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Contribution of changes in demography and in the risk factors to the predicted pattern of cancer mortality among Spanish women by 2022

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ABSTRACT

Background: Changes in the burden of cancer mortality are expected to be observed among Spanish women. We predict those changes, in Spain, for breast cancer (BC), colorectal cancer (CRC), lung cancer (LC) and pancreatic cancer (PC) from 2013 to 2022.
Methods: Bayesian age–period–cohort modeling was used to perform projections of the cancer burden in 2013–2022, extrapolating the trend of cancer mortality data from 1998 to 2012. We assessed the time trends of the crude rates (CRs) during 1998–2012, and compared the number of cancer deaths between the periods 2008–2012 and 2018–2022 to assess the contribution of demographic changes and changes in the risk factors for cancer.
Results: During 1998–2012, CRs of cancer decreased for BC (0.3% per year) and increased for LC (4.7%), PC (2%) and CRC (0.7%). During 2013–2022, CRs might level off for CRC, whereas the time trends for the remaining cancers might continue at a similar pace. During 2018–2022, BC could be surpassed by CRC as the most frequent cause of cancer mortality among Spanish women, whereas LC could be the most common cause of cancer mortality among women aged 50–69 years (N/year = 1960 for BC versus N/year = 1981 for LC). Comparing 2018–2022 and 1998–2012, changes in the risk factors for cancer could contribute 37.93% and 18.36% to the burden of LC and PC, respectively, and demographic shifts – mainly due to ageing (19.27%) – will drive the burden of CRC.
Conclusions: During 2018–2022, demographic changes (ageing) and changes in risk factors could have a different impact on the lifetime risk of cancer among Spanish women.

1. Introduction

During 2012, breast cancer (BC), colorectal cancer (CRC), lung cancer (LC) and stomach cancer were the four most common cancer types amongst European women [1]. A similar pattern was observed for cancer mortality, although the fourth position of stomach cancer was surpassed by pancreatic cancer (PC) and other cancers depending on the country and the cancer incidence in that country [1,2]. However, changes in the burden of cancer mortality are expected to be observed across Europe within the next 10 years [3], due mainly to a decreasing trend of BC mortality [4]. In parallel, an increasing trend of LC was detected [1,3] suggesting that LC might surpass BC mortality in some age groups [3]. On the other hand, PC mortality has shown a striking rising trend of incidence and mortality since the beginning of 2000s [1,3]. Similar patterns were observed in certain regions of Spain until 2010, where these four cancers accounted for at least 47% of the total deaths from cancer [5–8].

To interpret changes in the trends of all these cancers, it is important to take into account changes in the risk of developing cancer in parallel with changes in demographic factors such as ageing of the population [9]. This last factor is related to a lifetime

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risk of developing cancer, which has been found to increase over time due to longer life expectancy [10]. Since Spain is predicted to be one of the world's oldest countries in 2050, with 40% of its population aged over 60 (Population Ageing and Development, 2009: www.unpopulation.org), the assessment of its cancer mortality burden and the effect of ageing is of crucial interest. The analysis of these four cancer sites provides a useful tool for planning cancer treatment and prevention programs, since mortality reduction is the main objective of the interventions based on screening and early treatment, and it is an indicator to assess the effectiveness of cancer control strategies.

We analyzed these remarkable changes of the top four cancer killers in Spain during 1998–2012 among women, and predicted their burden for 2018–2022, assessing how changes in the risk of death from cancer and changes in demographic factors may affect the number of cancer deaths in the future.

2. Materials and methods

2.1. Data

The National Institute of Statistics of the Spanish Government (INE, http://www.ine.es/) provided data on cancer mortality and age distribution of the female population for the period 1998–2012. Cancer mortality data for BC, CRC, LC and PC were arranged in three 5 year periods (1998–2002, 2003–2007, 2008–2012) and 18 5-year age groups (from 0 to 4 years to 85–89 years). Cancer codes were classified using International Classification of Diseases 10th revision, and these were C50 for BC, C33–C34 for LC, C18–C21 for CRC (colon, rectum and anus) and C25 for PC. Projections of future population counts and age distribution for the periods 2013–2017 and 2018–2022 were provided by the INE, which can project population data using rates of mortality, fertility and migration within a multiregional model [11].

2.2. Bayesian age–period–cohort modeling of the projections

We adapted the age–period–cohort modeling previously used for projecting breast cancer mortality in Spain up to 2020, considering temporal structures of model parameters [6]. For each cancer site, the annual percent change of the crude rates (CRs) during 1998–2012 and 2013–2020 was estimated through an age-drift model [6]. Details of the models used can be ound in the Supplementary material (Section 1) at the end of this paper.

2.3. Separating the contribution of the changes in demography and changes in the risk of death from cancer

Differences in the numbers of BC, CRC, LC and PC deaths across the 10-year period 2008–2012 and 2018–2022 were evaluated, separating changes due to demography and risk factors for cancer according to the method of Bashir and Estève [12] and adapting these to the Bayesian framework. For each age group, the number of deaths in 2018–2022 was broken down into those due to changes in demography (size and age distribution) and those due to changes in the risk of death from cancer using the reference period 2008–2012. We calculated the absolute net percentage of change between these two time periods as $Net(\%) = Demography(\%) + Risk(\%)$ (See Section 1 of the Supplementary material for mathematical details), and, making use of the predictive distribution of the number of deaths during 2018–2022, we presented the 95% prediction intervals (PIs) of those percentage changes. The inclusion of the 0 value within the PI of the percentage change due to any of the two additive percentages shows that the corresponding percentage might not be influencing the absolute percentage net change between periods.

3. Results

3.1. Time trends during 1998–2012

Table 1 shows the CRs and annual average of the number of deaths for the periods 1998–2002, 2003–2007 and 2008–2012, as well as their annual percentage change by age groups. The number of deaths increased for all cancers and in all age groups with the exception of BC among women aged 50–69. For this cancer, we detected a 0.7% decrease in the number of deaths and a levelling off of the CRs among women aged 69 and older. In this age group, CRC was still the cancer with the largest number of deaths, showing a rise of 0.3% of the CRs during 1998–2012. On the other hand, among women younger than 69 years, CRs of BC and CRC decreased substantially. Finally, the CRs of LC rose in all age groups, whereas for PC they rose among women older than 50 years.

Table 1
Time trends of the burden of breast, colorectal, lung and pancreatic cancer among Spanish women during the period 1998–2012 by age groups, and their corresponding median and 95% credible interval of the annual percentage change.

	Period 1998–2002			Period 2003–2007			Period 2008–2012			Annual percentage change 1998–2012								
Age group	<50	50–69	>69	<50	50–69	>69	<50	50–69	>69	<50			50–69			>69		
		(*N*)			(*N*)			(*N*)		Me	LL	UL	Me	LL	UL	Me	LL	UL
Breast	770	2111	2754	789	1957	3086	822	1970	3427	0.6%	0.2%	1.1%	−0.7%	−1.0%	−0.4%[a]	2.2%	1.9%	2.4%
Colorectal	216	1211	3563	209	1156	4084	219	1321	4532	0.1%	−0.8%	0.7%	0.9%	0.5%	1.2%	2.4%	2.2%	2.6%
Lung	236	620	1011	348	877	1281	358	1442	1610	3.8%	3.1%	4.5%	9.1%	8.6%	9.4%	4.7%	4.3%	5.1%
Pancreas	61	489	1310	82	541	1563	93	673	1901	5.2%	1.6%	7.9%	3.7%	2.9%	4.5%	4.5%	3.5%	5.7%

	Period 1998–2002			Period 2003–2007			Period 2008–2012			Annual percentage change 1998–2012								
Age group	<50	50–69	>69	<50	50–69	>69	<50	50–69	>69	<50			50–69			>69		
		(CR)			(CR)			(CR)		Me	LL	UL	Me	LL	UL	Me	LL	UL
Breast	5.9	48.5	99.2	5.6	42.2	97.1	5.5	37.7	99.6	−0.7%	−1.1%	−0.3%[a]	−2.5%	−3.0%	−2.2%[a]	0.1%	−0.4%	0.3%
Colorectal	1.7	27.8	128.3	1.5	24.9	129.1	1.5	25.3	132.1	−1.2%	−2.0%	−0.4%[a]	−1.1%	−1.5%	−0.6%[a]	0.3%	0.1%	0.5%
Lung	1.8	14.2	36.4	2.5	18.9	40.3	2.4	27.6	46.8	2.5%	1.9%	3.2%	6.9%	6.5%	7.3%	2.5%	2.2%	2.9%
Pancreas	0.7	11.1	46.1	0.8	11.5	48.9	0.8	12.1	55.3	0.1%	−0.5%	0.4%	0.1%	−0.4%	0.3%	3.8%	2.2%	4.2%

N: number of deaths (annual average); CR: crude rate per 100,000 women-years; Me: median of the estimated annual percentage change; LL: lower limit of the 95% credible interval; UL: upper limit of the 95% credible interval.
[a] Decreasing annual percentage changes.

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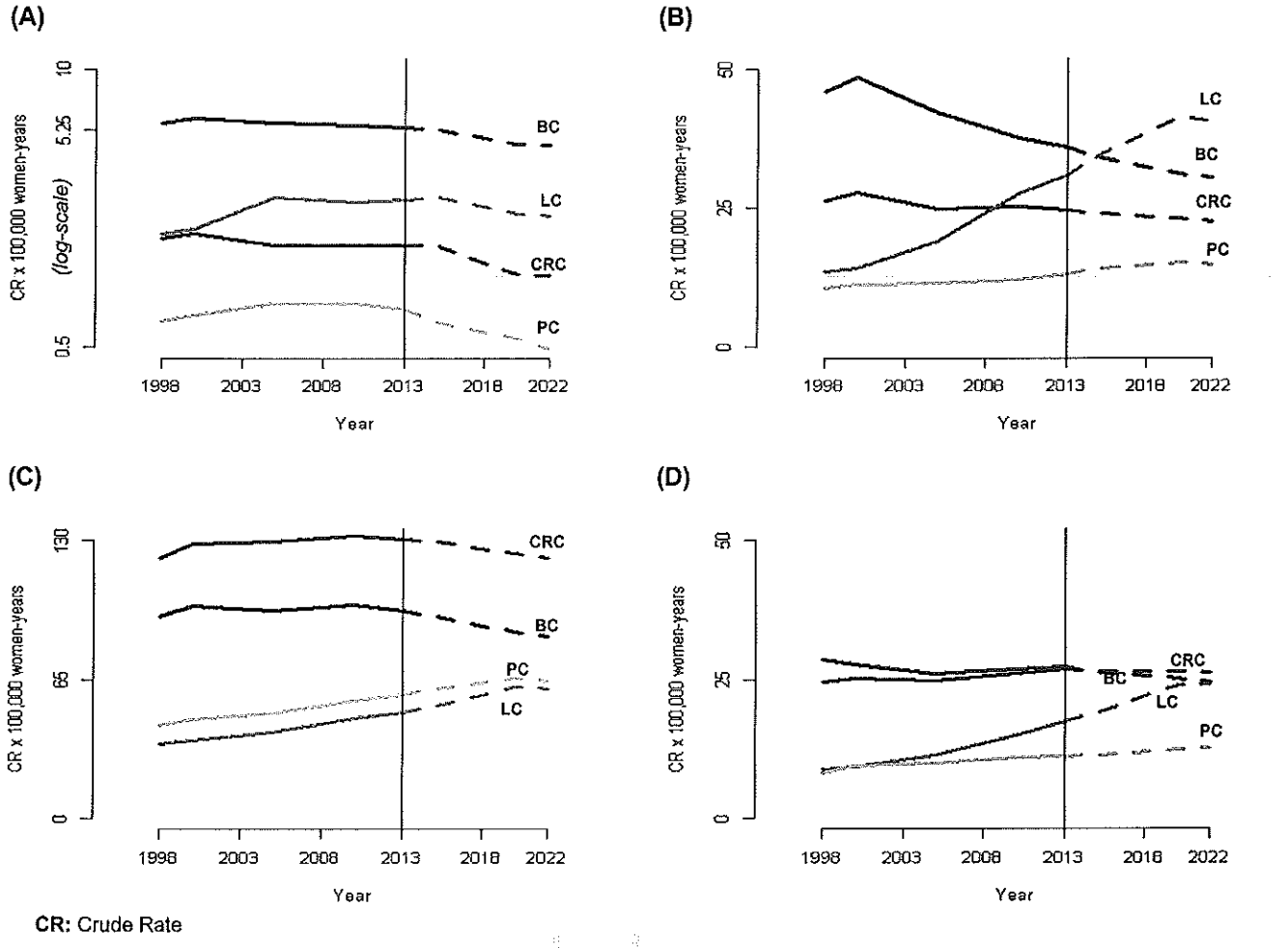

Fig. 1. Time trends of breast, colorectal, lung and pancreatic cancer mortality rates among Spanish women during the period 1998–2012 by age-groups and their projections beyond 2013: (A) women younger than 50 years, (B) women aged between 50 and 69 years, (C) women older than 69 years and (D) all age groups.

3.2. Projections for 2013–2022

Age-cohort models were those which had the best fit to data from 1998 to 2012 (see Sections 1 and 2, Table S1 and Fig. S1 of the Supplementary material) and they were used to predict the cancer burden to 2022. Table S2 of the supplementary material presents the annual average of the predicted number of deaths for the selected cancer sites during the periods 2013–2017 and 2018–2022 by age groups. The time trends of the CRs of cancer mortality during 1998–2012 and their projections up to 2022 are presented in Fig. 1. Complementary to Fig. 1, Table S2 and Table S3 of the supplementary material provide the predicted number of deaths and the CRs by selected age groups (Table S2) and the observed and predicted annual percentage change of the CRs (Table S3). Up to 2022, BC will continue to be the leading cause of cancer mortality among women younger than 50 years (Fig. 1A). Among women aged 50–69 years, BC will continue to decrease and it will be surpassed by LC between 2013 and 2017 (N/year = 1960 for BC versus N/year = 1981 for LC, Table S2) (Fig. 1B). Among women older than 69 years, CRC will continue as the leading cause of cancer mortality (Fig. 1C), and by 2022 it will overtake BC as the first cause of cancer mortality considering all age groups aggregated (Fig. 1D). In this line, the CRs of LC observed during 1998–2012 will continue to rise beyond 2013 at the same pace (1998–2012 by 4.7% per year; 2013–2017 by 4.1% per year, Table S3) as well as the CRs of PC (1998–2012 by 2.0% per year; 2013–2017 by 1.2% per year, Table S3). In contrast, BC rates might continue their decreasing trend beyond 2013 (1998–2012 by −0.3% per year; 2013–2017 by −0.8% per year, Table S3) whereas CRC rates might be stable beyond 2013.

3.3. Changes due to demography and risk of death from cancer between 2008–2012 and 2018–2022

Fig. 2 shows the age-specific burden of the selected cancers, comparing the age-specific number of deaths between the periods 2008–2012 and 2018–2022 (Fig. 2A and B) and showing the contribution of demographic factors and risk of death to the changes between those periods (Fig. 2C and D). Demographic shifts in the Spanish population will have a huge influence on the burden of BC and CRC mortality among women older than 69 years (Fig. 2C). On the other hand, the number of deaths attributable to changes in the risk of death (Fig. 2D) show three patterns: (1) the dramatic rise of the number of deaths from LC in the age group 50–69 and its levelling off beyond the age of 69, (2) the continuous rise in the number of deaths from PC due to changes in the risk of death beyond the age of 50 years, and (3) the decreasing risk of death from BC and CRC.

Table 2 summarizes the absolute percentage changes due to demography and risk of death in each cancer site comparing time period 2018–2022 with 2008–2012. For BC, the median net percentage change decline (−4.67%) would be due mainly to the decrease in the risk of death (−21.05%), since demographic changes would contribute to a median increase of 16.38%. However, the

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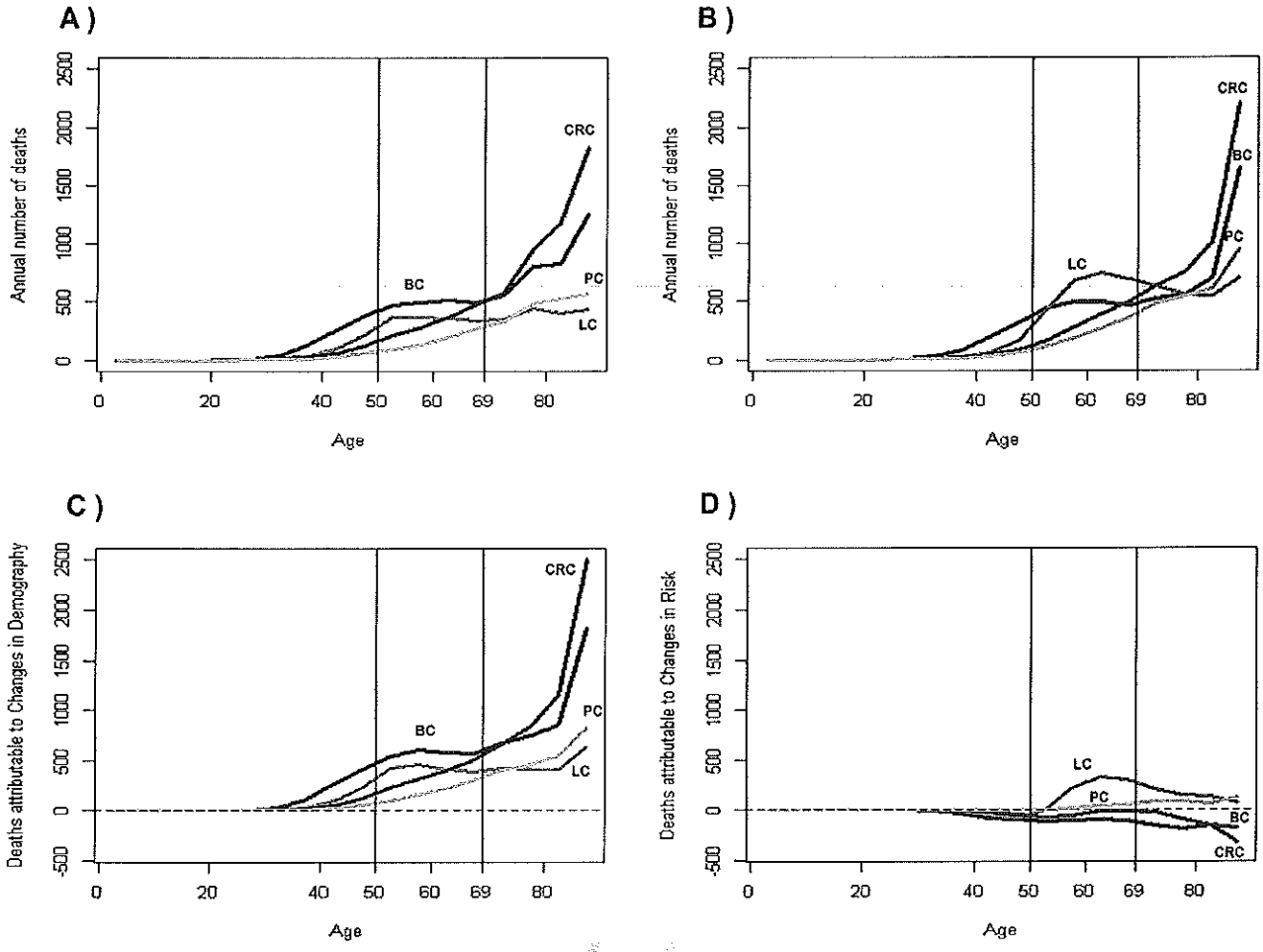

Fig. 2. Annual number of cancer deaths from breast, colorectal, lung and pancreatic cancer among Spanish women in 2008–2012 (A) and their predicted figures in 2018–2022 (B), assessing the number of deaths attributable to changes in demography (C) and risk (D) during 2018–2022.
Note: (B) can be partitioned into two figures, (C) and (D), since (C) and (D) show the annual average of the attributable number of cancer deaths due age-specific changes in demography and in risk, respectively, comparing the time periods 2018–2022 with 2008–2012 (reference period). (C) could be interpreted as the expected age-specific number of cancer deaths if the age-specific rates during 2008–2012 were applied to population distribution in 2018–2012. Therefore, (D) was obtained as the difference between the age-specific number of cancer deaths predicted in 2018–2012 and the corresponding expected number of deaths due to demographic changes.

expected increase in the number of deaths from CRC (6.06%) would be due mainly to the demographic changes (19.27%) that surpass the decreasing change in the risk of death from this tumor (−13.22%). On the other hand, the increase in the number of LC deaths would be due mainly to the 37.93% increase in the risk of death, which is more than twice the effect of demographic changes (15.38%). Finally, changes in demography (16.30%) and in the risk of death (18.36%) equally contribute to the net percentage change in the number of PC deaths between the two periods.

Table 2
Comparison of the total number of breast, colorectal, lung and pancreatic cancer deaths in Spain for the time periods 2018–2022 and 2008–2012, their 95% prediction interval for the time period 2018–2022, and the contributing factors to the net percentage change in the number of deaths from 2018 to 2022 compared with those from 2008 to 2012.

	Time period				Change in the burden: 2018–2022/2008–2012[a]								
	2008–2012	2018–2022			Percentage change (%)								
	(*N*)	(*N*)			**Net**			**Demographic**			**Risk**		
		Me	LL	UL	Me	LL	UL	Me	LL	UL	Me	LL	UL
Breast	6219	5928	5795	6059	**−4.67**	**−5.91**	**−3.35**	16.38	16.36	16.38	**−21.05**	**−22.29**	**−19.73**
Colorectal	6072	6441	6324	6575	6.06	4.85	7.61	19.27	19.25	19.29	**−13.22**	**−14.42**	**−11.67**
Lung	3410	5230	5105	5362	53.34	51.06	55.84	15.38	15.36	15.39	37.93	35.68	40.44
Pancreas	2667	3593	3501	3684	34.67	32.33	37.02	16.30	16.29	16.31	18.36	16.03	20.71

N: number of deaths (annual average); Me: median of the 95% prediction interval; LL: lower limit of the 95% prediction interval; UL: upper limit of the 95% prediction interval; Net: net percentage change in the number of deaths between time periods 2018–2022 and 2008–2012; Demographic: percentage change in the number of deaths between time periods 2018–2022 and 2008–2012 due to demographic changes (population size + age distribution); Risk, percentage change in the number of deaths between time periods 2018–2022 and 2008–2012 due to changes in the risk of death from these cancers; In bold face: decreasing percentage change.
[a] 2008–2012: reference period.

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4. Discussion

We found that the absolute number of deaths from BC might be surpassed by those of CRC among Spanish women during 2018–2022. LC might also surpass BC as the leading cause of cancer mortality among Spanish women aged 50–69 years. The number of deaths from PC continues to rise beyond the age of 50 years and remains slightly ahead of those of LC among women aged 69 and older. The most striking finding is the pattern of the burden of cancer mortality. Changes in the risk of death will have the larger contribution to the burden of LC and PC mortality, whereas demographic shifts will contribute the most to the non-decreasing trend of CRC mortality.

We must take into account several limitations in the interpretation of the results of our study. First, we restricted our cancer mortality analysis to the female gender, and this is of scarce utility for non-gender-specific cancers; therefore, the results presented here must be interpreted in this context. Second, tumors such as CRC or LC are heterogeneous from the clinical point of view. The study of the burden of molecular heterogeneity of these cancers is of interest since clinical practice is often guided by the molecular analysis of primary tumors [13]. However, the use of mortality data implies the use of broad cancer groupings, and our analysis is limited to provide the global burden of these cancers. Another limitation in our study is that all calculations and conclusions are drawn under the assumption that observed historical trends will continue into the future without major changes [14,15]. Finally, information about recent BC and CRC incidence estimates was highly valuable in assessing interpretations of the results obtained, but cancer incidence in Spain is based only on data from seven cancer registries that cover only 20% of the Spanish territory, and it was only available until not available for the time period analysed.

In a population ageing scenario where life expectancy increases, the number of new cancer cases and deaths from cancer is expected to rise [10]. However, projections need to focus not only on demographic changes [16], they may also quantify the effect of the time lags between changes in risk factors and their effect on CRs such as those observed between smoking prevalence and LC [17]. As we quantified, the percentage change due to changes in risk for LC (37.93%) surpassed that due to demographic factors (15.38%), and these could be observed mainly among women over the age of 50 years.

Breast cancer mortality has shown a favorable decreasing trend since 1992 in Spain [18], as observed in most European countries [4]. The decrease in the number of deaths from BC comparing the periods 2013–2017 and 2018–2022, which is marked in all age groups, will be a consequence of the combined effects of earlier detection and a range of improvements in treatment [6]. We expect a decrease in the number of BC deaths among women aged 50–69 years (target population for breast cancer screening programs in Spain) during the period 2013–2022. In this age group, the decreasing BC mortality trend is expected to occur at the same time as increased access to mammography screening [19] and more effective BC treatments. Although BC incidence is levelling off in Spain [19], BC continues to be the leading cancer tumor in Spain [1]. The combination of this feature with favorable survival rates among middle-aged women may lead to increased long-term survival in these patients [20]. However, despite an improvement in life expectancy for these young BC patients 10 years or more after diagnosis [20], they may die of BC at advanced ages [20,21].

Similarly, the number of CRC deaths is expected to increase due to ageing of the population in parallel with a decrease towards a levelling off among younger age groups; this was previously detected at the beginning of the 2000s [22]. Dietary factors have been shown to confer an increased risk of colorectal cancer [23]. Since 70–75% of CRC cases are sporadic and thus related to lifestyle, a high percentage of CRC cases could be avoided with a healthy lifestyle [24]. The development of screening programs is a key issue for CRC since it improves the prognosis of CRC and even reduces incidence through the detection of adenomatous polyps [25]. Although CRC screening programs in Spain started at the beginning of 2000 [26], during the year 2015 it is expected that these programs will cover 50% of the Spanish population aged between 50 and 69 years [27]. In other countries, these programs have been shown to be effective [25], since the high morbidity and mortality of CRC cases may benefit from the improvements in treatment of the disease at the early stages or as a precursor lesion [24]. A recent study carried out in Europe and the USA suggests that elderly patients with CRC cancer receive surgery, chemotherapy or radiotherapy less often than younger patients, despite evidence that they could also benefit from an increase in survival [28]. Although some older patients are unsuitable for specific treatments [24], it has been shown that quality of life in patients aged over 80 years who underwent surgery for CRC was generally comparable to that of younger patients [28]. Since we found that 70% of the CRC deaths occur beyond the age of 69 years, focus on these age groups is called for.

The two-smoking related cancers have shown similar perspectives, since we found that the contribution of the changes in the risk of death were higher than those of demography when comparing time periods 2008–2012 and 2018–2022. A substantial rise in the number of deaths from LC was found among women aged 50–69, whereas this rise was less pronounced for PC.

The projected dramatic increase in LC deaths in middle-aged women shows that the number of deaths due to LC might clearly overtake those due to BC by 2018–2022. Assuming that the most recent trends continue, a recent study suggests a similar situation across Europe [3]. LC mortality rates in Spain are below the European average [1] but show a similar trend-pattern to those in other European countries, since cases started to decline from the year 2000 among men, in parallel with the rise among women in most European countries [3]. Smoking prevalence among Spanish women increased sharply during 1960–1990, and levelled off in the early 2000s, slowly decreasing thereafter [17]. Thus, from the 1980s, there has been a higher rate of cessation of smoking among men but not among women [29], and it is therefore reasonable to expect a continuous rise of LC among women. The late initiation to smoking among Spanish women might explain the recent rising trend of LC incidence and mortality rates[17]. However, the recent legislative changes in the anti-smoking law in Spain may have an additional impact on smoking prevalence [30]. This could be an indicator to investigate if the future curb of LC mortality among women can be observed, or if the increase in risk between time periods starts to level off.

On the other hand, the number of PC deaths has shown a rising trend among women aged 69 and older during 1998–2012; this is consistent with the recent predicted trends in Europe and the USA [3,31]. As with LC, PC has a low survival rate (below 5% at 5 years [32]). There is no early diagnosis or effective treatment for PC [33], and consequently primary prevention is the only way to reduce its incidence; control of tobacco smoking is the most reliable measure since it prevents between 20% and 25% of PC deaths [33]. This means that mortality trends for this tumor might be influenced by both risk and demographic changes.

To sum up, the results presented here might be used to alert public health planners to the need for preventative actions focusing on specific age groups. Demographic changes (ageing) and changes in risk factors could have different impacts on the lifetime risk of cancer among Spanish women. The non-decreasing burden of CRC mortality at advanced ages must be tackled, since

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newer data from studies specifically targeting older patients and subgroup analyses indicate that proper treatment planning and specific medical and geriatric assessment can achieve a safe and beneficial treatment result in these patients. On the other hand, the rising burden of LC mortality among middle-aged women adds evidence for extending preventive actions in smokers and developing guidance on preventing the uptake of smoking in adolescents. In addition, attention must be paid to the slow but rising burden of PC mortality at advanced ages. Research identifying risk factors and treatment strategies for this tumor are called for. Finally, the reduction in the risk of death from BC in all ages as a result of improvements in treatment and early detection through screening must be accounted for in planning the management of these tumors with their rising burden.

Conflict of interest

The authors declare that they have no conflict of interest.

Authorship contribution

RC hereby states that all authors participated in the conception and design, acquisition of data, and analysis and interpretation of data, and drafted the article or revised it critically for important intellectual content.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.canep.2015.12.002.

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