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Bayesian prediction of lung and breast cancer mortality among women in Spain (2014–2020)

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ABSTRACT

Background: Breast cancer (BC) is the main cause of cancer mortality among women, and mortality from lung cancer (LC) is increasing among women. The purpose of the present study was to project the mortality rates of both cancers and predict when LC mortality will exceed BC mortality.
Methods: The cancer mortality data and female population distribution were obtained from the Spanish National Statistics Institute. Crude rate (CR), age-standardized rate (ASR), and age-specific rate were calculated for the period 1980–2013 and projected for the period 2014–2020 using a Bayesian log-linear Poisson model.
Results: All calculated rates were greater for BC than for LC in 2013 (CR, 27.3 versus 17.3; ASR, 13.5 versus 9.3), and the CR was not projected to change by 2020 (29.2 versus 27.6). The ASR for LC is expected to surpass that of BC in 2019 (12.9 versus 12.7).
Conclusions: By 2020 the LC mortality rates may exceed those of BC for ages 55–74 years, possibly because of the prevalence of smoking among women, and the screening for and more effective treatment of BC. BC screening could be a good opportunity to help smokers quit by offering counseling and behavioral intervention.

1. Introduction

Cancer is among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases and 8.2 million cancer-related deaths in 2012 [1]. The leading cancers are lung, prostate, colorectal, stomach, and liver among men and breast, colorectal, lung, cervix, and stomach among women [2].

The incidence age-standardized rate (ASR) of breast cancer (BC) in women varies widely, from 19.3 in Eastern Africa to 89.7 in Western Europe [3]. The 5-year relative survival is over 80% in developed countries [4], which usually have more extensive screening programs. Thus far, mammography is the only screening program proven to be effective for BC, but it is only possible in countries with the appropriate health infrastructure [5]. The most common treatments can be classified as local therapies (treating the tumor at the site), such as surgery and radiation, or systemic therapies (to reach cancer cells anywhere in the body), such as hormone and targeted therapy.

The incidence ASR of lung cancer (LC) in women is lower than the incidence rate of BC, ranging from 0.9 in Central Africa to 35.8 in North America [3]. However, LC has a worse survival prospect, with a 5-year net survival under 20% in developed countries [6,7] and a 5-year relative survival of 13% in Europe [8]; it is the leading cause of cancer mortality [2]. At diagnosis, most LC patients have an advanced stage of disease, which is associated with poorer prognosis. The most common LC screening tests for early detection are chest x-ray, sputum cytology, and low-dose

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computed tomography (LDCT). LDCT is the most promising test, with a reduction of 20% of mortality in a study in the United States [9]; still, LDCT identifies a high number of false positives with harmful implications. Moreover, there is no evidence of a reduction in the smoking prevalence among those screened [10–12]. The poor prognosis at the time of detection of the LC provides greater value to primary prevention for lowering mortality.

In Europe, cancer mortality per year for women decreased by 1% from 1993 to 2009, with the exceptions of lung and pancreatic cancers which increased during the same period of time [13]. Moreover, the incidence of major tobacco-related cancers, including LC, have increased for women in Europe [14]. These opposite trends between LC and BC imply an important reduction in the difference in the mortality of both cancers (2009: an observed ASR of 13.05 by LC versus 15.85 by BC; 2015: a predicted ASR of 14.24 by LC versus 14.22 by BC) [15].

In Spain, a similar pattern has been observed: the cancer mortality in women has decreased, with the exceptions of LC and BC which lead the mortality rate [16]. In 2012, the incidence ASR estimates were 67.3 for BC and 11.3 for LC, and the mortality ASR estimates were 11.3 and 9.4 [17]. The BC mortality in Spain is one of the lowest in Europe; it was low at the end of the 1980s and is decreasing faster than the European average [18]. The LC mortality is low compared to the rest of Europe but has been increasing faster in the last few years. This suggests that LC mortality among women could surpass BC mortality in Spain in the next few years.

Moreover, the shape of the Spanish population pyramid has changed in the last 20 years. The proportion of subjects aged >65 years was 10% in 1975 and 17% in 2010, and the prospect is that this will grow to 32% in the coming 40 years [19]. Spain is one of the countries with higher life expectancy in the world, and Spanish women have a high life expectancy at birth (85 years) [20].

The objectives of this study were to project the mortality rates of LC and BC in women in Spain and to predict when LC mortality will exceed BC mortality.

2. Methods

2.1. Data sources

The data were obtained from the National Statistics Institute (INE) [21]. Mortality data were available for women during the period 1980–2013. Deaths due to LC and BC were grouped by year and age (18 groups, from 0 to 4 years to 85 or more years). Population data were also available during the study period, and future population estimations were obtained from 2014 to 2020 and provided by the INE.

2.2. Outcomes

For each age group we calculated the crude mortality rate (CR), the ASR using the direct method with the world standard population [22], and the age-specific mortality rate for the following groups: 45–54 years, 55–64 years, 65–74 years, and ≥75 years. All rates were calculated for LC and BC in women and reported as per 100,000 person years.

2.3. Statistical analysis

A log-linear model was used to predict the future mortality rates of LC and BC in women. Assuming the number of deaths for the i^{th} age group and the t^{th} year following a Poisson distribution of average $\mu_{i,t}$ the following Bayesian model was suggested according to previous studies [23,24]:

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

where $Y_{i,t}$ is the population and t_0 is the reference year. Note that $(e^{\beta} - 1)$ is the annual percentage change (APC) in the mortality rate. This value is a good indicator of the trend in the rate; the sign indicates an increase (positive) or decrease (negative) and the magnitude indicates the intensity of the trend [23].

By applying a Bayesian model we avoid fitting problems in those age groups with low rates and small counts of deaths, as it could happen in a classical approach making use of a similar model, and even in this situation one could produce predictive and credible intervals. Before applying the model, two decisions must be made: the number of years used to estimate the model and the number of years predicted. Using all 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 best meet the condition of log-linearity, but they produce estimates with poor accuracy. Evidence suggests that the linear trend of LC mortality has not changed since 2007 in any age group [25]. On the other hand, the most reliable prediction base for a log-linear model could be 5 years, with 10 years or more not covering the observed number of deaths [26]. According to these points, we have fitted our model to the period 2007–2013 and used it to predict rates during the period 2014–2020. Regarding the predictions, as we move forward in time the compliance of the log-linear assumption becomes questionable and the precision decreases.

A Gaussian distribution as prior was applied 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 hyper-priors $\tau_\alpha \sim$ 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 [27,28]. 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 for all α_i and β_i obtained from a normal distribution of mean 0 and precision 0.01. Therefore, we obtained 30,000 samples of the model parameters, which allowed us to predict the future number of deaths by LC and BC in each age group. Once the predicted number of deaths was obtained, the distribution of the mortality rates could be described.

The results were reported as the median and the 95% credible interval (95% CI) predicted for LC and BC each year in the period 2014–2020. We reported all mortality rates, the annual percentage change in the mortality rate by age group, and the LC/BC ratio for the calculated rates. If the 95% CI of the ratio included 1, we assumed that the LC and BC rates did not differ.

2.4. Comparison of the cumulative risk of death

We calculated the cumulative rate (C) for LC and BC for the years 2013 and 2020 by adding age-specific absolute rates (in 5-year age groups) and then the lifetime cumulative risk up to 80 years of age using the following standard formula:

$$100\left(1 - e^{-5 \times \frac{C}{10^5}}\right)$$

The cumulative risk may be interpreted as the probability that an individual will die from the cancer of interest before a certain age (up to 80 years in our analysis) in the absence of competing causes of death [29].