty-four of these countries belong to the high-income group, where the highest lung cancer and breast cancer ASMR are observed.

Previous studies (3, 22) have shown that crude mortality rates in women for breast and lung cancer are higher in more developed countries. This is partially due to the demographics in these countries, where the oldest population strata are increasing (23). In our age-adjusted models, high-income countries still have the highest mortality rates, although the gap with middle-income countries is narrow.

Our study shows that the first countries where lung cancer mortality surpassed breast cancer mortality in women are mostly developed countries. This could be explained by two main factors. On the one hand, there is a downward trend for breast cancer mortality in these countries as a result of an early detection, mainly due to widespread screening programs (24, 25), and improvements in treatment (26–28), in spite of some of the main risk factors for breast cancer (1, 3) being more prevalent in developed countries. On the other hand, because lung cancer mortality rates rely heavily on the prevalence of tobacco consumption due to the limited 5-year survival rate shown by this type of cancer (6, 7), the countries with the highest current lung cancer mortality rates are those where women smoked more in the past. In some of these countries, lung cancer mortality has even started to decline. In addition to smoking, exposure to radon, associated with up to 14% of lung cancers (29), or occupational exposures (e.g., asbestos) (30) may also add in different proportion to lung cancer mortality.

The strength of this study is the coverage and completeness of the data (31). Furthermore, lung and breast cancer diagnosis and certification has long been validated (32). The main assumption of the log-linear Poisson model used to obtain projections is that the log-linear trends observed in recent years will continue into the future (18). More complex models can be used, such as age–period–cohort models, but these require a long period of observation as a basis for prediction and may present interpretation difficulties in practice with wider credible or prediction intervals than those based on simple linear or log-linear models (18). On the other hand, the over 15 years of prediction span may be influenced by cohort effects not included in the model. For mid-term projections, up to the year 2030, a simple log-linear model has performed better than other models in this particular situation (19, 33, 34). As we move forward in time the compliance of the log-linear assumption becomes questionable and the precision decreases.

Moreover, the projected rates should be interpreted assuming that the recent trends continued for the next two decades. For both types of cancer, especially for lung cancer, this situation is unlikely to happen. First, the shift from conventional cigarettes and other combustible products to electronic nicotine and nonnicotine delivery systems (e.g., electronic cigarettes, IQOS) could have an impact in the decrease of lung cancer mortality rates. In this sense, the use of electronic cigarettes or heat-not-burn tobacco devices could be a useful tool to quit or reduce tobacco consumption. However, current scientific evidence on the effectiveness of these devices for quitting smoking is contradictory and scarce. A meta-analysis (35) of three randomized controlled trials and 21 cohort studies conclude that there is no strong evidence that electronic cigarettes may help smokers to stop smoking in the long term, as well as to prevent relapse among former smokers. Furthermore, other studies conducted in Europe (36) and the United States (37) found a high percentage of "dual" use (i.e., use of e-cigarettes plus use of other tobacco products). In this sense, a recent study (38) that assesses potential scenarios to shift the conventional to electronic cigarettes has shown a potential reduction in the projection of premature death in the United States. In addition, a study (39) conducted in Spain showed that the projection of smoking status among women is going to increase until 2025. The real impact of heat-not-burn tobacco products (electronic cigarettes, IQOS, etc.) in lung cancer mortality rates should still be assessed. On the other hand, due to recommendations from independent experts (40, 41) and scientific societies (42), mainly arising from the results of the US National Lung Screening Trial, where a reduction of 20% in the lung cancer mortality and of 6.7% in all-cause mortality were observed in the group undergoing low-dose computer tomography versus the group undergoing chest X-ray (43), lung cancer screening programs may be implemented in the near future in different countries worldwide, subsequently reducing our projected mortality rates. Regarding breast cancer mortality rates, the use of digital and state-of-the-art technology for mammography has improved cancer detection (44), improving mortality rates eventually and treatment is progressively improving. Another limitation is that Africa and low-income countries were not included in the study, due to lack of data.

In conclusion, lung and breast cancer mortality is higher in high-income countries, where lung cancer mortality has surpassed or will surpass breast cancer within the next years. Being that low-dose computer tomography implementation is still a matter of debate and with breast cancer mortality decreasing, prevention efforts should focus on smoking avoidance and cessation.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

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Development of methodology: J.C. Martín-Sánchez, R. Clèries, C. La Vecchia, J.M. Martínez-Sánchez
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): M. Malvezzi, E. Negri
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): J.C. Martín-Sánchez, N. Lunet, A. González-Marrón, N. Matilla-Santander, R. Clèries, M. Malvezzi, C. La Vecchia, J.M. Martínez-Sánchez
Writing, review, and/or revision of the manuscript: J.C. Martín-Sánchez, N. Lunet, A. González-Marrón, C. Lidón-Moyano, N. Matilla-Santander, R. Clèries, E. Negri, S. Morais, A.R. Costa, A. Ferro, L. Lopes-Conceição, C. La Vecchia, J.M. Martínez-Sánchez
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): J.C. Martín-Sánchez

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