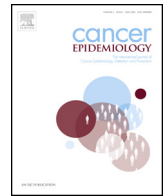




Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

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



Juan Carlos Martín-Sánchez^a, Ramon Clèries^{b,c}, Cristina Lidón^a, Luís González-de Paz^{d,e}, Nuno Lunet^{f,g}, Jose M. Martínez-Sánchez^{a,h,i,*}

^a Biostatistics Unit, Department of Basic Sciences, Universitat Internacional de Catalunya, Sant Cugat del Vallès, Spain

^b Plan for Oncology of the Catalan Government, L'Hospitalet de Llobregat, Spain

^c Department of Clinical Sciences, School of Medicine, Universitat de Barcelona, Barcelona, Spain

^d Centre Atenció Primària Les Corts. Transverse Group for Research in Primary Care, IDIBAPS, Barcelona, Spain

^e Public Health Unit, Department of Medicine, Universitat Internacional de Catalunya, Sant Cugat del Vallès, Spain

^f EPIUnit – Instituto de Saúde Pública da Universidade do Porto (ISPUP), Porto, Portugal

^g Department of Clinical Epidemiology, Predictive Medicine and Public Health, University of Porto Medical School, Porto, Portugal

^h Tobacco Control Unit, Cancer Prevention and Control Programme, Catalan Institute of Oncology-ICO, L'Hospitalet de Llobregat, Spain

ⁱ Cancer Control and Prevention Group, Bellvitge Biomedical Research Institute-IDIBELL, L'Hospitalet de Llobregat, Spain

ARTICLE INFO

Article history:

Received 8 February 2016

Received in revised form 11 April 2016

Accepted 30 May 2016

Available online 16 June 2016

Keywords:

Lung cancer

Breast cancer

Projections & predictions

Bayesian models

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.

© 2016 Elsevier Ltd. All rights reserved.

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

* Corresponding author at: Biostatistics Unit, Department of Basic Sciences, Universitat Internacional de Catalunya, Carrer de Josep Trueta s/n 08195 Sant Cugat del Vallès, Barcelona, Spain.

E-mail address: jmmartinez@uic.es (Dr. J.M. Martínez-Sánchez).

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]:

$$\frac{\mu_{i,t}}{Y_{i,t}} = e^{(\alpha_i + \beta_i(t-t_0))},$$

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 $\alpha_i \sim \text{normal}(0, \tau_\alpha)$ and $\beta_i \sim \text{normal}(0, \tau_\beta)$ with precision parameters τ_α and τ_β having flat hyper-priors $\tau_\alpha \sim \text{gamma}(\psi, \phi)$ and $\tau_\beta \sim \text{gamma}(\psi, \phi)$, 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].

Table 1 Observed rates (per 100,000 people years) of lung and breast cancer mortality (1980–2013) and median (95% credible intervals) for the projected rates (per 100,000 people years) in the period 2014–2020.

Type of rate	Observed					Projected						
	1980	2007	2013	2014	2015	2016	2017	2018	2019	2020		
Crude rate	LC 6.2	12.3	17.3	18.4 (17.6–19.1)	19.6 (18.7–20.5)	20.9 (19.9–21.9)	22.4 (21.2–23.6)	24.0 (22.6–25.4)	25.7 (24.1–27.4)	27.6 (25.7–29.6)		
	BC 19.0	26.4	27.3	27.7 (26.8–28.5)	27.9 (27.0–28.9)	28.2 (27.2–29.3)	28.5 (27.4–29.7)	28.8 (27.5–30.0)	29.0 (27.7–30.4)	29.2 (27.7–30.7)		
Age-standardized rate	LC 4.4	7.0	9.3	9.8 (9.4–10.2)	10.3 (9.8–10.8)	10.9 (10.3–11.5)	11.5 (10.8–12.2)	12.1 (11.4–12.9)	12.9 (12.0–13.8)	13.6 (12.6–14.7)		
	BC 15.3	14.5	13.5	13.3 (12.8–13.8)	13.2 (12.7–13.7)	13.1 (12.5–13.6)	12.9 (12.4–13.5)	12.8 (12.2–13.4)	12.7 (12.0–13.4)	12.6 (11.9–13.3)		
45–54 y	LC 5.1	17.2	17.6	18.2 (16.3–20.0)	18.4 (16.4–20.5)	18.6 (16.3–20.9)	18.8 (16.4–21.4)	19.0 (16.4–22.0)	19.2 (16.3–22.6)	19.4 (16.2–23.0)		
	BC 33.8	27.2	25.4	24.6 (22.5–26.8)	24.3 (22.1–26.6)	24.0 (21.6–26.4)	23.6 (21.1–26.3)	23.3 (20.7–26.1)	23.0 (20.2–26.0)	22.6 (19.6–25.8)		
55–64 y	LC 11.3	21.1	37.0	40.3 (37.1–43.7)	44.0 (40.2–48.1)	48.2 (43.6–53.1)	52.7 (47.2–58.5)	57.6 (51.2–64.8)	63.0 (55.3–71.6)	69.0 (59.7–79.3)		
	BC 44.3	42.5	39.7	37.7 (34.8–40.7)	37.3 (34.2–40.4)	36.8 (33.6–40.2)	36.4 (33.0–40.1)	36.0 (32.3–40.0)	35.7 (31.8–39.9)	35.3 (31.1–39.8)		
65–74 y	LC 25.2	28.2	41.7	43.7 (40.0–47.6)	46.7 (42.5–51.2)	49.9 (44.9–55.1)	53.2 (47.5–59.4)	56.8 (50.2–64.2)	60.6 (53.0–69.2)	64.7 (55.9–74.8)		
	BC 52.8	55.8	51.2	50.1 (46.5–53.9)	49.9 (45.9–54.0)	49.5 (45.2–53.9)	49.1 (44.6–54.0)	48.8 (43.8–54.0)	48.5 (43.2–54.0)	48.0 (42.4–54.1)		
≥75 y	LC 41.1	47.8	57.2	57.8 (54.0–61.7)	59.6 (55.4–64.0)	61.2 (56.4–66.2)	62.9 (57.5–68.5)	64.5 (58.6–71.1)	66.1 (59.5–73.3)	67.5 (60.3–75.7)		
	BC 80.3	113.6	115.7	119.1 (113.7–124.5)	120.4 (114.6–126.5)	120.7 (114.2–127.4)	121.6 (114.5–128.9)	122.1 (114.4–130.2)	121.7 (113.3–130.5)	120.8 (111.9–130.2)		

LC: lung cancer, BC: breast cancer.

3. Results

Table 1 and Fig. 1 show the LC and BC mortality rates in women between 1980 and 2013 and the projections for 2014–2020.

The LC mortality rates clearly increased during the period 1980–2013 (Table 1) starting in the mid-1990s (Fig. 1). In 2007–2013, the period used to estimate the model, all rates also increased approximately 5% annually (CR: 12.3 to 17.3 and ASR: 7.0 to 9.3), whereas the maximal increase in age-specific rates was 10% for the 55–64 age group (21.1 to 37.0).

BC mortality rates were lower in 2013 than in 1980 (with the exception of the CR and for those aged ≥ 75 years). The rates increased until the first half of the 1990s but decreased thereafter (Fig. 1). During the period 2007–2013 there were small variations not greater than 10%, with an increased CR (26.4 to 27.3) and age-specific rates for those aged ≥ 75 years (113.6 to 115.7), the others decreasing approximately 1.5% annually.

The predicted LC mortality for 2014–2020 showed an increase. The ASR would exceed 10 (95% CI 10.3–11.5) in 2016 and would be just under 15 in 2020 (95% CI 12.6–14.7). The CR would exceed 20 in 2017 (95% CI 21.2–23.56), almost reaching 30 in 2020 (95% CI 25.7–29.6). The predicted BC mortality indicates a slow increase in the CR, which will be below 30 until 2016 (95% CI 27.2–29.3) but will be greater later (2020: 95% CI 27.7–30.7), and a slow decrease in the ASR, which will be over 12 until 2018 (95% CI 12.2–13.4) (Table 1).

Fig. 2 shows the different patterns in the APC according to age group for both cancers, modeled from observations during the period 2007–2013. The 95% CI shows an increase of over 3% and up to 12% in LC for the 55–74 age group. The APC in BC mortality according to age group has an estimate below 0 with a 95% CI which includes 0, the exceptions being the age group 80–84, where the estimate is above 0, and the age group 45–49 where the 95% CI does not include 0.

Table 2 shows the LC/BC ratios for all predicted mortality rates reported as the median and 95% CI. LC will reach and even exceed BC in the next few years, but not in all predicted rates. The 95% CI was >1 for the 55–64 age group from 2015 (95% CI 1.05–1.34), and the 65–74 age group from 2019 (95% CI 1.05–1.49). The 95% CI included 1 for the CR from 2020 (95% CI 0.86–1.03), the ASR from 2018 (95% CI 0.88–1.03), and the 45–54 age group from 2019 (95% CI 0.68–1.03). The 95% CI ratio was <1 from 2014 to 2020 in the age group ≥ 75 years (2020: 95% CI 0.49–0.64).

Fig. 3 shows the cumulative risk of BC and LC death up to 80 years of age, comparing the years 2013 and 2020. The cumulative risk of BC death was higher than that of LC in all age groups during 2013, reaching 2.23% at up to 80 years of age (Fig. 3a). On the basis of the predicted age-specific BC and LC mortality rates in 2020, the cumulative risk of LC death could surpass that of BC for those between 55 and 75 years of age (Fig. 3b). The difference in the cumulative risks of death between the years 2020 and 2013 shows a decreasing risk of BC death in all age groups but an increasing cumulative risk of LC death beyond 45 years of age (Fig. 3c).

4. Discussion

The predictions indicate that the mortality rate for LC will reach and/or exceed the mortality rate for BC in the next few years, and that LC will become the leading type of cancer mortality for women in Spain. If not for all ages, it has been well established for women 55–64 years of age (expected from 2014). A study in the European Union predicted that LC mortality would slightly exceed BC mortality in 2015, not in the number of deaths but in the ASR, but for Spain BC mortality is still predicted to be greater than LC

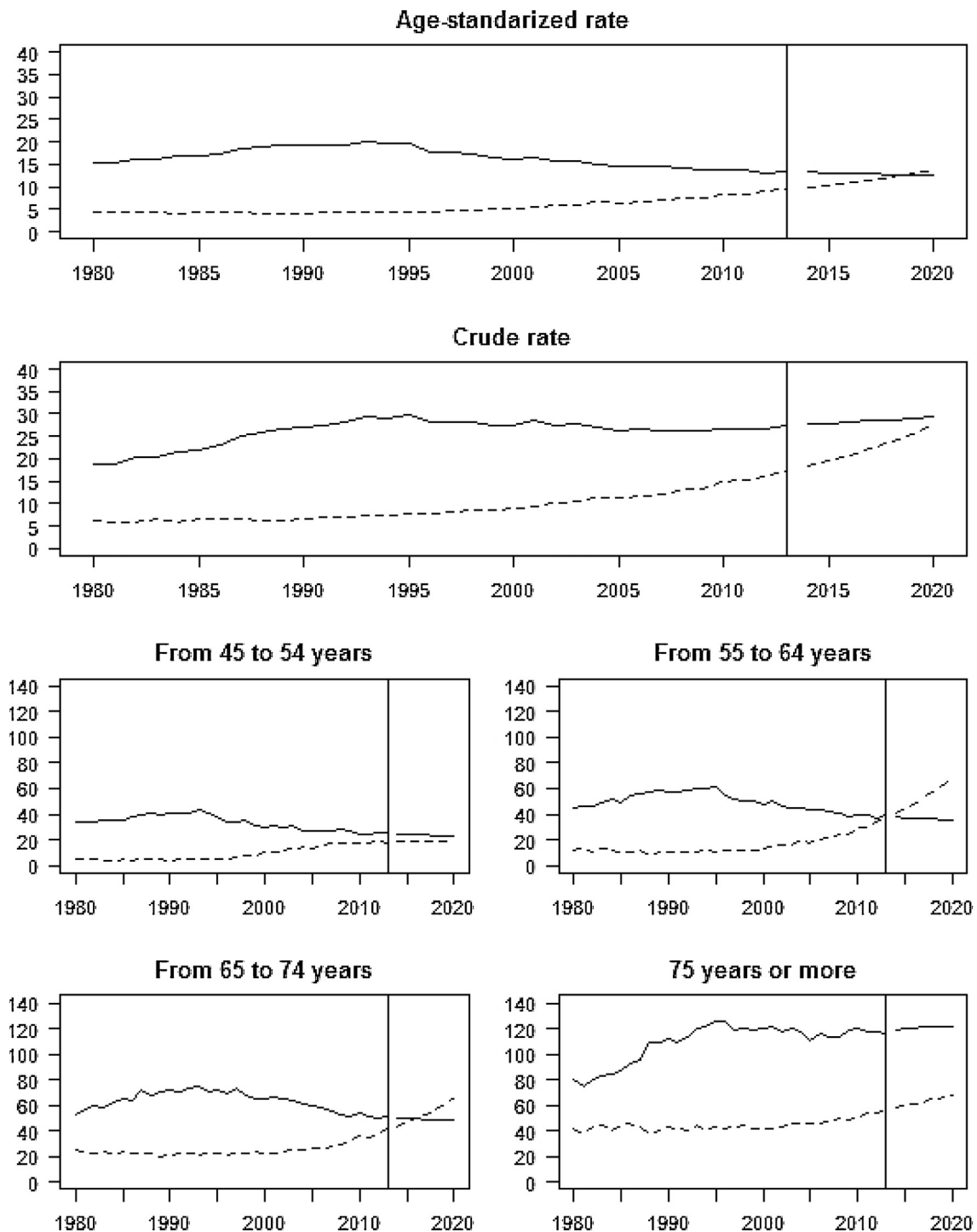


Fig. 1. Observed rate (per 100,000 people years) of breast cancer (continuous lines) and lung cancer (dashed lines) mortality (1980–2013) and median for the projected rates (per 100,000 people years) in the period 2014–2020.

mortality. This study uses a similar model but obtained the years used from a JoinPoint Regression [15].

Since the 1980s, BC has been the first cause of death from cancer in women in Spain, but mortality rates decreased by 1.8% from 1997 to 2006 [30]. This downward trend can be attributed to treatment and screening programs. Since the 1980s there have been continuous advancements in treatment, such as the use of adjuvant therapy to reduce the risk of BC recurrence [31], new chemotherapy drugs to slow cancer growth [32], and the introduction of sentinel-lymph-node biopsy to assess BC spread [33]. Currently, clinicians approach

this disease with a rapidly evolving multidisciplinary treatment [34]. BC screening is the second key factor to explain the decrease in BC mortality. The age group considered for breast screening in Spain is 45 or 50 to 70 years depending on the autonomous community (AC), and the geographical coverage is 100% according to international recommendations. Screening was initiated in 1990 in Navarre and progressively implemented in all the ACs. Women of 50–64 years of age are included in all programs, starting at 45 years or finishing at 69 years in some ACs. The mean overall participation was 67.0% [35]. Spain currently has a lower BC mortality rate among

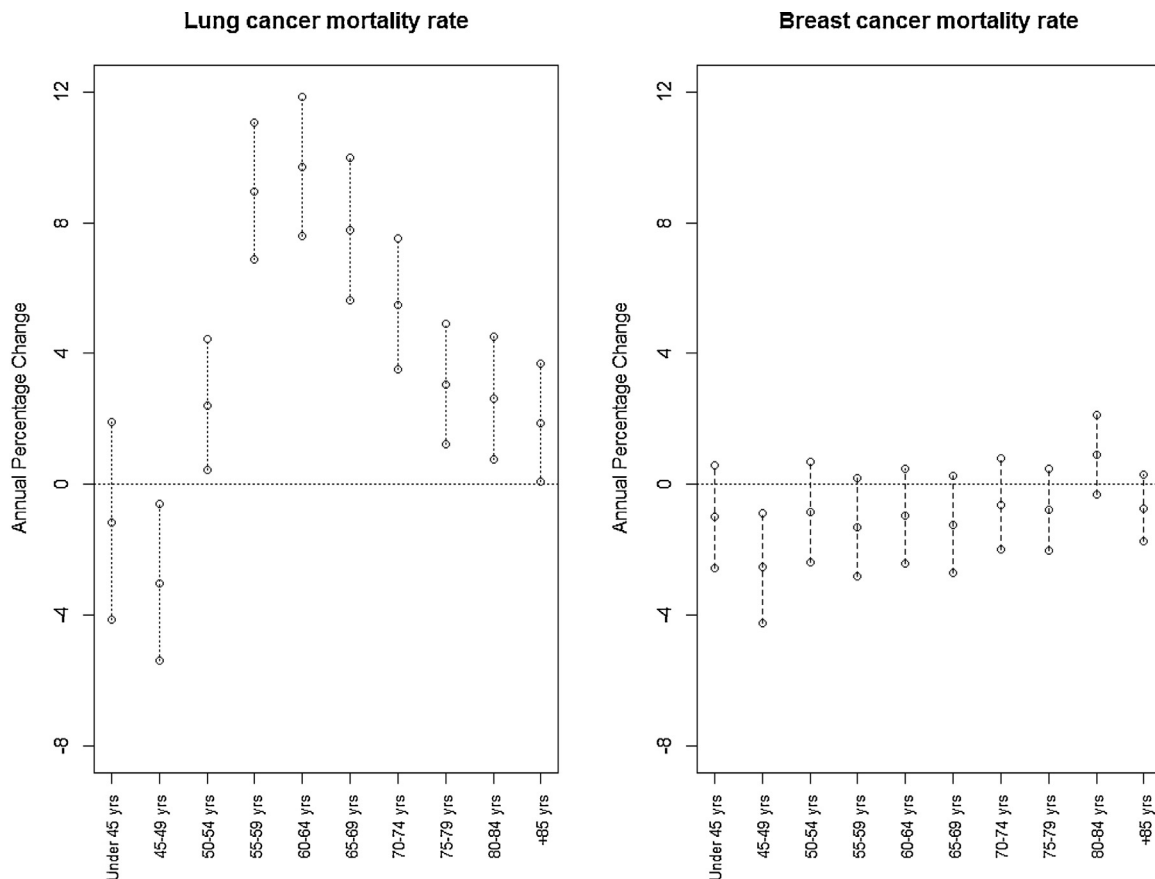


Fig. 2. Median and 95% credible interval of annual percentage change in lung cancer and breast cancer mortality by age group in the period 2007–2013.

the European countries [18,36]. Undoubtedly, the coverage of BC screening has been successful and screening should be used in other diseases when possible.

On the other hand, the breast cancer mortality is still increasing in older women (≥ 75 years), as previously observed in other studies [37]. In the analysis by 5-year age groups, mortality rates are increasing only in the 80–84 years group, though not significantly. The difference in the patterns observed between women 50–74 years old and those over 75 years could be partially explained by the different years of implementation of breast cancer screening programs across 17 autonomous regions of Spain [37] and the lower participation rate in the first years of breast cancer screening in Spain [38]. As a result of this, a smaller proportion of older women may have benefited from the breast screening program, which may result in less favorable mortality trends.

The main risk factor for LC is tobacco consumption [39]. Time trends for tobacco use could predict the incidence and mortality of LC [40]. However, there is a gap in time between the beginning of smoking habits and the diagnosis of LC; when smoking prevalence

decreases the mortality due to LC may still increase because of the effect of previous smoking. The gap between the smoking prevalence rates and the smoking-caused mortality is estimated to be approximately 30–40 years [40], with the highest correlation for women with a lag of 40 years [41]. The actual increase in LC mortality rates among women could be explained by 40 years having passed since the 1970s, when the prevalence of tobacco use increased the most, from 5.8% in 1970 to 15.0% in 1980 [42], reaching 26.5% in 1990 and leveling off until the 2000s, when it started to decrease [41]. The gap of 40 years and the maximum smoking prevalence achieved in the early 1990s indicate that the maximum age-adjusted mortality could be achieved around 2030. This is in line with our projections of increasing age-adjusted rates in the analyzed period (2014–2020).

No population screening program is currently available for LC in Spain [43]. If such a program was implemented, the usual target population would be actual smokers 50–74 years of age who smoke at least 20 cigarettes per day. The program could also include ex-smokers from the last 10–15 years. This approach would include approximately 400,000 women and 900,000 men [10]. The

Table 2

Median (95% credible intervals, 95% CIs) for the ratio of lung cancer and breast cancer mortality for the projected rates in the period 2014–2020.

Type of rate	2014	2015	2016	2017	2018	2019	2020
Crude rate	0.66 (0.63–0.70)	0.70 (0.66–0.74)	0.74 (0.70–0.79)	0.78 (0.73–0.84)	0.83 (0.77–0.90)	0.88 (0.82–0.96)	0.94 (0.86–1.03)
Age-standardized rate	0.74 (0.70–0.78)	0.78 (0.73–0.83)	0.83 (0.78–0.89)	0.89 (0.83–0.96)	0.95 (0.88–1.03)	1.01 (0.93–1.11)	1.08 (0.99–1.19)
45 to 54 y	0.74 (0.64–0.84)	0.76 (0.65–0.87)	0.77 (0.66–0.91)	0.79 (0.67–0.94)	0.82 (0.67–0.98)	0.84 (0.68–1.03)	0.85 (0.69–1.07)
55 to 64 y	1.07 (0.96–1.20)	1.18 (1.05–1.34)	1.31 (1.15–1.49)	1.45 (1.25–1.67)	1.60 (1.37–1.88)	1.77 (1.49–2.10)	1.96 (1.62–2.36)
65 to 74 y	0.87 (0.78–0.98)	0.94 (0.83–1.06)	1.01 (0.88–1.15)	1.08 (0.93–1.26)	1.16 (0.99–1.37)	1.25 (1.05–1.49)	1.35 (1.12–1.63)
≥ 75 y	0.49 (0.45–0.53)	0.49 (0.45–0.53)	0.51 (0.46–0.56)	0.52 (0.46–0.57)	0.53 (0.47–0.59)	0.54 (0.48–0.62)	0.56 (0.49–0.64)

Bolded if the 95% credible interval is over 1.

Italics if the 95% credible interval is under 1.

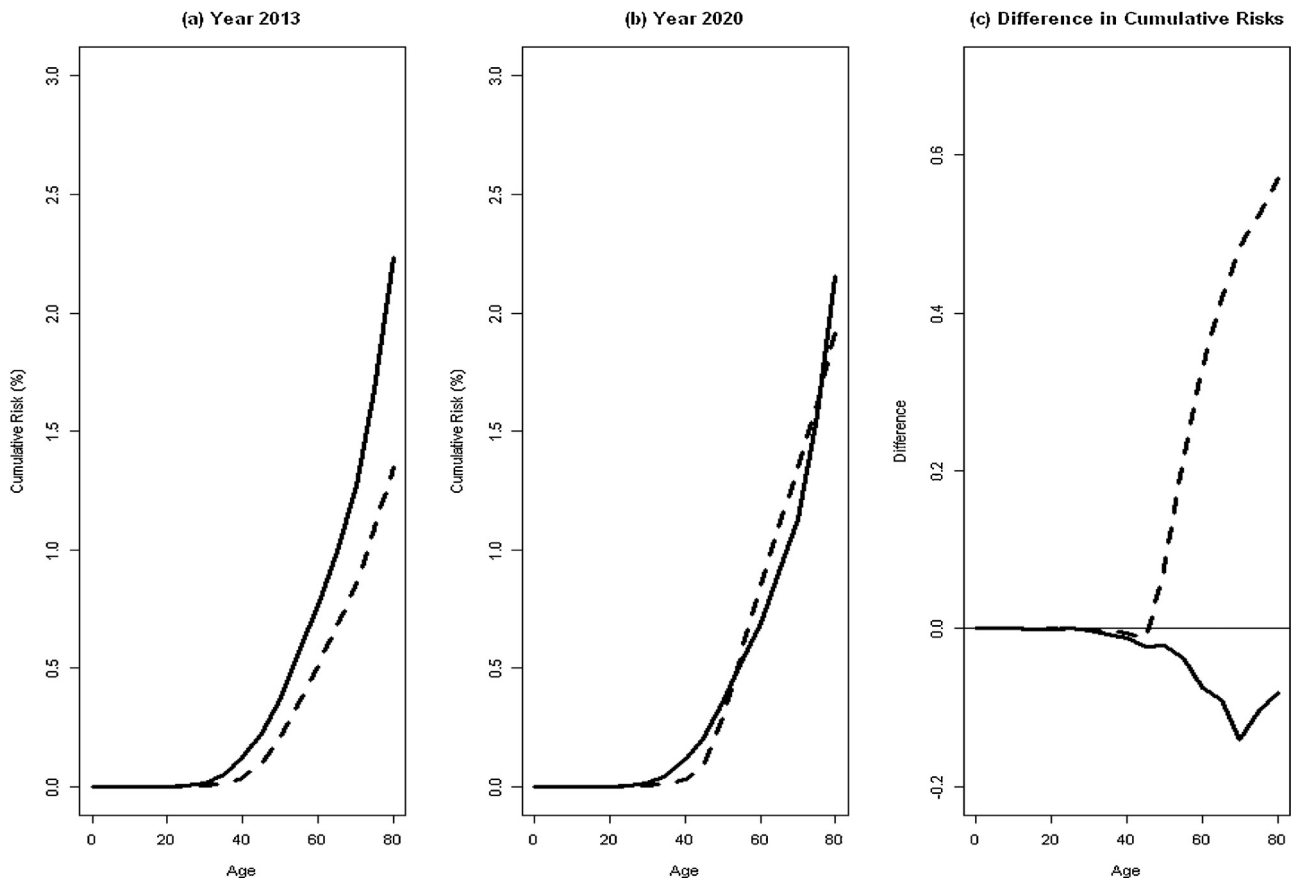


Fig. 3. Cumulative risk of death from breast cancer (continuous line) and lung cancer (dashed line) up to 80 years of age (2013 versus 2020).

available scientific evidence does not support the implementation of population screening programs for this type of cancer [44], but there is strong evidence for smoking cessation programs. A systematic review showed that interventions combining pharmacotherapy and behavioral support increase smoking cessation success in a wide range of populations, in comparison to the usual care [45]. The systematic review included some Spanish studies which showed good results after 1 year of treatment [46,47] – one study with diabetics and the other with the general population – and in both cases more than 20% of the sample intervened was not smoking 1 year later. Even when the program is successful in a minority of the participants, there is an effect on mortality [48]. Also, former smokers who stopped less than 10 years previously have a risk of LC decreased by one third [49] and a similar risk to non-smokers after more than 20 years of not smoking [50]. In this sense, the use of electronic cigarettes (e-cigarettes) could be a useful tool to quit or reduce tobacco consumption. However, current scientific evidence on the effectiveness of e-cigarettes for quitting smoking is contradictory and scarce. A meta-analysis [51] based on 13 studies (two randomized controlled trials and 11 cohort studies) has failed to prove that e-cigarettes help smokers to stop smoking in the long term compared with placebo e-cigarettes, and that e-cigarettes could help prevent relapse among former smokers or that they could promote smoking cessation among current smokers. Furthermore, other studies [52] found a high percentage of “dual” use (i.e. use of e-cigarettes plus use of other tobacco products), including in Spain [53,54].

Taking advantage of the infrastructure and coverage of BC screening, we recommend including initiatives in this program to reduce smoking, the main risk factor for LC, among women.

Moreover, breast cancer screening could be an appropriate “teachable moment” [55] to promote healthy behaviors such as quitting smoking among women. For these reasons, we suggest that combining both programs (tobacco cessation and breast cancer screening) could be useful in reducing lung cancer. These initiatives should not be targeted for early detection of the disease, but for the primary prevention of the disease. Most ex-smokers quit smoking without treatment, but there are effective treatments for smokers who need help [56]. Brief counseling and behavioral interventions can be effective, and there are also effective medications, such as nicotine replacement products. Both counseling and medication are effective, even more so when used together [56]. A limitation of this intervention is that it could not avoid the majority of the deaths by LC in the first years, as the women involved may have been exposed to tobacco for decades. However, starting the intervention at 45 years of age when the risk is starting to increase should be beneficial in the long term: some deaths by LC will be avoided, and some others will be delayed. While there is no proposal of a better LC screening program, especially with a smaller number of false-positive tests, smoking cessation remains the most important approach to reduce LC mortality.

The strength of this study is the validity and reliability of the data recorded by the INE. Some studies on the accuracy of cancer death have shown that these data cannot always be trusted, but BC and LC are among the well-certified cancers, with a confirmation rate and a detection rate >90% [57]. The mortality registry is complete and covers all Spanish territories. This avoids the inherent problems of working with a sample. A weakness of the study is the use of mortality as an indicator of the presence of the disease, which would be accurate for a cancer with a low survival rate (lung) but not for one

with a high survival rate (breast) [58]. Therefore the outcome of interest must be mortality, and we should not consider it a replacement for the incidence, as these data are not available. We used a simple log-linear Poisson model to obtain projections in which the main assumption of this model is that log-linear trends will continue into the future [24]. 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 in practice present difficulties in interpretation, with wider credible or prediction intervals than those based on simple linear or log-linear models [24]. In addition, we performed short-term projections, up to the year 2020, and a simple log-linear model would perform better than other models in this particular situation [26,59].

In conclusion, the LC mortality rates are expected to exceed the rates for BC in the next few years. The BC screening program in Spain could be a helpful tool, as it has full coverage in the territory, a high participation rate, and is indicated in an age group that coincides with the moment when LC mortality strongly increases. BC screening offers a good opportunity to implement measures to help dependent women smokers quit smoking, in addition to public health national campaigns.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Source of funding

This project was funded by the Instituto de Salud Carlos III, Government of Spain (RTICC, RD12/0036/0053), and by the Ministry of Universities and Research, Government of Catalonia (grant 2009SGR192). The funding organizations had no role in the study design, data collection, analysis, or interpretation, writing of the report, or the decision to submit it for publication.

Authorship contribution

JMMS conceived the study. JCMS collected the data, prepared the database, and analyzed the data. JCMS drafted the manuscript, which was critically revised by JMMS. All authors substantially contributed to interpreting the data and revising the manuscript. All authors approved the final version of the manuscript.

References

- [1] B. Stewart, C. Wild (Eds.), *World Cancer Report*, International Agency for Research on Cancer, Lyon, France, 2014, pp. 2014.
- [2] World Health Organization, *Cancer*. Fact sheet n° 297, (2015). Available from: <http://www.who.int/mediacentre/factsheets/fs297/en/> (accessed 11.04.16).
- [3] J. Ferlay, H.R. Shin, F. Bray, D. Forman, C. Mathers, D.M. Parkin, Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008, *Int. J. Cancer* 127 (2010) 2893–2917.
- [4] C. Allemani, H.K. Weir, H. Carreira, R. Harewood, D. Spika, X.-S. Wang, et al., Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2), *Lancet* 385 (2015) 977–1010.
- [5] World Health Organization, *Breast Cancer: detection and control*, (2015). Available from: <http://www.who.int/cancer/detection/breastcancer/en/> (accessed 11.04.16).
- [6] National Cancer Institute, *Cancer of the Lung and Bronchus – SEER Stat Fact Sheets*, (2015). Available from: <http://seer.cancer.gov/statfacts/html/lungb.html> (accessed 11.04.16).
- [7] Cancer Research UK, *Lung Cancer Survival Statistics*, (2015). Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer/survival> (accessed 11.04.16).
- [8] S. Francisci, P. Minicozzi, D. Pierannunzio, E. Ardanaz, A. Eberle, T.K. Grimsrud, et al., Survival patterns in lung and pleural cancer in Europe 1999–2007: Results from the EUROCARE-5 study, *Eur. J. Cancer* 51 (2015) 2242–2253.
- [9] D.R. Aberle, A.M. Adams, C.D. Berg, W.C. Black, J.D. Clapp, R.M. Fagerstrom, et al., Reduced lung-cancer mortality with low-dose computed tomographic screening, *N. Engl. J. Med.* 365 (2011) 395–409.
- [10] A. Rubio, A., Ravina, *Cribado de cáncer de pulmón*, Madrid, 2007.
- [11] P.B. Bach, M.J. Kelley, R.C. Tate, Screening for lung cancer: a review of the current literature, *Chest* 123 (2003) 725–82.
- [12] V.A. Moyer, Screening for lung cancer: u.S. preventive services task force recommendation statement, *Ann. Intern. Med.* 160 (2014) 330–338.
- [13] C. Bosetti, P. Bertuccio, M. Malvezzi, F. Levi, L. Chatenoud, E. Negri, et al., Cancer mortality in Europe 2005–2009, and an overview of trends since 1980, *Ann. Oncol.* 24 (2013) 2657–2671.
- [14] J. Lortet-Tieulent, E. Renteria, L. Sharp, E. Weiderpass, H. Comber, P. Baas, et al., Convergence of decreasing male and increasing female incidence rates in major tobacco-related cancers in Europe in 1988–2010, *Eur. J. Cancer* 51 (2013) 1144–1163.
- [15] M. Malvezzi, P. Bertuccio, T. Rosso, M. Rota, F. Levi, C. La Vecchia, et al., European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? *Ann. Oncol.* (2015) 1–8.
- [16] M.J. Sánchez, T. Payer, R. De Angelis, N. Larrañaga, R. Capocaccia, C. Martinez, et al., Cancer incidence and mortality in Spain: estimates and projections for the period 1981–2012, *Ann. Oncol.* 21 (2010) 30–36.
- [17] J. Ferlay, I. Soerjomataram, M., Ervik, R., Dikshit, S., Eser, C. Mathers, et al., GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase., Lyon, Fr. *Int. Agency Res. Cancer.* 11 (2013). Available from: <http://globocan.iarc.fr> (accessed 11.04.16).
- [18] P. Autier, M. Boniol, C. La Vecchia, L. Vatten, A. Gavin, C. Héry, et al., Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database, *BMJ* 341 (2010) c3620.
- [19] IMSERSO, *Envejecimiento activo. Libro blanco*, 2011. Available from: http://www.imserso.es/InterPresent1/groups/imserso/documents/binario/8088_8089libroblancoenv.pdf. (accessed 11.04.16)
- [20] Global Health Observatory. WHO, *Life expectancy*, (2016). Available from: http://www.who.int/gho/mortality_burden_disease/life_tables/en/ (accessed 11.04.16).
- [21] Instituto Nacional de Estadística (2015). Available from: www.ine.es (accessed 11.04.16).
- [22] O.B. Ahmad, C. Boschi-pinto, A.D. Lopez, C.J. Murray, R. Lozano, I. Mie, Age standardization of rates: a new who standard (2001).
- [23] T. Dyba, T. Hakulinen, Comparison of different approaches to incidence prediction based on simple interpolation techniques, *Stat. Med.* 19 (2000) 1741–1752.
- [24] R. Cléries, J. Ribes, M. Buxo, A. Amejjide, R. Marcos-Gragera, J. Galceran, et al., Bayesian approach to predicting cancer incidence for an area without cancer registration by using cancer incidence data from nearby areas, *Stat. Med.* 31 (2012) 978–987.
- [25] J.C. Martín-Sánchez, R. Cléries, C. Lidón-Moyano, L. Gonzalez-de Paz, J.M. Martínez-Sánchez, Differences between men and women in time trends in lung cancer mortality in Spain (1980–2013), *Arch. Bronconeumol.* (2016) (in press).
- [26] J. Valls, G. Castellà, T. Dyba, R. Cléries, Selecting the minimum prediction base of historical data to perform 5-year predictions of the cancer burden: the GoF-optimal method, *Cancer Epidemiol.* 39 (2015) 473–479.
- [27] R. Development Core Team, *R: A Language and Environment for Statistical Computing*, R Foundation for Statistical Computing, 2003.
- [28] S. Sturtz, U. Ligges, A. Gelman, *R2WinBUGS: a package for running WinBUGS from R*, *J. Stat. Softw.* 12 (2005) 1–16.
- [29] B.N. Breslow, N. Day, *New York Toronto delhi bombay Calcutta madras karachi kuala lumpur Singapore Hong Kong tokyo. STATISTICAL METHODS IN CANCER RESEARCH VOLUME II – THE DESIGN AND ANALYSIS OF COHORT STUDIES*, *Int. Agency Res. Cancer.* 150 (1987).
- [30] A. Cabanes Domenech, B. Perez-Gamez, N. Aragonés, M. Pollán, G. López-Abente, *La situación del cáncer en España, 1975–2006*, Instituto de Salud Carlos III, Madrid, 2009.
- [31] M. Baum, D.M. Brinkley, J.A. Dossett, K. McPherson, J.S. Patterson, R.D. Rubens, et al., Improved survival among patients treated with adjuvant tamoxifen after mastectomy for early breast cancer, *Lancet* 2 (1983) 450.
- [32] F.A. Holmes, R.S. Walters, R.L. Theriault, A.D. Forman, L.K. Newton, M.N. Raber, et al., Phase II trial of taxol, an active drug in the treatment of metastatic breast cancer, *J. Natl. Cancer Inst.* 83 (1991) 1797–1805.
- [33] J.J. Albertini, G.H. Lyman, C. Cox, T. Yeatman, L. Balducci, N. Ku, et al., Lymphatic mapping and sentinel node biopsy in the patient with breast cancer, *JAMA* 276 (1996) 1818–1822.
- [34] S. Rajan, J. Foreman, M.G. Wallis, C. Caldas, P. Britton, Multidisciplinary decisions in breast cancer: does the patient receive what the team has recommended? *Br. J. Cancer.* 108 (2013) 2442–2447.
- [35] N. Asuncion, D. Salas, R. Zubizarreta, R. Almazán, J. Ibáñez, M. Ederla, et al., Cancer screening in Spain, *Ann. Oncol.* 21 (2010) 43–51.
- [36] J. Amaro, M. Severo, S. Vilela, S. Fonseca, F. Fontes, C. La Vecchia, et al., Patterns of breast cancer mortality trends in Europe, *Breast* 22 (2013) 244–253.
- [37] C. Vidal Lancis, J.M. Martínez-Sánchez, M.M. Mazon, M.P. Tuser, Breast cancer mortality trend in Spain and its autonomous communities during the period 1980–2005, *Rev. Esp. Salud Pública.* 84 (2010) 53–59.
- [38] S. Esnaola, E., Elorriaga, E., Aldasoro, A., Bacigalupe, M. de Diego, G. Sarriguarte, et al., Evolución de la participación y las desigualdades sociales en los cribados de cáncer de mama y de cáncer de cuello uterino en la CAPV, 1992–2013., *Vitoria-Gasteiz*, 2015. Available from: http://www.osakidetza.euskadi.eus/contenidos/informacion/osagin/es_profesio/adjuntos/cribado_mama_cito_cas.pdf (accessed 11.04.16).

- [39] World Health Organization, Cancer Prevention, (2015). Available from: <http://www.who.int/cancer/prevention/en/> (accessed 11.04.16).
- [40] A. Lopez, N. Collishaw, T. Piha, A descriptive model of the cigarette epidemic in developed countries, *Tob. Control.* 3 (1994) 242–247.
- [41] U. Bilal, E. Fernández, P. Beltran, A. Navas-Acien, F. Bolumar, M. Franco, Validation of a method for reconstructing historical rates of smoking prevalence, *Am. J. Epidemiol.* 179 (2014) 15–19.
- [42] E. Fernández, A. Schiaffino, M. García, E. Saltó, Prevalencia del consumo de tabaco en España entre 1945 y 1995. Reconstrucción a partir de las Encuestas Nacionales de Salud, *Med. Clin. (Barc.)* 120 (2003) 14–16.
- [43] Red de Programas de Cribado de Cancer, Cancer de Pulmon, (2015). Available from: <http://www.cribadocancer.es/index.php/otros-cribados/cancer-pulmon> (accessed 01.01.15).
- [44] M.K. Gould, Lung cancer screening and elderly adults: do we have sufficient evidence, *Ann. Intern. Med.* 161 (2014) 672–673.
- [45] L.F. Stead, T. Lancaster, Combined pharmacotherapy and behavioural interventions for smoking cessation, *Cochrane Database Syst. Rev.* 10 (2012) CD008286.
- [46] S. Perez-Tortosa, L. Roig, J.M. Manresa, C. Martin-Cantera, E. Puigdomenech, P. Roura, et al., Continued smoking abstinence in diabetic patients in primary care: a cluster randomized controlled multicenter study, *Diabetes Res. Clin. Pract.* 107 (2015) 94–103.
- [47] F. Rodriguez-Artalejo, P. Lafuente Urdinguio, P. Guallar-Castillon, P. Garteizurrekoa, O. Sainz Martinez, J.I. Diez Azcarate, et al., One year effectiveness of an individualised smoking cessation intervention at the workplace: a randomised controlled trial, *Occup. Environ. Med.* 60 (2003) 358–363.
- [48] N.R. Anthonisen, M.A. Skeans, R.A. Wise, J. Manfreda, R.E. Kanner, J.E. Connett, The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial, *Ann. Intern. Med.* 142 (2005) 233–239.
- [49] R. Peto, S. Darby, H. Deo, P. Silcocks, E. Whitley, R. Doll, Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies, *BMJ* 321 (2000) 323–329.
- [50] K. Wakai, N. Seki, A. Tamakoshi, T. Kondo, Y. Nishino, Y. Ito, et al., Decrease in risk of lung cancer death in males after smoking cessation by age at quitting: findings from the JACC study, *Jpn. J. Cancer Res.* 92 (2001) 821–828.
- [51] C. McRobbie, Electronic cigarettes for smoking cessation and reduction (Protocol), *Cochrane Libr.* 12 (2014) CD010216.
- [52] S. Carroll Chapman, L.T. Wu, E-cigarette prevalence and correlates of use among adolescents versus adults: a review and comparison, *J. Psychiatr. Res.* 54 (2014) 45–54.
- [53] J.M. Martínez-Sánchez, M. Ballbè, M. Fu, J.C. Martín-Sánchez, E. Saltó, M. Gottlieb, et al., Electronic cigarette use among adult population: a cross-sectional study in Barcelona, Spain (2013–2014), *BMJ Open* 4 (2014) 8.
- [54] C. Lidón-Moyano, J. Martínez-Sánchez, M. Fu, M. Ballbè, J. Martín-Sánchez, E. Fernandez, Prevalence and use profile of electronic cigarette in Spain (2014), *Gac. Sanit.* (2016) (in press).
- [55] C. Senore, L. Giordano, C. Bellisario, F. Di Stefano, N. Segnan, Population based cancer screening programmes as a teachable moment for primary prevention interventions. a review of the literature, *Front. Oncol.* 2 (2012) 1–10.
- [56] Centers for Disease Control and Prevention, Quitting Smoking – Smoking & Tobacco Use, (2015). Available from: http://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/quitting/index.htm (accessed 11.04.16).
- [57] B. Pérez-Gómez, N. Aragonés, M. Pollán, B. Suárez, V. Lope, A. Llácer, et al., Accuracy of cancer death certificates in Spain: a summary of available information, *Gac. Sanit.* 20 Suppl 3 (2006) 42–51.
- [58] M.D. Chirlaque, D. Salmerón, E. Ardanaz, J. Galceran, R. Martínez, R. Marcos-Gragera, et al., Cancer survival in Spain: estimate for nine major cancers, *Ann. Oncol.* 21 (2010).
- [59] T. Dyba, T. Hakulinen, Do cancer predictions work? *Eur. J. Cancer* 44 (2008) 448–453.