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RESEARCH ARTICLE

Cancer incidence in Spain, 2015

J. Galceran[1,2] · A. Ameijide[1] · M. Carulla[1] · A. Mateos[3] · J. R. Quirós[4] · D. Rojas[5] · A. Alemán[6] · A. Torrella[7] · M. Chico[8] · M. Vicente[9] · J. M. Díaz[10] · N. Larrañaga[11,12] · R. Marcos-Gragera[13,14] · M. J. Sánchez[12,15,16] · J. Perucha[17] · P. Franch[18] · C. Navarro[12,19,20] · E. Ardanaz[12,21] · J. Bigorra[1] · P. Rodrigo[22] · R. Peris Bonet[23] · REDECAN Working Group

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Abstract
Purpose Periodic cancer incidence estimates of Spain from all existing population-based cancer registries at any given time are required. The objective of this study was to present the current situation of cancer incidence in Spain.
Methods The Spanish Network of Cancer Registries (REDECAN) estimated the numbers of new cancer cases occurred in Spain in 2015 by applying the incidence-mortality ratios method. In the calculus, incidence data from population-based cancer registries and mortality data of all Spain were used.
Results In 2015, nearly a quarter of a million new invasive cancer cases were diagnosed in Spain, almost 149,000 in men (60.0%) and 99,000 in women. Globally, the five most common cancers were those of colon–rectum, prostate, lung, breast and urinary bladder. By gender, the four most common cancers in men were those of prostate (22.4%), colon–rectum (16.6%), lung (15.1%) and urinary bladder (11.7%). In women, the most common ones were those of breast (28.0%), colon–rectum (16.9%), corpus uteri (6.2%) and lung (6.0%). In recent years, cancer incidence in men

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✉ J. Galceran
jgalceran@grupsagessa.com

1 Tarragona Cancer Registry, Fundation Society for Cancer Research and Prevention (FUNCA), Pere Virgili Health Research Institute (IISPV), Reus, Spain

2 University Rovira i Virgili, Reus, Spain

3 Albacete Cancer Registry, Health and Social Welfare Authority, Castile-La Mancha, Spain

4 Asturias Cancer Registry, Public Health Directorate, Department of Health, Asturias, Spain

5 Canary Islands Cancer Registry (Gran Canaria), Public Health Directorate, Canary Islands Government, Las Palmas de Gran Canaria, Spain

6 Canary Islands Cancer Registry (Tenerife), Public Health Directorate, Canary Islands Government, Tenerife, Spain

7 Castellón Cancer Registry, Public Health Directorate, Valencian Government, Castellón, Spain

8 Ciudad Real Cancer Registry, Health and Social Welfare Authority, Castile-La Mancha, Spain

9 C. Valenciana Childhood Cancer Registry, Public Health Directorate, Valencian Government, Valencia, Spain

10 Cuenca Cancer Registry, Health and Social Welfare Authority, Castile-La Mancha, Spain

11 Basque Country Cancer Registry, Health Department, Basque Government, Vitoria-Gasteiz, Spain

12 CIBER of Epidemiology and Public Health (CIBERESP), Madrid, Spain

13 Epidemiology Unit and Girona Cancer Registry (UERCG), Oncology Coordination Plan (PDO), Department of Health, Autonomous Government of Catalonia, Descriptive Epidemiology, Genetics and Cancer Prevention Group [Girona Biomedical Research Institute] IDIBGI, Catalan Institute of Oncology-Girona (ICO), Girona, Spain

14 University of Girona (UdG), Girona, Spain

15 Registro de Cáncer de Granada, Escuela Andaluza de Salud Pública, Instituto de Investigación Biosanitaria ibs.GRANADA, Hospitales Universitarios de Granada/Universidad de Granada, Granada, Spain

16 Hospitales Universitarios de Granada/Universidad de Granada, Granada, Spain

17 La Rioja Cancer Registry, Epidemiology and Health Prevention Service, Logroño, Spain

18 Mallorca Cancer Registry, Public Health and Participation Department, Palma de Mallorca, Spain

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seems to have stabilized due to the fact that the decrease in tobacco-related cancers compensates for the increase in other types of cancer like those of colon and prostate. In women, despite the stabilization of breast cancer incidence, increased incidence is due, above all, to the rise of colorectal and tobacco-related cancers.

Conclusion To reduce these incident cancer cases, improvement of smoking control policies and extension of colorectal cancer screening should be the two priorities in cancer prevention for the next years.

Keywords Cancer · Cancer cases · Cancer statistics · Incidence · Trends · Spain

Introduction

Cancer is one of the diseases that causes major public health problems in Spain. Currently, it is the second most frequent cause of death overall but, since 2000, it has been the leading one in men. In 2014, the last year with available data, three in ten deaths in men and two in ten in women were caused by cancer. Crude mortality rates in 2014 were 294.6 per 100,000 in men and 182.1 in women [1]. Nevertheless, trends in incidence and mortality of some types of cancer are starting to show a stabilization or a decrease, and this fact suggests a certain degree of effectiveness of therapeutic improvements and of preventive policies, primary as well as secondary.

Cancer incidence within a geographically determined population can be established by means of population-based cancer registries, the main aim of which is the identification and counting of all incident cases (new cases) diagnosed among the residents of this geographical area. Furthermore, these registries are essential in determining survival of all cancer patients of the area, as well as the prevalence of cancer. These registries also have many other objectives such as the evaluation of cancer screening programmes [2].

[19] Department of Epidemiology, Murcia Regional Health Council, IMIB-Arrixaca, Murcia, Spain

[20] Department of Health and Social Sciences, Universidad de Murcia, Murcia, Spain

[21] Navarre Cancer Registry, Navarre Public Health Institute, IdiSNA, Navarra Institute for Health Research, Pamplona, Spain

[22] Zaragoza Cancer Registry, Aragon Health Science Institute, Saragossa, Spain

[23] Spanish Childhood Cancer Registry, Spanish Society of Paediatric Haematology and Oncology, University of Valencia, Valencia, Spain

Some cancer incidence estimations for Spain have been calculated in different moments. The first one was published by Moreno [3] in 2001 for the period 1993–1996 using an incidence-mortality ratio method. In 2004, López-Abente [4] published the estimation for the period 1997–2000 using the same method. In 2010, Sánchez [5], using the MIAMOD method, estimated the cancer incidence for 2006 and a projection for 2012. At international level, cancer incidence in Spain was sometimes estimated by the EUCAN and GLOBOCAN projects [6, 7] using previously published data in Cancer Incidence in Five Continents series and incidence-mortality ratio methods. The results of these estimations were commented in some reports of other institutions. The latest estimates of cancer incidence in Spain were calculated for 2012 and need to be updated. Furthermore, a stable and robust methodology is required to periodically obtain incidence data with the participation of all existing PBCRs at any given time.

In this paper, we present the current situation of cancer incidence in Spain. We provide the estimated incidence for 2015 by gender and type of cancer for Spain as a whole, the evolution of incidence in the different territories where population-based cancer registries exist and the estimated incidence trends in Spain from 1993 to 2007 in addition to the estimated projections until 2015. A comparison of cancer incidence in Spain with those of other countries of the European Union in 2012 (EU-27) is also provided. This information is useful in defining priorities for the cancer strategies and policies in Spain with the ultimate goal of contributing to the decrease in the burden of cancer in the population and inequalities among geographical areas of Spain.

REDECAN (Red Española de Registros de Cáncer) is the network of Spanish population-based cancer registries (PBCRs) (http://redecan.org/es/index.cfm). The consolidated registries which comprise REDECAN are the following ones: Albacete, Asturias, Canary Islands, Castellón, Ciudad Real, Cuenca, Girona, Granada, La Rioja, Mallorca, Murcia, Navarra, Basque Country and Tarragona, and the Valencian Childhood Cancer Registry, as well as the Spanish Registry of Childhood Cancer (Registro Español de Tumores Infantiles—RETI) which is a multi-institutional-based registry. The results of this paper have been obtained from the data of the cited consolidated general cancer registries of REDECAN and that of Zaragoza (Fig. 1). A summary of the history of Spanish population-based cancer registries was presented in 2010 [8].

Materials and methods

Data sources

Data on population and mortality of all Spain and data of cancer incidence of the areas covered by cancer registries

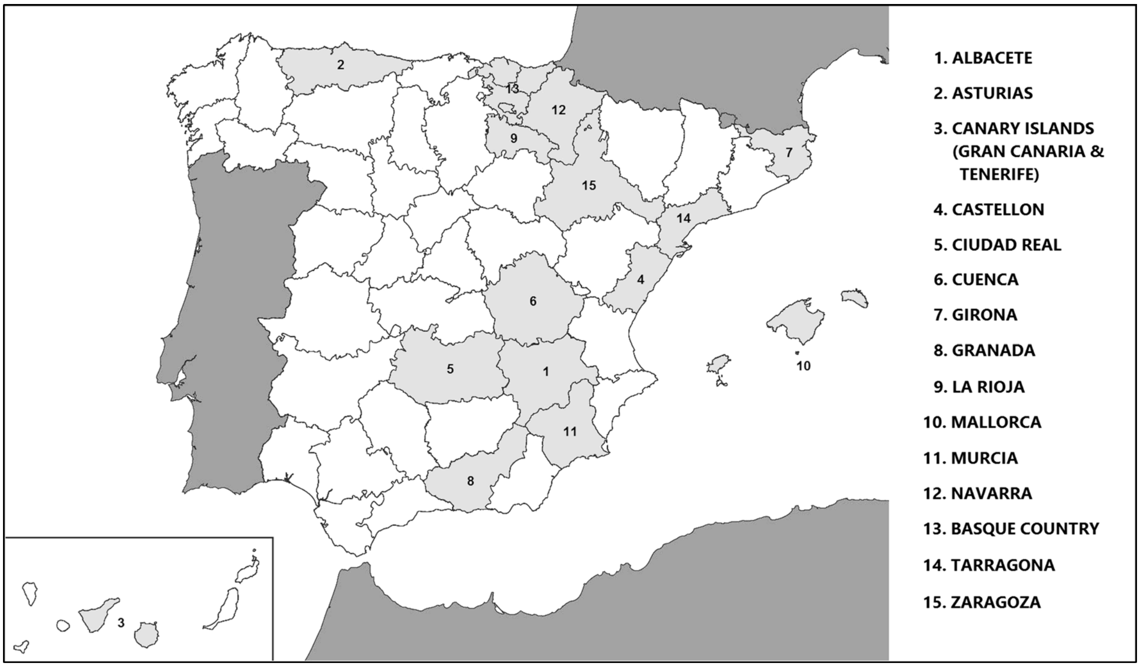

Fig. 1 Spanish population-based cancer registries which provided data for the calculation of estimates of cancer incidence in Spain. Source: Spanish Network of Cancer Registries (REDECAN)

were used to calculate the estimates of cancer incidence in Spain. Cancer mortality data (period 1993–2012) were provided by the National Statistics Institute (Instituto Nacional de Estadística—INE).

Cancer incidence data (period 1993–2007) were provided by the 15 Spanish global PBCRs (Database of REDECAN). Each registry provided available incidence period data: 1993–2007 (Albacete, Asturias, Canary Islands, Cuenca, Basque Country, Girona, Granada, La Rioja, Mallorca, Murcia, Navarra and Tarragona), 2004–2007 (Ciudad Real and Castellon) and 1993–2005 (Zaragoza) (Fig. 1). In January 2015, PBCRs covered 28.8% of the Spanish population (13,373,357 out of 46,449,565).

Population data: Annual inter-census estimates from 1993 to 2011 by province and Spain as a whole were provided by the National Statistics Institute. For 2012 to 2015, National short-term population estimates from the National Statistics Institute were used [1].

For international comparisons of incidence data (Tables 8, 9), in addition to data from REDECAN, results of the project EUCAN were used. This project provided national estimates of incidence, mortality and prevalence for 24 types of cancer in 40 European countries for 2012 in the Website of the European Cancer Observatory (ECO) [6].

Cancer types

Types of cancer studied (in International Classification of Diseases-10 classification) [9] were: lip, oral cavity and pharynx (C00–14), oesophagus (C15), stomach (C16), colon (C18), rectum (C19–21), liver (C22), gallbladder and biliary tract (C23–24), pancreas (C25), larynx (C32), lung (C33-C34), skin melanoma (C43), female breast (C50), cervix uteri (C53), corpus uteri (C54), ovary (C56), prostate (C61), testis (C62), kidney (C64), urinary bladder (C67, D09.0, D41.4), brain and central nervous system (C70–72), thyroid (C73), Hodgkin's lymphoma (C81), non-Hodgkin's lymphoma (C82–85, C96), myeloma (C90), leukaemia (C91–95) and all except non-melanoma skin cancer (C00–43, C45–96, D09.0, D41.4).

Estimates of cancer cases in 2015

The number of incident cases for the year 2015 was estimated by applying the incidence/mortality ratios (I/M ratios) to the estimated national mortality according to several scenarios. In fact, the methods used in this study are an adaptation of the I/M ratio method used by Moreno [3], López-Abente [4] and Bray [10] to estimate cancer incidence in Spain for previous periods.

Mortality rates for the period 2013–2017 for Spain as a whole, for each combination cancer type and gender, were estimated applying the NORDPRED [11] model to the 1993–1997, 1998–2002, 2003–2007 and 2008–2012 mortality periods. It was assumed that the mortality rates of 2015 are the same as that of the 2013–2017 period and the number of cancer deaths of 2015 was estimated applying the mortality rates of 2015 to the estimated population of the same year.

The estimates of I/M ratios were calculated using the hypothesis that, for each cancer type and gender, the I/M ratios were similar in all provinces. Incidence and mortality data between 1993 and 2007 of the provinces with population-based cancer registries were used to calculate the estimate of I/M ratios of this period. A third of the Uterus NOS (C55) mortality data was assigned to Cervix uteri (C53), another third to Corpus uteri (C54) and another third to Other cancers. These assignations were applied based on internal studies made in Tarragona and Girona cancer registries focused on the mortality of uterus NOS cases (data not published). For each combination cancer type and gender, the I/M ratios were estimated by means of a generalized linear mixed model (GLMM). The GLMM assumed that the number of incident cases in each province is the dependent term and follows a Poisson distribution; the number of deaths is the offset and the independent terms are the age, the year of diagnosis and the province of residence. The effect "year of diagnosis" was analysed by means of a polynomial function of second degree. The effect of age was smoothed by means of a linear spline with four nodes (10th percentile, first tertile, second tertile and 90th percentile of the mortality pool) and the province of residence was considered as a random effect to take into account the possible heterogeneity of I/M ratios among provinces. In the combinations cancer type and gender with less than 1000 cases in the study period (men: testis, thyroid and Hodgkin's lymphoma; women: oesophagus, larynx, thyroid and Hodgkin's lymphoma), the effect of province was not included.

The estimation of the parameters of the models was made based on a Bayesian statistic approach using Markov Chain Montecarlo Methods (MCMC). The R packages "R2WinBUGS" and "BRugs" and OpenBUGS software were used [12].

Three chains of simulations were calculated with 10,000 burn-in cycles and another one of 40,000 cycles for the analysis. One of every five cycles was selected to obtain a matrix of 24,000 estimations of the parameters.

The incidence between 1993 and 2007 was estimated applying to each year the I/M ratios estimated by the model to the annual national mortality.

The number of incident cases for 2015 was estimated, applying to the national mortality of 2015, the I/M ratios estimated for the model to this year, with three possible scenarios; these suppose three different hypotheses on the evolution of the estimation of the I/M ratio between 2007 and 2015. In the scenario A (constant I/M): I/M ratio was stable from 2007 to 2015 and equal to the I/M ratio of 2007. In the scenario B (linear I/M): the linear trends of the I/M ratio of the period between 1993 and 2007 were extended until 2015. In the scenario C (quadratic I/M): the quadratic trend of the I/M ratio between 1993 and 2007 was prolonged until 2015.

For each combination cancer type, gender and scenario, estimates were generated for number of incident cases (*N*), crude incidence rate (CR), age-standardized incidence rate to the World population (ASIRw) and age-standardized incidence rate to the European population (ASIRe). The percentiles 2.5 and 97.5 of the distribution of the generated values were used as 95% credibility intervals of each indicator (95% CI). All (crude and age-standardized) rates are expressed per 100,000 person-years (men or women).

Once the indicators had been calculated for each scenario, a group of epidemiologists and statisticians of REDECAN defined, by consensus, the most plausible scenario for each combination cancer type and gender. For the selection of the scenario for each cancer type we take into account the knowledge of the descriptive and aetiological epidemiology of each type of cancer, as well as other criteria such as the evolution of incidence rates in the last few years, the preference of selection of the same scenario for a similar pattern of evolution graphic of the I/M ratio, the coherence between the solution applied to men and women if the epidemiology of the cancer is not clearly different for both genders, and the avoiding of non-plausible situations such as decreasing of the I/M ratio or high increments of I/M ratio.

Scenario A was applied to the following cancers: lip, oral cavity and pharynx (women), liver, pancreas, larynx (men), skin melanoma, corpus uteri, ovary, testis, kidney, brain and CNS, thyroid, Hodgkin's lymphoma, Non-Hodgkin's lymphoma and Other cancers. Scenario B was applied to lip, oral cavity and pharynx (men), oesophagus, stomach, colon (women), rectum (men), gallbladder and biliary tract, lung (women), cervix uteri and urinary bladder cancers and leukaemia. And scenario C was used in colon (men), rectum (women), larynx (women) and lung (men) cancers and myeloma.

For prostate cancer, none of the three scenarios was valid, because I/M ratio trend had shown substantial and artificial variations due to the effect of the widespread use of the prostate test antigen. So, and as done by other authors, the same rates that the model estimated for 2007 were assigned to 2015 [13, 14].

For breast cancer, none of the three scenarios seems valid, either. Incidence trends in the participating registries are very different for this cancer. Taking into account that breast cancer screening programmes show differences by region, the same rates that the model estimated for 2007 were also assigned to 2015 [15].

The total number of incident cases for all types of cancer except non-melanoma skin cancer was obtained by adding the number of incident cases of the chosen scenario for each cancer studied.

Geographical differences in cancer incidence in Spain

The geographical cancer incidence variations in Spain have been presented through comparison of the ASIRe among cancer registries for the periods 1993–1997, 1998–2002 and 2003–2007 for all cancers as a whole except non-melanoma skin cancers by gender.

These data correspond to the population-based cancer registries that provided data to, at least, one of the volumes of the series *Cancer Incidence in Five Continents* published by the *International Agency for Research on Cancer* and the *International Association of Cancer Registries* and corresponding to these periods (Volumes VIII, IX and X) [16–18] plus the Castellón Cancer Registry which provided data of good quality for the period 2004–2007.

Risk of cancer incidence according to age

From the cancer estimates in Spain for the period 2003–2007, the risk of developing any type of cancer except those of non-melanoma skin cancer from birth to before a certain age was calculated. In addition, for the ten most frequent male and female cancer types, the risk of developing a cancer before 40, 50, 60, 70, 80 and 85 years old was calculated.

Trends of cancer incidence in Spain

The annual ASIRe was estimated for the period between 1993 and 2015, for all the cancers as a whole except non-melanoma skin cancer and for the five most frequent male and female cancers. The annual ASIRe between 2008 and 2015 was calculated using linear interpolation of ASIRe of 2007 and 2015.

Percentage change in number of incident cases separated by factor

The percentage change in the total number of incident cases between 1995 and 2005 and between 2005 and 2015 has been broken down into three components (size and population structure and risk) using the method described by Bashir and Esteve [19].

Childhood cancer

Childhood cancer is very infrequent. Therefore, incidence estimation was not calculated for these cancers using this methodology in this paper. However, crude and age-standardized incidence rates for all cancers as a whole are presented based on data provided by the Spanish Registry of Childhood Cancer.

International comparison of cancer incidence

As previously noted, for international comparisons of incidence data, results of the EUCAN project were used [6]. For all the cancers as a whole except non-melanoma skin cancer, and for the ten most common male and female cancers, the incidence ASIRe of Spain of the year 2012 estimated by the REDECAN method was compared with that of the same year in the EU-27 as a whole as well as each of its 27 countries as shown by the EUCAN project.

Because of the differences in the definition and inclusion criteria of urinary bladder tumours, the REDECAN estimates were not comparable with those of EUCAN-2012. So, for this type of cancer, European incidence was compared with that estimated by EUCAN-2012 for Spain.

For all cancers as a whole except non-melanoma skin cancer, the value of incidence of Spain corresponds to the sum of REDECAN estimates of all cancers except those of urinary bladder plus the value for urinary bladder estimation for Spain by EUCAN-2012.

In the comparison of Spanish incidence for 2012 with those other European countries for the same year, we used REDECAN data because REDECAN data are more up to date than EUCAN-2012 data of Spain.

In the “Selected cancers” section, all sentences that include comments on rates specify if they are World age-standardized (ASIRw) or European age-standardized (ASIRe).

Results

Estimates of cancer cases in 2015

Tables 1 and 2 present the estimated cancer incidence of Spain in 2015 by each combination of gender and cancer type (annual number of new (incident) cases, crude rate, and World and European age-standardized incidence rates). All rates are per 100,000 person-years (men or women). For each one of these parameters, the credibility interval is also shown.

The total number of new invasive cancer cases in 2015 in Spain was 247,771 (148,827 in men and 98,944 in women). The five most common cancers were those of colon–rectum with 41,441 new cases, prostate (33,370 new cases), lung (28,347 new cases), breast (27,747 new cases) and urinary bladder (21,093 new cases). By gender, the

Table 1 Estimates of cancer incidence by type of cancer; Spain 2015 (men). Source: Spanish Network of Cancer Registries (REDECAN)

Type of cancer	*N* cases	95% CI	CR	95% CI	ASIRw	95% CI	ASIRe	95% CI
Lip, oral cavity and pharynx	4980	3896–6225	21.9	17.1–27.3	12.4	9.6–15.6	17.4	13.5–21.9
Oesophagus	1979	1746–2238	8.7	7.7–9.8	4.7	4.1–5.3	6.7	5.9–7.6
Stomach	5150	4681–5660	22.6	20.5–24.8	10.8	9.8–11.9	16.2	14.7–17.8
Colon	15,808	13,436–18,500	69.4	59.0–81.2	32.1	27.3–37.6	49.0	41.6–57.3
Rectum	8956	7968–10,026	39.3	35.0–44.0	19.4	17.2–21.7	28.8	25.6–32.3
Colon–rectum	24,764	22,194–27,661	108.7	97.4–121.4	51.5	46.2–57.4	77.8	69.8–86.8
Liver	4252	3645–4911	18.7	16.0–21.6	9.7	8.3–11.2	14.1	12.1–16.3
Gallbladder and biliary tract	1104	876–1369	4.8	3.8–6.0	2.1	1.7–2.6	3.3	2.6–4.1
Pancreas	3513	3159–3901	15.4	13.9–17.1	7.5	6.8–8.4	11.3	10.1–12.5
Larynx	3426	2988–3899	15.0	13.1–17.1	8.6	7.4–9.8	12.1	10.5–13.9
Lung	22,430	19,740–25,420	98.4	86.6–111.5	50.5	44.4–57.4	74.1	65.2–84.1
Skin melanoma	2577	2211–2976	11.3	9.7–13.1	6.1	5.3–7.1	8.6	7.4–10.0
Prostate	33,370	27,439–40,101	146.4	120.4–176.0	67.6	55.2–81.6	103.4	84.8–124.5
Testis	974	871–1084	4.3	3.8–4.8	4.2	3.7–4.7	4.3	3.9–4.8
Kidney	3590	3188–4027	15.8	14.0–17.7	8.5	7.5–9.6	12.2	10.8–13.7
Urinary bladder	17,439	15,695–19,304	76.5	68.9–84.7	37.2	33.3–41.2	55.7	50.1–61.7
Brain and central nervous system	2332	2091–2596	10.2	9.2–11.4	6.4	5.7–7.1	8.3	7.4–9.2
Thyroid	865	767–973	3.8	3.4–4.3	2.4	2.1–2.7	3.2	2.8–3.6
Hodgkin's lymphoma	943	837–1057	4.1	3.7–4.6	3.7	3.3–4.2	4.0	3.5–4.5
Non-Hodgkin's lymphoma	4190	3667–4760	18.4	16.1–20.9	10.6	9.3–12.0	14.3	12.5–16.2
Myeloma	1489	984–2248	6.5	4.3–9.9	3.0	2.0–4.5	4.6	3.0–6.9
Leukaemia	3782	3161–4494	16.6	13.9–19.7	9.5	8.1–11.2	12.6	10.6–14.8
Other cancers	5678	4857–6578	24.9	21.3–28.9	13.2	11.4–15.2	18.6	15.9–21.5
All except non-melanoma skin	148,827	141,329–157,285	653.1	620.2–690.2	330.1	314.0–348.2	482.7	458.8–509.6

All rates are expressed per 100,000 person-years

N cases number of cases, *95% CI* 95% credibility interval, *CR* crude rate, *ASIRw* age-standardized incidence rate (World), *ASIRe* age-standardized incidence rate (Europe)

four most common cancers in men were those of prostate (33,370 cases), colon–rectum (24,764 cases), lung (22,430 cases) and urinary bladder (17,439 cases). These four cancers represent 66% of all invasive cancers in men. In women, the four most common ones were those of breast (27,747 cases), colon–rectum (16,677 cases), corpus uteri (6160 cases) and lung (5917 cases). Breast and colon–rectum cancers represent 45% of all invasive cancers in women (Fig. 2).

Geographical differences in cancer incidence in Spain

The incidence of cancer is not homogeneous in all the Spanish population. Table 3 shows the differences in ASIRe for all cancers except non-melanoma skin cancer in 15 registries during three consecutive 5-year periods (1993–1997, 1998–2002 and 2003–2007) obtained from the REDECAN database.

An obvious variability of incidence rates is observed in both women (differences up to 70 points) and men (differences up to 146 points). Regarding temporal trends, incidence rates increased between the first and the third 5-year periods in all registries in a greater or lesser degree. With the exception of Canary Islands, where incidence rates only increased by 15 points, all other incidence rates of Spanish registries increased by 30 or more points. Generally speaking, cancer registries which presented lower rates during the first 5-year period increased their rates more than those with higher rates during the first period. For example, in men, Albacete had the second lowest rate in 1993–1997 (346.2 per 100,000) and presented the highest increase (85 points), Cuenca grew from 336.8 to 404.1 per 100,000 (68 points of increase) and Zaragoza grew from 375.4 to 446.7 per 100,000 (71 points of increase). The exception was the Basque Country which, starting from the highest rate in 1993–1997 (483.2 per 100,000), increased to 549.9 per 100,000 in 2003–2007 (66

Table 2 Estimates of cancer incidence by type of cancer; Spain 2015 (women). Source: Spanish Network of Cancer Registries (REDECAN)

Type of cancer	*N* cases	95% CI	CR	95% CI	ASIRw	95% CI	ASIRe	95% CI
Lip, oral cavity and pharynx	1690	1489–1908	7.2	6.3–8.1	3.3	2.9–3.8	4.7	4.2–5.3
Oesophagus	379	293–483	1.6	1.2–2.0	0.7	0.5–0.9	1.0	0.8–1.3
Stomach	3306	2968–3672	14.0	12.6–15.5	5.4	4.8–5.9	8.0	7.2–8.8
Colon	11,927	10,733–13,216	50.5	45.4–56	19.9	18.0–22.0	29.7	26.8–32.8
Rectum	4750	3705–6069	20.1	15.7–25.7	8.4	6.5–10.7	12.4	9.6–15.8
Colon—rectum	16,677	15,090–18,521	70.6	63.9–78.4	28.3	25.6–31.5	42.0	38.1–46.7
Liver	1610	1337–1917	6.8	5.7–8.1	2.4	2.0–2.8	3.7	3.1–4.4
Gallbladder and biliary tract	1009	850–1189	4.3	3.6–5.0	1.4	1.1–1.6	2.1	1.8–2.5
Pancreas	3401	3030–3805	14.4	12.8–16.1	5.1	4.6–5.7	7.9	7.0–8.8
Larynx	299	113–764	1.3	0.5–3.2	0.7	0.3–1.9	1.0	0.4–2.6
Lung	5917	5301–6591	25.1	22.4–27.9	12.7	11.4–14.3	17.9	16.0–20.0
Skin melanoma	2313	2003–2652	9.8	8.5–11.2	5.6	4.8–6.4	7.3	6.3–8.4
Breast	27,747	24,027–31,957	117.5	101.7–135.3	65.2	56.1–75.5	88.3	76.1–102.1
Cervix uteri	2399	1985–2874	10.2	8.4–12.2	6.3	5.2–7.6	8.2	6.7–9.9
Corpus uteri	6160	5405–6984	26.1	22.9–29.6	13.1	11.4–15.0	18.7	16.3–21.3
Ovary	3228	2861–3627	13.7	12.1–15.4	7.2	6.3–8.1	9.9	8.7–11.2
Kidney	1989	1716–2296	8.4	7.3–9.7	4.1	3.5–4.8	5.7	4.9–6.6
Urinary bladder	3654	3114–4249	15.5	13.2–18.0	6.0	5.2–7.0	9.0	7.7–10.5
Brain and central nervous system	1710	1500–1939	7.2	6.4–8.2	4.0	3.5–4.6	5.2	4.6–6.0
Thyroid	2442	2276–2617	10.3	9.6–11.1	6.6	6.1–7.0	8.8	8.2–9.5
Hodgkin's lymphoma	646	562–739	2.7	2.4–3.1	2.5	2.1–2.8	2.6	2.3–3.0
Non-Hodgkin's lymphoma	3480	3089–3903	14.7	13.1–16.5	7.0	6.2–7.8	9.7	8.6–10.8
Myeloma	1240	824–1848	5.3	3.5–7.8	1.9	1.3–2.9	3.0	2.0–4.4
Leukaemia	2736	2292–3242	11.6	9.7–13.7	5.8	4.9–6.8	7.5	6.3–8.8
Other cancers	4913	4175–5716	20.8	17.7–24.2	8.7	7.5–9.9	12.2	10.6–14.0
All except non-melanoma skin	98,944	94,512–103,989	419.0	400.2–440.3	204.1	193.9–215.7	284.5	270.7–300.2

All rates are expressed per 100,000 person-years

N cases number of cases, *95% CI* 95% credibility interval, *CR* crude rate, *ASIRw* age-standardized incidence rate (World), *ASIRe* age-standardized incidence rate (Europe)

Fig. 2 Ten leading incident cancer types by gender in Spain, 2015. Source: Spanish Network of Cancer Registries (REDECAN)

points of increase). In women, similar patterns were observed although with lower rates and lower differences between 1993–1997 and 2003–2007. In them, the two registries with the highest rates in 1993–1997, Tarragona and Girona, slightly increased their rates in 1998–2002 but presented a slight decrease in the last 5 years period.

Table 3 Age-standardized cancer incidence rates to the European standard population by cancer registry, sex and period. All cancers except non-melanoma skin cancer. Source: Spanish Network of Cancer Registries (REDECAN)

Cancer registry	Men			Women		
	1993–1997	1998–2002	2003–2007	1993–1997	1998–2002	2003–2007
Albacete	346.2	377.0	431.6	224.3	225.9	235.0
Asturias	455.4	471.1	506.8	245.8	254.2	265.2
Basque Country	483.2	531.5	549.9	258.3	276.7	286.9
Canary Islands	460.2	472.7	475.0	266.7	279.9	278.6
Castellón			458.6			256.8
Ciudad Real			434.9			243.3
Cuenca	336.8	340.8	404.1	220.8	213.7	222.0
Girona	467.4	506.1	508.8	275.5	292.1	282.9
Granada	376.6	380.0	406.4	218.4	245.5	254.7
La Rioja	407.7	459.9	459.8	236.9	250.1	264.5
Mallorca	475.5	489.1	507.2	265.2	273.0	278.1
Murcia	414.9	444.5	476.8	241.6	272.1	280.0
Navarra	460.3	487.7	488.5	264.0	286.8	292.2
Tarragona	422.5	476.1	484.5	279.0	293.7	283.6
Zaragoza	375.4	438.6	446.7	219.6	250.4	249.7

All rates are expressed per 100,000 person-years

Risk of cancer incidence according to age

Figure 3 shows the risk of developing any type of cancer (except those of non-melanoma skin cancer) from birth to just before some defined ages. The risk is slightly higher in women than in men up to 50 years old (4.1 vs. 3.2%). From this age, the risk is higher in men and the difference is progressively higher. The difference at age 84 is of 22.5 points (50.9% in men vs. 28.3% in women).

Table 4 shows the same risks by gender and age, for the ten leading incident types of cancer. Under the age of 40, only female breast cancer (0.4%) and hematologic cancers presented a risk greater than 0.1% and the global risk of cancer is slightly higher than 1% in both genders. Breast cancer in women is the type of cancer which constantly presented the highest risk up to 69 years of age. When people arrive at the end of their seventies, prostate cancer presents the highest risk (11.1%) followed by lung cancer in males (8.8%), breast cancer in women (7.9%) and

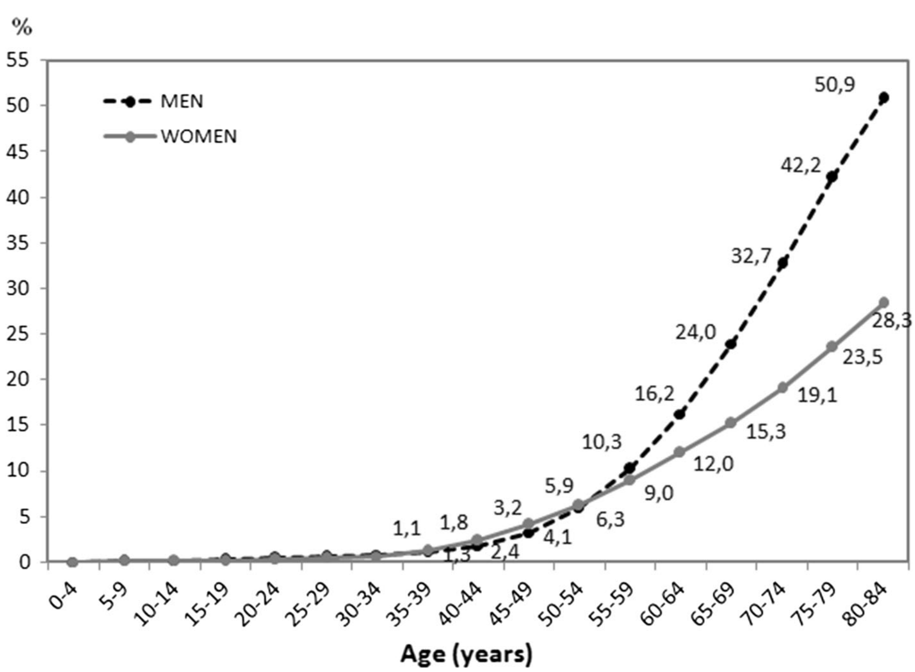

Fig. 3 Probability (%) of developing invasive cancers from birth to selected ages by gender, in Spain, 2003–2007. All cancers except non-melanoma skin cancer. Source: Spanish Network of Cancer Registries (REDECAN)

Table 4 Probability (%) of developing invasive cancers from birth to selected ages for the ten leading incident cancer types, by sex, in Spain, 2003–2007. Source: Spanish Network of Cancer Registries (REDECAN)

Type of cancer	0–39	0–49	0–59	0–69	0–79	0–84
Men						
Prostate	0.00	0.06	0.96	4.66	11.12	14.46
Colon–rectum	0.05	0.28	1.19	3.43	7.41	9.96
Lung	0.04	0.40	1.85	4.63	8.77	11.02
Urinary bladder	0.02	0.16	1.02	3.04	6.00	7.95
Stomach	0.02	0.11	0.38	0.98	2.11	2.90
Lip, oral cavity and pharynx	0.03	0.23	0.80	1.54	2.29	2.64
Non-Hodgkin's lymphoma	0.13	0.28	0.51	0.85	1.43	1.76
Liver	0.02	0.09	0.33	0.83	1.69	2.14
Leukaemia	0.17	0.24	0.37	0.69	1.34	1.76
Kidney	0.02	0.11	0.35	0.71	1.25	1.54
All except non-melanoma skin	1.14	3.25	10.25	23.96	42.17	50.90
Women						
Breast	0.44	1.86	3.82	5.80	7.88	8.99
Colon–rectum	0.05	0.24	0.80	1.91	3.87	5.24
Corpus uteri	0.01	0.07	0.39	1.02	1.60	1.83
Lung	0.02	0.17	0.42	0.71	1.10	1.32
Urinary bladder	0.01	0.04	0.13	0.36	0.73	1.01
Non-Hodgkin's lymphoma	0.08	0.16	0.34	0.61	1.06	1.32
Ovary	0.04	0.17	0.42	0.70	1.06	1.24
Stomach	0.02	0.07	0.19	0.41	0.90	1.27
Pancreas	0.01	0.03	0.11	0.32	0.70	1.01
Leukaemia	0.11	0.16	0.25	0.43	0.76	1.00
All except non-melanoma skin	1.27	4.09	8.98	15.25	23.51	28.35

colon–rectum cancer in men (7.4%). By the age of 84, prostate cancer presented the highest risk again (14.5%), followed by lung cancer in men (11.0%), colon–rectum in men (10.0%) and breast in women (9.0%).

Trends of cancer incidence in Spain

Figure 4 presents the evolution of the estimated cancer ASIRe from 1993 to 2007 in Spain for both genders as a whole and by gender. The linear projections of rates from 2007 to the estimated rates of 2015, globally and by gender, are also shown.

Global rates increased from 334 per 100,000 in 1993 to 379 in 2007 with an initial period (1993–2003) of increase and a subsequent stabilization. The estimated rate of 2015 is very similar to that of 2007 (384).

In men, the rate in 1993 was 427 and increased to 493 in 2004. From this year to 2007, rates were stable and the estimated rate for 2015 is 483, slightly lower than that of 2007. In women, the rate of 1993 was 240 and the increase persisted until 2003. Despite a stabilization observed from 2003 until 2007, a slight increase is estimated from this year until 2015 (ASIR = 285).

Figures 5a, b and 6a, b present the evolution of the estimated cancer ASIRe from 1993 to 2007 in Spain by gender for the ten leading cancer types. Their linear projections until 2015 are also shown.

In men, rates of lung cancer, the leading cancer type in 1993, remained stable around 80–84 per 100,000 until 2001, year of the start of a decrease. We estimate that lung cancer incidence continued its decrease until 2015. The estimated rate for this year is 74.

Urinary bladder cancer incidence rates occupied the second position in 1993 with a rate slightly higher than that of colon–rectum cancer. Although cancer incidence rates for this cancer seem to have remained stable at around 50 per 100,000 in the nineties, in the first decade of 2000 rates slightly increased to around 55 per 100,000. The estimated rate for 2015 is 56 per 100,000.

Colon–rectum cancer incidence rates steadily increased from 1993 (48 per 100,000) until 2007 (68 per 100,000) and in 2015 the projected incidence rate reached 78 per 100,000.

Prostate cancer incidence rates increased sharply from 1993 to 2007 mainly due to the introduction of new diagnostic techniques like the prostatic specific antigen (PSA).

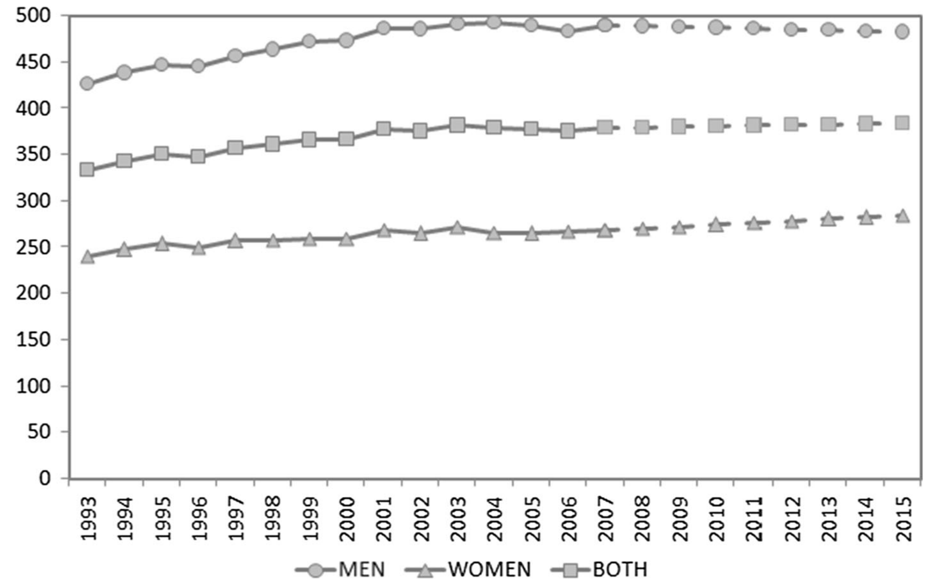

Fig. 4 Trends in cancer incidence rates 1993–2007 and projections until 2015 by gender. All cancers except non-melanoma skin cancer; Spain. Rates are standardized to the European standard population and expressed per 100,000 person-years. Source: Spanish Network of Cancer Registries (REDECAN)

The projection of prostate cancer incidence rates until 2015 could be heavily affected by changes in the use of PSA and its saturation as it has happened in other countries. To estimate incidence of 2015, the rate of 2007 has been applied to 2015 assuming that it is impossible for rates to increase permanently and as in similar projections by other scientists.

Stomach cancer rates decreased steadily from 1993 (27 per 100,000) to 2007 (18 per 100,000). The estimated rate for 2015 is 16 per 100,000.

Incidence rates of cancer of lip, oral cavity and pharynx remained stable around 30 per 100,000 from 1993 until 1997. From this year, rates decreased to 20 per 100,000 in 2007 and the estimated rate for 2015 is 17 per 100,000.

Non-Hodgkin's lymphoma incidence rates increased from 1993 to 2007 (12–15 per 100,000) and the estimation from this year until 2015 shows a stabilization around 14.

Incidence of liver cancer also showed an initial increase from 1993 (13 per 100,000) reaching a rate of 15 per 100,000 in 2002 and followed by a very slight decrease until 2007. The estimate for 2015 is 14 per 100,000.

Leukaemias show stable rates along all the period from 1993 to 2015 with a rate of around 12–14 per 100,000.

Rates of kidney cancer increased from 1993 (8 per 100,000) until 2004 (12 per 100,000) and maintained stable from then. The estimated rate for 2015 is 12 per 100,000.

In women, breast cancer was by far the leading cancer type during the period. In 1993, the rate was 77 per 100,000 and increased until 2001 (89 per 100,000); from this year until 2007, a stabilization is observed and the estimated rate for 2015 is 88 per 100,000.

Colon–rectum cancer incidence increased during the period by a lower degree than in men. In 1993, rate was 32 per 100,000 and the value of the estimate for 2015 is 42.

Corpus uteri cancer incidence also showed a steady increase from 1993 (10 per 100,000) to 2015 (19 per 100,000) and a very similar trend is observed for lung cancer but with slightly lower rates (from 6 to 18 per 100,000). In 1993, urinary bladder cancer rates had a similar rate to lung cancer but its annual rates increased by a lower degree than this cancer and the estimate for 2015 is 9 per 100,000.

Incidence of ovarian cancer increased from 1993 to 1996 and from this year decreased steadily until 2007. The estimate for 2015 is 10 per 100,000, similar to that of 2007.

Non-Hodgkin's lymphoma incidence showed a rising trend from 1993 to 2001; followed by a stabilization until 2005 and a very slight decrease until the estimate of 2015 (10 per 100,000). As in men, stomach cancer incidence shows a steady decrease from 1993 (12 per 100,000) and the estimated rate for 2015 is 8 per 100,000. Incidence of leukaemia fluctuates around 7–9 per 100,000 during the studied period and the estimated rate for 2015 is 8 per 100,000. A rising trend is observed in pancreas cancer incidence from 5 per 100,000 in 1993 to 7 in 2007; the estimate for 2015 being 8 per 100,000.

For more detail, Table 5 presents the ASIRe by cancer type and gender for 5 years periods and for the year 2015, for 25 cancer types.

Percentage change in number of incident cases separated by factors

Tables 6 and 7 present the percentage change in the total number of incident cases between the years 1995 and 2005

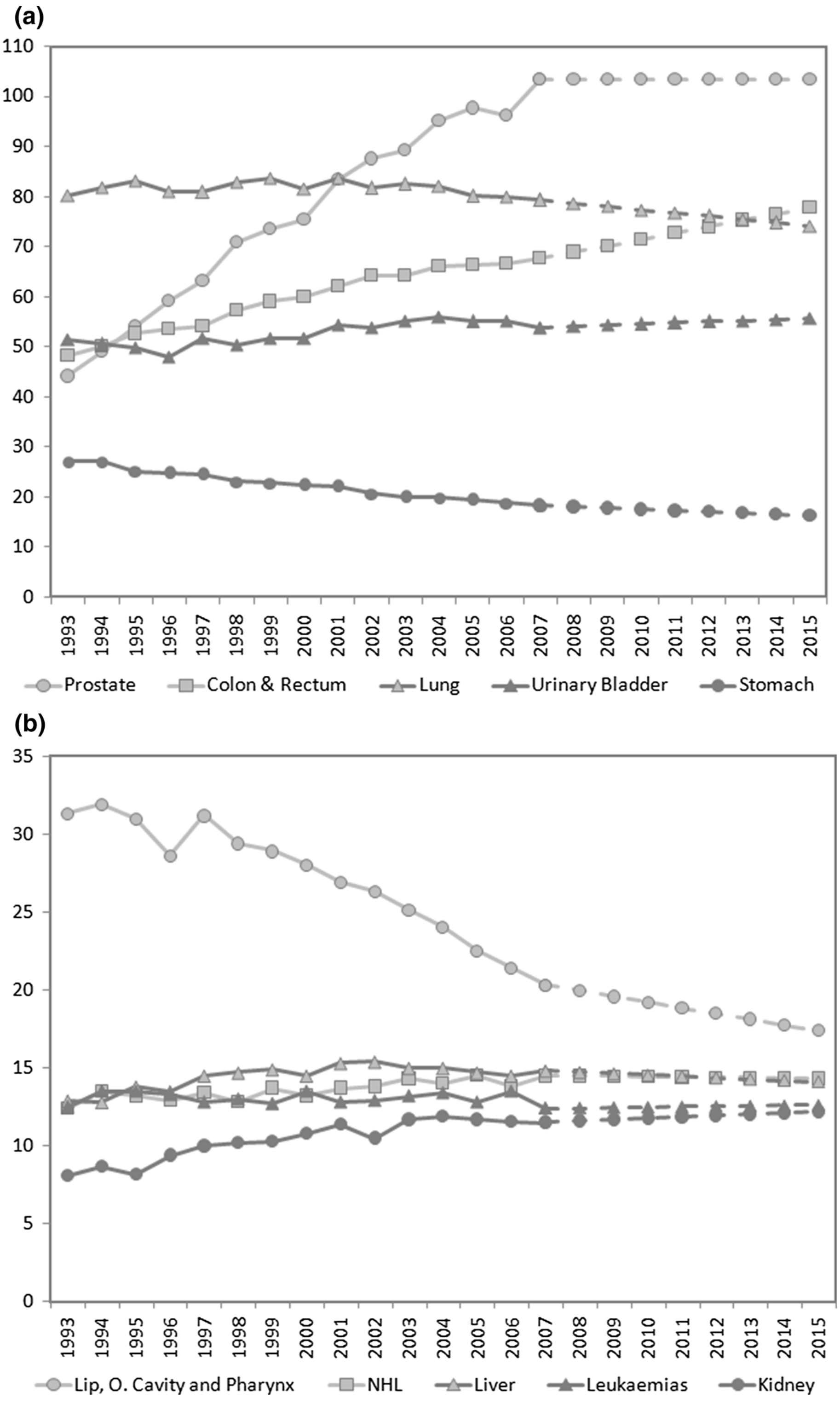

Fig. 5 **a** Trends in incidence rates 1993–2007 of five leading cancer types and projections until 2015 in Spain; men. Rates are standardized to the European standard population and expressed per 100,000 person-years. **b** Trends in incidence rates 1993–2007 of sixth to tenth leading cancer types and projections until 2015 in Spain; men. Rates are standardized to the European standard population and expressed per 100,000 person-years. Source: Spanish Network of Cancer Registries (REDECAN)

and between the years 2005 and 2015, respectively, according to three components (population size, population structure and risk factors).

In men, the absolute number of incident cases increased by 35.4% during the period 1995–2005: 14% because of the increase in the population size, 9% because of population ageing and 12.4% because of cancer risk factors. The most influential cancer that explains the global increase due to risk factors is prostate cancer which presented an 84% increase. In this

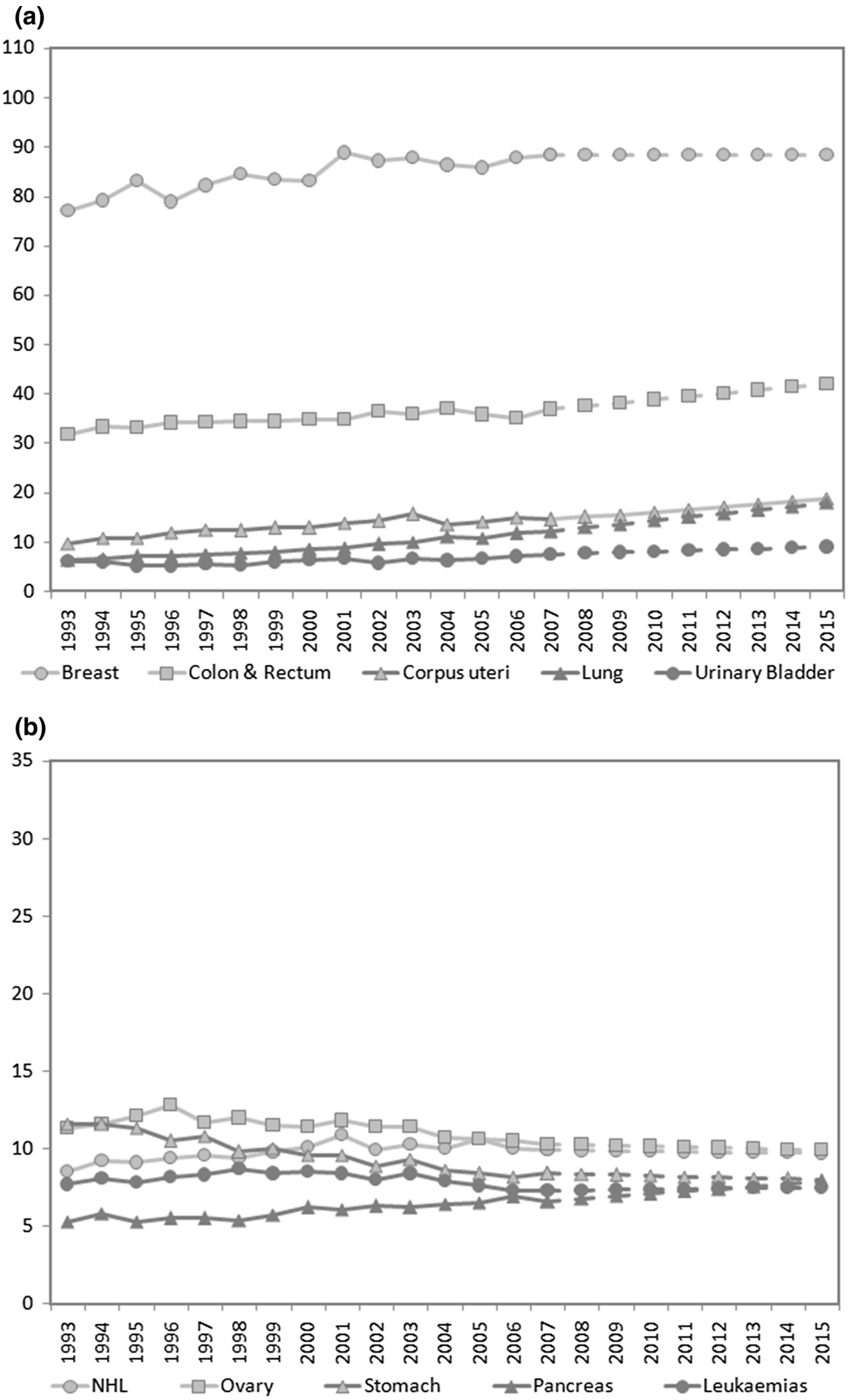

Fig. 6 **a** Trends in incidence rates 1993–2007 of five leading cancer types and projections until 2015 in Spain; women. Rates are standardized to the European standard population and expressed per 100,000 person-years. **b** Trends in incidence rates 1993–2007 of sixth to tenth leading cancer types and projections until 2015 in Spain; women. Rates are standardized to the European standard population and expressed per 100,000 person-years. Source: Spanish Network of Cancer Registries (REDECAN)

case, as noted previously, the increase is, above all, due not to actual risk factors but to the introduction of new diagnostic techniques that increased the diagnostic rate for this type of cancer. During the next decade (2005–2015), the estimate of the total increase is clearly lower (20.6%), and produced only by the two population factors: 6.7% because of the increase in the population size and 15.4% because of the population ageing. Globally, the influence of cancer risk factors was less and decreased 1.5% mainly due to the influence of tobacco-related cancers such as lung, larynx, urinary bladder, oral cavity and pharynx.

Table 5 Age-standardized cancer incidence rates to the European standard population by cancer type and all cancers except non-melanoma skin cancer, by sex and period (1993–1997, 1998–2002 and 2003–2007) and projection to 2015; Spain. Source: Spanish Network of Cancer Registries (REDECAN)

Type of cancer	Men				Women			
	1993–1997	1998–2002	2003–2007	2015	1993–1997	1998–2002	2003–2007	2015
Lip, oral cavity and pharynx	30.8	27.9	22.6	17.4	3.5	4.0	4.5	4.7
Oesophagus	8.9	8.1	7.5	6.7	0.9	0.9	0.9	1.0
Stomach	25.7	22.2	19.2	16.2	11.1	9.6	8.6	8.0
Colon	31.3	37.7	42.1	49.0	22.6	23.9	25.1	29.7
Rectum	20.4	22.8	24.1	28.8	10.7	11.1	11.1	12.4
Liver	13.5	15.0	14.8	14.1	4.6	4.6	4.1	3.7
Gallbladder and biliary tract	3.3	3.5	3.4	3.3	4.3	3.9	3.2	2.1
Pancreas	9.1	10.1	10.5	11.3	5.5	5.9	6.5	7.9
Larynx	20.3	18.4	15.5	12.1	0.6	0.6	0.8	1.0
Lung	81.5	82.7	80.7	74.1	7	8.6	11.2	17.9
Skin melanoma	4.7	6.3	7.2	8.6	6.4	7.3	7.9	7.3
Breast					80.1	85.5	87.3	88.3
Cervix uteri					6.7	7.1	6.5	8.2
Corpus uteri					11.2	13.2	14.5	18.7
Ovary					11.9	11.6	10.7	9.9
Prostate	54.1	78.3	96.4	103.4				
Testis	2.5	2.8	3.7	4.3				
Kidney	8.9	10.6	11.7	12.2	4.2	4.5	5.0	5.7
Urinary bladder	50.3	52.4	55.0	55.7	5.5	5.9	6.8	9.0
Brain and CNS	8.2	8.0	8.2	8.3	5.7	5.5	5.3	5.2
Thyroid	1.8	2.1	2.5	3.2	6.1	6.1	8.2	8.8
Hodgkin's lymphoma	2.9	2.9	3.4	4.0	1.7	2.3	2.4	2.6
Non-Hodgkin's lymphoma	13.1	13.5	14.2	14.3	9.2	10.0	10.2	9.7
Myeloma	4.4	5.1	4.9	4.6	3.4	3.6	3.3	3.0
Leukaemia	13.1	13.0	13.1	12.6	8.0	8.4	7.7	7.5
Other cancers	34.5	33.1	28.6	18.6	18.8	18.2	16.3	12.2
All	443.3	476.3	489.3	482.7	249.8	262.4	267.9	284.5

All rates are expressed per 100,000 person-years

In women, the differences between the two decades are much smaller. During the first decade (1995–2005), the absolute number of incident cases increased by 29.9%: 12% because of the increase in the population size, 9.1% because of the population ageing and 8.9% because of cancer risk factors. Breast cancer, the main incident cancer, presented a 13% increase because of the influence of risk factors. The main tobacco-related cancers represented a small proportion of all cancers but all of them showed high values of the risk component. During the decade 2005–2015, the total increase in the absolute number of cases was less (25.6%) than that in the previous decade. The value of population size decreased to 7.9%, that of population ageing increased to 12% and that of cancer risk factors decreased to 5.6%. It is worth highlighting that the value for risk factors of breast cancer has been stable (1.1%) and those of the tobacco-related cancers have maintained high values.

Childhood cancer

Childhood cancer deserves a special mention. According to the areas with population coverage of the Spanish Childhood Cancer Registry (Aragón, Catalonia, Madrid, Navarra y Basque Country), which covers 39% of the Spanish childhood population, the estimated childhood crude incidence rate (0–14 years) in Spain for the period 2000–2013 was 154 per million boys and girls, and the ASIRw was 156 (95% CI 152–160) per million boys and girls [20].

Table 6 Estimation of the percentage change in number of incident cases separated in factors by type of cancer and sex; Spain 1995–2005

Type of cancer	Men					Women				
	Total	Population	Structure	Risk	APC	Total	Population	Structure	RISK	APC
Lip, oral cavity and pharynx	−11.5	9.2	7.6	−28.3	−3.3	50.9	13.9	10.4	26.6	2.4
Oesophagus	2.9	10.7	7.2	−15.0	−1.6	16.9	10.8	12.3	−6.1	−0.6
Stomach	−7.1	9.7	10.5	−27.2	−3.1	−6.6	8.6	12.4	−28.0	−3.2
Colon	67.0	17.4	10.9	38.7	3.3	37.5	12.7	10.0	14.8	1.4
Rectum	44.4	15.0	10.1	19.3	1.8	26.4	11.6	9.9	4.9	0.5
Colon–rectum	58.2	16.4	10.6	31.1	2.7	34.0	12.3	10.0	11.6	1.1
Liver	32.4	13.8	7.7	10.9	1.0	12.0	10.3	10.1	−8.4	−0.9
Gallbladder and biliary tract	26.8	13.2	12.0	1.6	0.2	−6.6	8.6	11.9	−27.0	−3.1
Pancreas	40.9	14.7	10.2	16.1	1.5	44.9	13.3	11.7	19.9	1.8
Larynx	−9.2	9.4	6.2	−24.9	−2.8	49.4	13.7	10.3	25.3	2.3
Lung	19.8	12.5	8.4	−1.1	−0.1	76.9	16.3	9.6	51.1	4.2
Skin melanoma	92.1	20.0	10.3	61.8	4.9	52.6	14.0	8.8	29.8	2.6
Breast						33.8	12.3	8.5	13.0	1.2
Cervix uteri						17.9	10.9	10.0	−2.9	−0.3
Corpus uteri						53.3	14.1	4.1	35.2	3.1
Ovary						10.3	10.1	7.8	−7.7	−0.8
Prostate	116.3	22.5	10.1	83.8	6.3					
Testis	71.1	17.8	2.6	50.7	4.2					
Kidney	58.4	16.5	7.9	34.0	3.0	44.4	13.3	7.5	23.6	2.1
Urinary bladder	32.5	13.8	9.2	9.5	0.9	44.0	13.3	11.4	19.3	1.8
Brain and CNS	20.6	12.5	6.9	1.1	0.1	11.9	10.3	5.6	−4.0	−0.4
Thyroid	73.0	18.0	10.6	44.4	3.7	56.9	14.4	7.0	35.4	3.1
Hodgkin's lymphoma	33.4	13.9	5.0	14.5	1.4	54.8	14.2	1.7	38.9	3.3
Non-Hodgkin's lymphoma	32.9	13.8	7.9	11.2	1.1	39.6	12.9	6.6	20.2	1.9
Myeloma	40.1	14.6	9.6	15.9	1.5	25.8	11.6	8.2	6.1	0.6
Leukaemia	21.6	12.6	7.1	1.9	0.2	19.8	11.0	7.0	1.8	0.2
Other cancers	3.1	10.7	10.0	−17.6	−1.9	7.2	9.9	11.4	−14.0	−1.5
All except non-melanoma skin	35.4	14.1	9.0	12.4	1.2	29.9	12.0	9.1	8.9	0.9

APC annual percentage change of the incidence rates

Comparison of cancer incidence in Spain with Europe

Tables 8 and 9 present estimated cancer ASIRe for the 10 leading cancers and for all cancers as a whole (except for non-melanoma skin cancer) by gender in the 27 countries of the European Union for 2012 from EUCAN-2012. The values for Spain have been calculated from the more up-to-date REDECAN cancer registries data than those of EUCAN-2012 with the exception of the urinary bladder cancer for which EUCAN-2012 values have been used.

In men, rates vary from 289 per 100,000 in Greece to 551 per 100,000 in France. The rate of Spain at 470 per 100,000 is slightly higher than that of the European average (453 per 100,000). By contrast, in women the value of the Spanish rate (273 per 100,000) is clearly lower than that of the EU-27 (330 per 100,000). The variability of rates in this gender is lower than that in men (254–394) with the exception of Greece (192) and Denmark (454).

It is estimated that by 2012 a total of 2,634,582 new cancer cases in all 27 countries of the European Union as a whole were diagnosed, 1,434,263 men and 1,200,319 women. In men, the most frequent was prostate cancer (359,942 cases), followed by lung cancer (211,401 cases) and colon–rectum cancer (191,623 cases). In women, the most diagnosed was breast cancer (364,449 cases), followed by colon–rectum cancer (150,514 cases) and lung cancer (98,188 cases).

For all cancers as a whole in men, Spain (469.6 per 100,000) has a slightly higher rate than the average for the EU-27 (452.9 per 100,000) occupying the twelfth position in the classification in which Greece had the lowest rate

Table 7 Estimation of the percentage change in number of incident cases separated in factors by type of cancer and sex; Spain 2005–2015

Type of cancer	Men					Women				
	Total	Population	Structure	Risk	APC	Total	Population	Structure	Risk	APC
Lip, oral cavity and pharynx	−4.5	5.3	15.6	−25.4	−2.9	28.1	8.0	12.9	7.2	0.7
Oesophagus	11.1	6.1	15.9	−10.9	−1.2	29.0	8.1	14.7	6.2	0.6
Stomach	3.6	5.7	17.1	−19.3	−2.1	9.4	6.9	14.8	−12.0	−1.3
Colon	44.0	8.0	16.8	19.2	1.8	41.3	8.9	13.8	18.6	1.7
Rectum	46.9	8.1	16.1	22.7	2.1	31.4	8.2	12.4	10.8	1.0
Colon–rectum	45.0	8.0	16.6	20.4	1.9	38.3	8.7	13.4	16.3	1.5
Liver	14.1	6.3	14.8	−7.0	−0.7	6.4	6.7	12.0	−12.0	−1.3
Gallbladder and biliary tract	23.0	6.8	20.3	−4.1	−0.4	−17.6	5.2	15.1	−38.0	−4.6
Pancreas	33.1	7.4	16.8	8.9	0.9	46.6	9.2	14.8	22.6	2.1
Larynx	−4.2	5.3	14.9	−24.4	−2.8	47.8	9.3	10.7	27.9	2.5
Lung	11.7	6.2	15.4	−9.9	−1.0	87.2	11.7	12.5	62.9	5.0
Skin melanoma	43.9	8.0	13.0	23.0	2.1	8.0	6.8	8.8	−7.6	−0.8
Breast						20.1	7.5	11.4	1.1	0.1
Cervix uteri						47.7	9.3	8.7	29.8	2.6
Corpus uteri						52.3	9.5	10.0	32.8	2.9
Ovary						10.1	6.9	11.1	−7.9	−0.8
Prostate	31.4	7.3	16.1	8.0	0.8					
Testis	−3.5	5.3	−16.2	7.4	0.7					
Kidney	26.7	7.0	14.9	4.8	0.5	32.8	8.3	10.8	13.7	1.3
Urinary bladder	25.3	6.9	17.0	1.3	0.1	56.1	9.8	14.7	31.7	2.8
Brain and CNS	19.0	6.6	10.9	1.5	0.1	16.4	7.3	7.7	1.4	0.1
Thyroid	50.7	8.3	11.5	30.9	2.7	28.8	8.1	12.0	8.8	0.8
Hodgkin's lymphoma	16.2	6.4	−5.3	15.1	1.4	8.2	6.8	−8.4	9.7	0.9
Non-Hodgkin's lymphoma	20.7	6.7	12.4	1.5	0.2	14.8	7.2	9.5	−2.0	−0.2
Myeloma	16.1	6.4	16.4	−6.7	−0.7	8.6	6.8	12.1	−10.0	−1.1
Leukaemia	16.8	6.5	13.2	−2.9	−0.3	16.5	7.3	10.8	−1.6	−0.2
Other cancers	−20.8	4.4	16.9	−42.1	−5.3	−11.0	5.6	15.6	−32.0	−3.8
All except non-melanoma skin	20.6	6.7	15.4	−1.5	−0.2	25.6	7.9	12	5.7	0.6

APC annual percentage change of the incidence rates

(289.0 per 100,000) and France the highest one (550.7 per 100,000).

By type of cancer and for the ten cancer types with the highest rates, Spain presented a prostate cancer ASIRe slightly lower than the average for the EU27 although, as noted, the estimation of incidence of this cancer has major difficulties in all countries and, therefore, the comparison is less reliable than that for other cancer types. Lung cancer had a higher incidence in Spain (76.8 per 100,000) than in the whole EU-27 (66.3 per 100,000). The same is observed with colon–rectum cancer (73.0 vs 59.0 per 100,000), stomach cancer (16.9 vs 15.2 per 100,000), non-Hodgkin's lymphomas (14.6 vs 13.8 per 100,000), liver cancer (14.1 vs 11.1 per 100,000), leukaemias (12.4 vs 11.8 per 100,000) and larynx cancer (12.9 vs 8.3 per 100,000). Cancer of the lip, oral cavity and pharynx (18.5 vs 18.3 per 100,000) presented a very similar ASIRe in Spain and the EU-27.

Urinary bladder cancer deserves special consideration. Inclusion, coding and classification criteria of tumours of this organ vary slightly from one registry to another [21]. Subtypes included in the results can also vary depending on the project (EUCAN-2012, *Cancer Incidence in Five Continents*…). Therefore, to make the rates of this cancer more comparable among countries, all values in the table correspond to EUCAN-2012 project. Spain has a higher urinary bladder cancer ASIRe than the average of the EU-27 (39.0 vs 29.1 per 100,000).

Regarding all cancers as a whole in women, Spain (278.3 per 100,000) has a lower ASIRe than that of the EU average (330.1 per 100,000) occupying the twenty-second position in the classification in which, again, Greece had the lower ASIRe (192.0 per 100,000) and Denmark the highest one (454.4 per 100,000).

By cancer type and for the 10 types with the highest ASIRe, Spain presented a lower incidence than the EU-

Table 8 Age-standardized cancer incidence rates to the European standard population of 10 types of cancer and all cancers in the European Union countries (UE-27) in 2012; men

Type of cancer Country	Prostate	Lung	Colon–rectum	Urinary bladder	Lip, oral cavity and pharynx	Stomach	Non-Hodgkin's lymphomas	Liver	Leukaemia	Larynx	All (but skin)
Total UE-27	110.8	66.3	59.0	29.1	18.3	15.2	13.8	11.1	11.8	8.3	452.9
Austria	110.0	54.2	51.3	29.5	16.5	13.9	11.9	12.1	11.3	5.0	423.9
Belgium	134.6	83.2	67.5	47.6	21.9	12.2	16.6	6.7	13.4	9.4	525.1
Bulgaria	37.1	73.1	58.7	28.0	15.1	21.4	6.6	9.2	8.3	14.0	367.0
Cyprus	85.9	38.1	41.6	35.8	4.2	11.4	10.8	6.3	15.9	4.1	322.3
Czech Republic	110.3	75.0	81.1	28.9	18.0	15.5	10.6	9.4	9.7	7.9	503.4
Denmark	138.4	62.5	69.2	35.2	18.0	12.3	16.2	6.4	10.1	6.1	515.0
Estonia	145.4	70.7	53.1	21.8	15.1	28.7	9.9	4.9	12.9	7.9	471.4
Finland	145.2	45.4	42.5	23.5	9.9	10.2	18.6	11.1	11.3	2.9	423.3
France	187.5	74.5	53.8	22.8	23.1	10.5	16.5	16.6	14.0	7.8	550.7
Germany	114.1	57.3	59.7	34.7	23.1	16.2	13.5	10.6	12.1	6.5	463.2
Greece	34.2	74.7	25.0	26.7	5.5	11.1	3.4	8.3	14.3	6.5	289.0
Holland	124.5	66.1	71.6	20.9	12.6	11.6	17.5	3.3	10.1	5.8	474.2
Hungary	56.6	109.3	86.7	34.3	39.8	20.3	8.8	8.0	11.3	16.6	500.3
Ireland	168.7	54.9	65.1	20.5	11.9	13.4	17.2	6.7	17.0	6.7	499.6
Italy	100.9	58.8	61.2	32.3	9.8	16.5	18.0	16.3	12.1	9.1	447.8
Latvia	127.2	83.9	45.5	26.5	14.8	33.7	7.9	8.4	11.4	11.9	472.7
Lithuania	93.8	80.8	47.4	23.7	19.1	33.5	10.3	6.9	13.3	11.2	454.1
Luxembourg	118.3	59.7	62.5	23.5	16.4	14.7	12.5	15.9	11.1	5.2	451.6
Malta	78.4	58.0	60.1	39.8	14.9	17.0	9.6	5.1	11.7	7.9	396.7
Poland	55.3	89.6	55.5	30.3	19.0	19.7	6.2	5.4	9.8	11.7	389.7
Portugal	95.1	49.1	61.4	33.4	27.5	26.7	16.4	11.9	9.8	13.0	429.7
Romania	37.9	83.3	50.3	27.4	29.6	23.7	7.2	13.1	9.3	14.1	381.6
Slovakia	78.3	69.9	92.2	28.2	30.3	21.0	10.1	10.0	14.8	9.6	488.9
Slovenia	124.9	78.9	74.5	28.1	20.6	23.3	11.9	12.5	10.4	7.2	514.0
Spain	103.4	76.8	73.0	39.0[a]	18.5	16.9	14.6	14.1	12.4	12.9	469.6[b]
Sweden	175.2	28.8	48.9	25.7	9.5	7.4	13.8	5.0	10.4	2.4	427.8
UK	111.1	53.3	55.7	14.8	13.9	10.0	16.8	6.8	12.4	4.8	415.8

All rates are expressed per 100,000 person-years

[a] Due to the differences in the definition and criteria of inclusion of urinary bladder cancers and to make the data more comparable, the estimate of EUCAN-2012 has been used for this type of cancer. The value of the REDECAN estimate is 54.6

[b] The presented value corresponds to the sum of REDECAN estimates of all types of cancer except non-melanoma skin cancer take away those of urinary bladder plus the EUCAN estimate of the urinary bladder. The value of the REDECAN estimate for all types of cancer except non-melanoma skin cancer is 485.2

27 average for breast cancer (88.3 vs. 108.8 per 100,000), lung cancer (15.3 vs 26.1 per 100,000) and cervical cancer (7.7 vs 11.3 per 100,000). ASIRe was slightly lower for cancers of corpus uteri (17.4 vs 17.9 per 100,000), ovary (10.2 vs 12.6 per 100,000) and thyroid (7.8 vs 9.3 per 100,000). Non-Hodgkin's lymphomas showed the same rate (9.6). Cancers of colon–rectum (39.9 vs 36.1 per 100,000), urinary bladder (8.4 vs 6.1 per 100,000) and stomach (8.1 vs 7.1 per 100,000) had higher ASIRe than those of the EU27 average.

Selected cancers

Tobacco-related cancers

Lung

In 2012, lung cancer was the most incident cancer in the world (1,825,000 new cases) [7] and the fourth most incident in the EU-27 (309,600 new cases). In this area, it occupied the second position in men and the third in women [22].

Table 9 Age-standardized cancer incidence rates to the European standard population of 10 types of cancer and all cancers in the European Union countries (UE-27) in 2012; women

Type of cancer Country	Breast	Colon–rectum	Corpus uteri	Lung	Ovary	Non-Hodkin's lymphomas	Thyroid	Urinary bladder	Cervix uteri	Stomach	All (but skin)
Total UE-27	108.8	36.1	17.9	26.1	12.6	9.6	9.3	6.1	11.3	7.1	330.1
Austria	90.7	29.3	14.8	27.8	10.2	8.5	17.6	7.6	7.0	7.3	304.0
Belgium	147.5	43.4	18.9	27.6	11.0	12.0	10.2	9.4	10.2	5.7	388.0
Bulgaria	76.3	36.4	24.3	12.4	17.9	4.9	5.7	6.5	28.5	10.4	290.5
Cyprus	104.3	33.2	15.4	10.7	9.4	9.1	16.7	3.8	5.2	4.8	270.3
Czech Republic	95.5	40.5	25.4	25.9	15.1	8.5	13.8	8.3	16.3	7.8	356.8
Denmark	142.8	53.4	19.2	54.9	14.3	11.6	4.8	10.7	12.1	4.4	454.4
Estonia	69.0	33.8	20.2	13.5	15.8	5.0	7.3	4.3	23.3	14.9	275.1
Finland	121.0	29.2	20.0	17.9	11.5	13.1	9.5	4.3	4.9	5.9	323.8
France	136.6	36.9	15.2	27.9	10.7	10.7	14.7	3.3	8.0	4.2	369.8
Germany	122.0	34.8	16.9	25.4	10.2	10.2	7.6	8.3	9.8	8.0	344.5
Greece	58.6	17.2	10.0	13.2	11.3	2.2	3.1	4.1	6.2	5.4	192.0
Holland	131.3	50.5	17.7	44.5	9.2	12.8	4.2	5.8	8.0	5.8	394.1
Hungary	72.3	44.6	10.5	46.5	14.1	7.0	8.8	10.5	20.5	9.7	319.4
Ireland	122.4	41.3	15.6	40.4	15.6	12.9	4.7	7.5	15.1	6.7	382.4
Italy	118.0	39.9	19.2	19.2	13.3	11.4	18.7	5.9	7.7	8.9	341.6
Latvia	69.8	30.0	23.2	11.7	18.9	5.4	8.8	5.9	20.7	12.6	280.5
Lithuania	65.2	28.1	24.5	10.4	16.2	7.2	24.2	6.8	31.6	11.8	302.6
Luxembourg	118.2	33.6	35.3	26.9	10.5	10.4	16.6	6.5	7.1	7.2	358.6
Malta	116.2	37.6	21.8	11.0	16.2	8.6	10.7	9.7	4.6	8.1	314.4
Poland	69.9	28.9	23.4	31.1	18.1	5.6	6.2	6.4	15.3	7.3	283.6
Portugal	85.6	33.8	18.0	11.7	8.2	10.6	6.4	5.4	10.8	12.8	263.0
Romania	66.2	29.2	11.6	15.8	13.6	5.5	5.3	4.1	34.9	8.5	253.7
Slovakia	78.1	43.6	26.8	20.5	15.4	9.0	7.2	5.9	19.4	9.8	327.8
Slovenia	88.4	40.1	20.8	24.8	13.8	9.4	13.3	6.5	11.8	9.6	339.1
Spain	88.3	39.9	17.4	15.3	10.2	9.6	7.8	5.5[a]	7.7	8.1	275.4[b]
Sweden	108.2	39.5	19.7	27.5	10.3	10.2	5.4	7.1	8.6	4.1	340.3
UK	129.2	36.7	19.7	38.5	16.0	12.0	5.7	4.5	7.9	4.8	370.5

All rates are expressed per 100,000 person-years

[a] Due to the differences in the definition and criteria of inclusion of urinary bladder cancers and to make the data more comparable, the estimate of EUCAN-2012 has been used for this type of cancer. The value of the REDECAN estimate is 8.4

[b] The presented value correspond to the sum of REDECAN estimates of all types of cancer except non-melanoma skin cancer take away those of urinary bladder plus the EUCAN estimate of the urinary bladder. The value of the REDECAN estimate for all types of cancer except non-melanoma skin cancer is 278.3

In Spain, a total of 28,347 new estimated cases were diagnosed in 2015, 22,430 in men and 5917 in women. It was the third most common cancer in men, after prostate and colorectal, and the fourth in women after breast, colorectal and corpus uteri. The ASIRe was 74.1 and 17.9 for men and women, respectively (Tables 1, 2).

The most important risk factor is smoking, and passive smoking is also a demonstrated risk factor [23]. Other risk factors are environmental pollution from motor vehicles or industries, occupational exposure to various substances, exposure to radon gas in homes and mines, and exposure to ionizing radiation [24]. As in other cancers, consumption of fruit and vegetables has a protective effect [25]. Exposure to these factors varies greatly between individuals and populations and this explains the wide geographical and temporal variability in the incidence of this cancer. Since tobacco is the most important risk factor, variations in the prevalence of smoking are the main explanatory factor of this variability.

In men, from a geographical point of view, in the period 2003–2007, La Rioja (42.1), Canary Islands (43.4) and Granada (43.4) presented the lowest rates and Mallorca (59.5) and Asturias (59.4) the highest [18].

In recent decades, there has been in Spain a significant decline in tobacco consumption in men and an increase followed by a stabilization in recent years in women. In 1978, smoking prevalence was 65% in men and 17% in women whereas in 2012 these values were 28% in men and 20% in women [26, 27]. This gradual abandonment of tobacco by men and the incorporation of the same by women have already had clear consequences in the incidence and mortality from this cancer by gender.

The incidence of lung cancer in men peaked in the year 2001 after many years of increase and a few of stability; since then, it has been declining. By contrast, in women, while ASIRe remained fairly low, incidence increased significantly from an ASIRe of 7.0 in the 1993–1997 to an ASIRe of 11.2 in the period 2003–2007. As a consequence, although the incidence remains much higher in men, the ratio between the incidence of lung cancer in men and women has decreased from 9.6 in the period 1993–1997 to 6.3 in 2003–2007. This decrease in differences of the incidence between genders is also observed in other tobacco-related tumours, but especially in the larynx, oral cavity and pharynx.

Lung cancer remains an important public health problem in Spain and the evolution of the prevalence of smoking indicates that a significant proportion of the population still smokes today, which highlights the need to improve the effectiveness of the strategy in the fight against smoking and, above all, that directed towards the female population.

Oral cavity and pharynx

In 2012, cancers of the oral cavity and pharynx as a whole occupied seventh position in incidence in the world with a total of 529,500 new cases [7]. In Europe, they occupied eleventh position [22] and in Spain too although the sex ratio (male/female) was slightly higher in Spain. In Spain, the estimated number of new diagnosed cases in 2015 was 6670 new cases, 4980 men and 1690 in women (Tables 1, 2). In the European context, the incidence of this cancer in Spain occupied an intermediate position [22].

The two main risk factors for this cancer are tobacco and alcohol consumption. The synergy between tobacco and alcohol use results in an increased risk up to 13 times compared to non-drinkers and non-smokers [28]. Another risk factor is infection by the human papillomavirus (HPV), especially for the tonsils, base of the tongue and other locations of the oropharynx [29].

Because of differences in exposure to these risk factors, the adjusted rates of Spanish cancer registries showed a strong variability. In the period 2003–2007, rates ranged from 10.3 in La Rioja to 20.6 in the Canary Islands in men and from 1.6 in La Rioja to 4.2 in the Basque Country in women [18]. Like other tobacco-related cancers, the ratio between cancer incidence rates in men and women decreased (6.8 in 1993–1997 to 4.0 in 2003–2007).

Larynx

Worldwide, laryngeal cancer occupies only the 21st position in the ranking of frequencies where 157,000 laryngeal cancers were diagnosed during 2012 [7].

It is estimated that in 2015 a total of 3725 new cases were diagnosed in Spain, 3426 men and 299 women (Tables 1, 2). In 2012, at the European level, ASIRw in men ranged from 1.4 in Iceland and 12.3 in Hungary and the incidence of this cancer in Spain occupied a medium–high position (rate of 7.8). In women, the rate in Spain was 0.7 occupying an intermediate position [7].

In the context of the cancer registries of Spain, a significant variability was also observed. In the period 2003–2007, incidence rates for men ranged from 8.9 in Albacete to 13.1 in the Basque Country. In women, it ranged from 0.1 in Cuenca to 0.8 in the Basque Country [18]. This variability, like in the cancer of oral cavity and pharynx, is strongly influenced by the prevalence of tobacco and alcohol.

Tobacco smoking is the main risk factor for this cancer. Alcohol is also another known risk factor for laryngeal cancer. The effect of the interaction of tobacco and alcohol appears to have a synergistic effect [28]. Although more limited, there is evidence of the role of HPV infection as a risk factor for larynx cancer [29].

Urinary bladder

In the European context, the incidence of urinary bladder cancer of Spain was, in men, the third highest only behind that of Belgium and Malta [22]. In 2012, urinary bladder cancer was the ninth most incident type of cancer in the world (430,000 new cases). In the EU-27, it is the fifth most incident cancer (123,000 new cases) and it is much more frequent in men (96,500) than in women (26,500) [7, 22].

A total estimation of 21,093 new cases was diagnosed in Spain in 2015, and although it occupied a similar position in their respective rankings (fourth position in men and fifth in women) it had a higher sex ratio than in Europe (17,439 cases in men and 3654 cases in women) (Tables 1, 2). In men, the estimated ASIRs for the year 2012 in the EU-27 ranged from 14.8 (UK) to 47.8 (Belgium) while in

Spain were 39.0. In women, the highest rate was in Denmark (10.7) and the lowest in France (3.3) while that of Spain (8.4) was placed in an intermediate position [22].

This cancer is caused by the contact of urothelial epithelium with substances excreted through the urine and coming directly from the inhaled or ingested, or from metabolism of other substances. Tobacco is the main risk factor for bladder cancer, being the attributable factor in more than 50% of cases. Smokers present nearly three times more risk than non-smokers [30]. Occupational exposure to aromatic amines (carcinogens present in tobacco and released in the textile industries among others) [31] and to polycyclic aromatic hydrocarbons, formaldehyde, asbestos and solvents also increases the risk [32]. Occupations such as those related to the manufacture of leather, aluminium or others are also associated with an increased risk [33]. Environmental exposure to arsenic increases the risk by more than three times in those exposed compared to unexposed [34].

As with incidence rates of lung cancer and especially due to the effect of differences in smoking prevalence, rates of urinary bladder cancer present a high geographical variability in Spain. Thus, for the period 2003–2007, the rates ranged from 24.4 in Cuenca and 44.5 in Mallorca in men. In women, they ranged from 2.6 in Cuenca to 6.8 in Navarra [18].

Digestive cancers

Oesophagus

Although this is the eighth most common cancer worldwide with 456,000 cases in 2012 [7], in Spain it is rare in men and very rare in women. The number of estimated new diagnosed cases in Spain in 2015 is 2358, 1979 in men and 379 in women (Tables 1, 2).

The aetiological factors of this cancer vary depending on histological type. The main risk factor is alcohol consumption, especially for squamous cell carcinoma [35]. Tobacco consumption is another risk factor for this cancer (both, for squamous cell carcinoma and for adenocarcinoma). These two factors together are synergistic and produce an increased risk of up to 100 times in major consumers of tobacco and alcohol compared to non-consumers [36]. Another known risk factor is obesity which increases risk for adenocarcinoma up to three times in obese people compared to non-obese [37]. Barrett's oesophagus (glandular metaplasia of oesophageal mucosa) also carries an increased risk for adenocarcinoma [38].

Because of its relationship with tobacco and alcohol consumption, there is also a pronounced geographical variability and the observed pattern is similar to that of larynx. Thus, in the period 2003-2007 the highest rates in men were observed in the Basque Country (7.6), Asturias (7.0) and the Canary Islands (6.4) and the lowest in Ciudad Real (3.3) and Granada (3.6). In women, the highest rates were observed in the Basque Country (0.9), Girona (0.9), Canary Islands (0.8) and Mallorca (0.8) and the lowest in Albacete and Cuenca (0.2) [18].

Stomach

It is estimated that in 2015 in Spain a total of 8456 new cases of stomach cancer were diagnosed, 5150 in men and 3306 in women (Tables 1, 2). In 2012, stomach cancer was the fifth most incident cancer in the world (951,500 new cases) and the eighth most incident in the EU-27 (80,500 new cases) [7, 22].

Its incidence worldwide has been declining over the last decades and has gone from being the most frequent digestive cancer to be the second, after colorectal cancer. Nevertheless, it still maintains a large geographical variability both worldwide and European level as in Spain. Thus, among the cancer registries of Spain, ASIRw ranged from 8.0 in Mallorca to 15.7 in the Basque Country in men in the period 2003–2007. In women, rates ranged from 3.9 in the Canary Islands to 6.3 in Cuenca and Ciudad Real [18]. Variability in Europe is even wider. In men, the estimated ASIRw for 2012 ranged from 5.0 (Switzerland) to 29.1 (Belarus) while in Spain it was 11.0 (intermediate-low position). In women, the highest ASIRw was in Albania (15.1) and the lowest in Sweden (2.7) while that of Spain (5.7) is also placed in a low-intermediate position [22]. It is more common in men than in women (sex ratio of the ASIR: 2.0) (Tables 1, 2).

One of the best known stomach cancer risk factors is Helicobacter Pylori infection. People infected by this bacterium have three times the risk of developing gastric adenocarcinoma compared to uninfected individuals [39]. This increased risk is not observed in the cardia, which seems to have a behaviour more related to risk factors of oesophageal cancer. Other known risk factors are the consumption of salt and salty foods. This consumption of salty foods may present a synergy with Helicobacter pylori infection, significantly increasing the risk [37]. Tobacco, as in other cancers, is also a risk factor, and increases 1.5 times the probability of developing cancer in smokers compared to non-smokers and can have synergies in increasing risk to infection by *Helicobacter pylori* [30]. Workers having contact with asbestos also present an increased risk of gastric adenocarcinoma [40]. Consumption of fruit and vegetables plays an important role as a protective factor in this cancer [37]. Socio-economic level is a variable that reflects exposure to multiple factors such as diet, infection with *Helicobacter pylori* and others, but does not adequately express all the known involved factors.

Thus, a country like Japan that has a high socioeconomic level has high rates of this cancer. Other risk factors of gastric cancer are pernicious anaemia, the A blood group, exposure to ionizing radiation and the background of partial gastrostomy [41].

Colon and rectum

Worldwide, colorectal cancer accounts for almost 10% of all cancers and it was the third most incident cancer with 1,360,500 new cases in 2012 [7]. In Europe and for both genders as a whole, it occupied the third position after prostate and breast [22] and in Spain it is in first position, and the estimation of the number of new cases for 2015 was 41,441, being more frequent in men (24,764) than in women (16,677) as in Europe. The estimated ASIRe for Spain was of 77.8 in men and 42.0 in women, respectively (Tables 1, 2). At European level, the incidence of this cancer in Spain occupied an intermediate position [22].

Among the cancer registries of Spain, ASIRw in men ranged from 32.7 in Cuenca to 50.2 in Tarragona in the period 2003-2007. In women, they ranged from 16.7 in Cuenca and 27.6 in Tarragona [18].

In Spain, the temporal evolution of this cancer has shown a steady increase, especially in men and until the mid-90s [42]. Thus, in colon cancer, the estimated ASIRe increased from 31.3 in the 1993–1997 5-year period to 42.1 in 2003–2007 in men (35% increase) and from 22.6 to 25.1 in women (11% increase). In rectum cancer, the equivalent percentage increases were 18.1% in men and 15.8% in women. Systematic screening cannot be the cause of this increase. Although at present screening programmes are more extended, the first population programmes began in 2000 in Catalonia and in 2006 in Valencia and Murcia. Thus, the increased incidence is mainly due to the influence of the risk factors.

As in most cancers, age is the main non-modifiable risk factor of this cancer. More than 90% of cases are diagnosed in people older than 50 years of age. In people with a genetic predisposition or with underlying diseases such as inflammatory bowel disease, an increased risk was also observed for colorectal cancer. There is an increased risk in people with inherited diseases such as familial colonic polyposis or Lynch syndrome, but the vast majority of colorectal cancers, over 90% of cases are sporadic [43].

Regarding the modifiable risk factors, one of the most important is the consumption of red and processed meat [37]. By contrast, consumption of fibre, fruits and vegetables as well as dairy or micronutrients, such as folate, calcium and vitamin D, is protective for this cancer [44]. All these dietary factors influence the risk of the cancer precursor lesions, the colorectal adenomas. It is estimated that 70% of colorectal cancers are avoidable with only dietary and nutritional measures [45]. Obesity is another risk factor for both genders, especially abdominal obesity. Instead, exercise and physical activity act as protectors. In both cases, hyperinsulinemia plays an important role and its presence implies an increased risk of colorectal adenomas [44]. In recent years, the role of alcohol above 100 g of consumption per week as risk factor has also been observed [46]. Some studies have pointed to the role of consumption of tobacco in colorectal cancer, especially in the cancer of the rectum, with increased risk of up to twice in relation to the risk of non-smokers [47]. Although it has been shown that consumption of acetylsalicylic acid is protective against this cancer, the appearance of side effects makes its administration not recommended systematically as chemoprevention [48].

Due to the high burden of colorectal cancer, its natural history and the possibility of early diagnosis by effective screening tests, this cancer is susceptible of population screening [49]. Population screening of this cancer has been implemented in various European countries during the last three decades (UK, Italy, Germany…). With regard to Spain, in 2012 population screening was implemented in a pilot phase in nine regions (Aragon, Canary Islands, Cantabria, Castile and Leon, Catalonia, Valencia, Murcia, Basque Country and La Rioja), by conducting a biennial faecal occult blood test on a population aged 50–69 years (except Cantabria: 55–69). However, all programmes together only covered 14% of the Spanish population of this age range [50].

Colorectal cancer is an important and still growing health problem in Spain. The evolution of incidence, the high prevalence of the main known risk factors (inadequate diet, overweight, sedentary lifestyle) and the possibility of its effective early diagnosis demonstrate the need to expand the early detection population programmes to cover 100% of the 50–69 years old population.

Pancreas

Pancreatic cancer ranks 15th in number of incident cases worldwide (338,000 new cases in 2012) [7] and in Europe it occupies eighth place with 3% of cases [22]. In Spain, the estimate of new cases for 2015 was 6914, 3513 in men (ASIRe = 11.3) and 3401 in women (ASIRe = 7.9) (Tables 1, 2). In the period 2003–2007, ASRw of existing Spanish cancer registries fluctuated between 4.3 and 8.3 in men and between 3.2 and 5.4 in women [18].

Tobacco is the best known risk factor for this cancer, with twice the risk in smokers compared with non-smokers [30]. Alcohol consumption has also been associated with increased risk, especially in heavy drinkers [51]. Obesity and a history of prior pancreatitis or gastric surgery are also risk factors [22, 52, 53] as well as diabetes [54]. The increase of pancreatic cancer incidence is probably related to an increase in some of these factors in the Spanish population.

Genital cancers

Breast

Breast cancer is by far the most common malignant tumour in women both worldwide and in Europe and in Western countries. In 2012, approximately 1,671,000 women were diagnosed from breast cancer worldwide and this represents 25% of all cancers in women. In the EU-27, the 364,500 breast diagnosed cancers accounted for a slightly higher proportion (30.4%) [7, 22]. The probability that a European woman presents a breast cancer before 75 years old is 8% [55]. In Spain, the number of female breast cancers diagnosed in 2015 was estimated in 27,747 (ASIRe = 88.3) (Table 2) which placed Spain in an intermediate situation at European level.

In Spain, where a north–south gradient is observed, the registries with highest ASIRw in the period 2003–2007 were Navarra (69.6), Tarragona (68.8) and Girona (67.8) and those with the lowest rates Cuenca (50.6), Ciudad Real (51.6) and Granada (54.8) [18].

Age is the main non-modifiable risk factor in breast cancer, with an increase in incidence from age 35 and a stabilization from age 55, coinciding with menopause. Hormonal status represents another important set of risk factors. A high age at first pregnancy increases the risk by 20%, while a high age of onset of menopause increases it to 30%. Conversely, a later age at menarche is a protective factor, with a decreased risk of 40% [56]. A family history of breast cancer is also another important non-modifiable risk factor and about 10% of cases of breast cancer have a hereditary component due to mutation of a gene. These cases usually occur in younger women [57]. In Spain, the cumulative risk of breast cancer at age 70 in carriers of the mutation in BRCA1 has been estimated at 52% (95% CI 26–69%) and at 47% in mutation carriers in BRCA2 (95% CI 29–60%) [58].

Among the modifiable risk factors, hormone replacement therapy (HRT) or taking oral contraceptives increases the risk in 20% compared to women who do not take them [59] although the risk associated with taking oral contraceptives depends on the hormonal combinations used. In Spain, the use of HRT is and has been very low [60]. Having given birth reduces by 10% the risk compared to women who have not given birth, like breastfeeding reduces risk by 2% for every 5 months of lactation [37]. Alcohol consumption has proved to increase risk up to 30% in female drinkers with respect to non-drinkers. Regarding tobacco, evidence of its role as a risk factor is more limited and more studies are required [35]. Physical activity has been linked as a protective factor for breast cancer in postmenopausal women, although the evidence is also limited. The presence of a higher proportion of body fat increases the risk of breast cancer in postmenopausal women up to 10% with respect to non-obese women [61]. Exposure to ionizing radiation in medical diagnostic or therapeutic processes also increases the risk of breast cancer [24].

Due to the high disease burden of breast cancer in the population, breast cancer screening programmes were implemented in the most developed countries several decades ago. In Spain, the first screening programme was implemented in 1990 in Navarre, and currently all regions offer such programmes, which cover more than 90% of the target population. In 2011, participation rate in these programmes was over 73% [62].

The implementation and operation of population screening programmes throughout the country altered for some years the temporal incidence trends by region depending on implementation strategies in each of them. Currently, screening has already reached a saturation point [63]. Screening causes a certain level of over-diagnosis (and, therefore, slightly higher rates than there would be if there was no screening). It also causes a proportion of in situ tumours somewhat higher than it would be without screening [64], higher survival rates and lower mortality rates. The magnitude of the effect that screening produced on these indicators is not quantifiable for different reasons. For example, increases in survival rates are caused by screening but also for opportunistic early diagnosis and by therapeutic improvements in this cancer and it is very difficult to assign which part corresponds to each factor.

However, due to its high impact, research, prevention, diagnosis and treatment of this cancer should be treated as priorities in oncology plans and the early diagnosis of this cancer through screening programmes should remain an important element together with other measures such as strategies for rapid diagnosis and ensuring the best therapeutic measures. Finally, aetiologic and therapeutic research must continue since many of the future improvements depend on it.

Cervix uteri

Uterine cancer, with 847,000 new cases in 2012, is the second most common cancer worldwide in women [20]. As this cancer encompasses two types of tumour (cervix and corpus uteri), which differ clearly both in their anatomical location and their aetiology and characteristics, they will be treated separately here.

Although worldwide cervix uteri cancer is the fourth most common cancer in women, at European level it occupied only ninth position [22]. In Spain, a country of low incidence, it was the twelfth most common cancer and it is estimated that 2399 new cases were diagnosed in 2015 (Table 2). During the period 2003–2007, ASIRw of registries ranged from 3.8 in Navarra to 8.5 in Tarragona [18] showing an important geographical variability. Compared to European countries, Spain presented in 2012 an ASIRe lower than the European average (7.7 vs 11.3) [22].

Between 1993–1997 and 2003–2007, a stabilization of incidence rates was observed although the projection for 2015 shows a slight increase in the ASIRe in relation to that of the period 2003–2007 (Table 5).

Infection by human papillomavirus (HPV) is the main risk factor for cervix uteri cancer. Some behaviours and sexual practices that favour HPV infection are associated with an increased risk, such as a greater number of sexual partners and young age of onset of sexual relationships [29]. Although HPV is a necessary factor for cervix uteri cancer, the presence of cofactors is required for the development and progression of this cancer. Immunosuppression status, multiparity, smoking, prolonged use of oral contraceptives and concomitant cervico-vaginal infections by chlamydia and herpes simplex virus can act as cofactors [65]. At the individual level, for primary prevention the most effective strategy is condom use as a method of preventing infection by HPV and other sexually transmitted diseases.

In Spain, different strategies for primary and secondary prevention are employed. On the other hand, all regions apply vaccination plans targeting the most common subtypes of HPV in their immunization schedule. Nevertheless, coverage rates with full schedule are lower than expected and vary between 50 and 98% by region.

As secondary prevention, opportunistic screening with cervical cytology using the Papanicolaou technique is performed. Currently, with the possibility of determining HPV infection, new protocols for screening for this cancer are taken into account for the near future.

Due to the introduction of the vaccine against HPV, it is expected that both, incidence and mortality, will decline in the future although, in the short term, this preventive action will have no significant effect on incidence. In the short term, incidence will depend on other factors such as the proportion of women of other countries with different prevalence of HPV infection due to migration, the modification in sexual behaviour and the intensity and the characteristics of screening programmes.

Corpus uteri

Although there are many types of cancer of the corpus uteri that can affect both the endometrium and the myometrium, the vast majority of them start in the endometrium. With 319,500 new cases worldwide in 2012, it occupied the fourth place in Europe (64,500 new cases) [7, 22].

In Spain, it was in third position since lung cancer remains less common than that of corpus uteri. It is estimated that 6160 new cases were diagnosed in Spain in 2015 (Table 2).

Variability in incidence rates is lower than that in other types of cancer. In the 2003–2007 period, the lowest ASIRw was observed in Albacete (10.5) and Canarias (10.9) and the highest ones in Murcia (15.9) and Granada (15.4) [18]. We have no information on whether this variability could be affected by regional differences in the rates of hysterectomies.

The main risk factors related to the most common subsite of the corpus uteri cancer, the endometrium, are related to the hormonal status of women, in particular to increased oestrogen exposure. Thus, nulliparous women and those with higher age at onset of menopause present a higher risk of endometrial cancer. HRT in menopause and treatment with tamoxifen increase the risk of endometrial cancer [66]. Some inherited syndromes such as Lynch syndrome are also risk factors for this cancer [67] and obesity and diabetes also increase the risk, while physical activity is probably a protective factor [37].

Incidence rates have increased steadily since 1993 and possibly this is due to the increasing prevalence of major risk factors such as obesity or oestrogen exposure.

Ovary

3228 estimated ovarian cancers (ASIRe = 9.9) were diagnosed in Spain in 2015 being, as in Europe, the fifth most common cancer in women (Table 2) [22]. As in corpus uteri cancer, variability within Spanish cancer registries was low. In the period 2003–2007, ASIRw ranged from 6.7 in the Canary Islands to 10.0 in Cuenca [18].

The incidence of this cancer showed a slight decrease between the 1993–1997 and 2003–2007 5-year periods. The estimated ASIRe moved from 11.9 to 10.7 (decrease of 9%) (Table 5).

Ovarian cancer is strongly related to hormonal and reproductive risk factors. Nulliparity is a known risk factor. The HRT for menopause or ovarian hyperstimulation treatments for fertility also increases the risk. Instead, long-term use of oral contraceptives reduces the risk [68]. Another important risk factor is the hereditary syndrome of cancer of breast and ovary with mutations BRCA1 and BRCA2. In Spain, the cumulative risk of ovarian cancer at age 70 has been estimated at 22% in BRCA1 mutation carriers and 18% in BRCA2 [58]. Lynch syndrome is also associated with an increased risk for this cancer [69].

Tobacco smoking increases the risk of ovarian cancer, particularly for one of the histological types, mucinous adenocarcinoma [70]. Obesity probably also increases the risk of this cancer in the same way as a high fat diet.

Due to the variety of factors involved and the lack of data, the slight decreasing incidence trend is difficult to interpret.

Prostate

Prostate cancer is the second most common cancer in men worldwide, but in Europe and Spain it has been, for some years, the first in number of diagnoses (360,000 in the EU-27 in 2012 and 33,370 in Spain in 2015). The estimated ASIRe for 2012 is slightly lower than that of the European average (103.4 versus 110.8) (Table 2) [7, 22].

In Spain, as in many Western countries, the incidence has increased dramatically since the early 1990s due to the introduction and widespread use of prostate-specific antigen (PSA) test [71]. It is estimated that in Spain ASIRe increased from 54.1 in 1993–1997 to 96.4 in 2003–2007 (Table 5). In the latter period, ASIRw varied from 44.1 in Granada to 73.8 in the Basque Country [18] and these differences are, above all, the consequence of the different degree of use of the PSA test than actual differences in incidence.

Prostate cancer presents a strong relationship with age, with an increasing incidence after age 50, and age constitutes the main risk factor for this cancer. In 5–10% of cases, a hereditary component has been found in family aggregations. Mutations in the BRCA1/BRCA2 genes (increased risk of male breast, pancreas and prostate cancers) and in p53 and CHEK2 genes (Li-Fraumeni syndrome) have also been observed [72]. There seems to be a moderately increased risk for this cancer in heavy smokers [73]. So far, a clear relationship with dietary factors has not established [74].

Two factors have been involved in temporal trends in the incidence and mortality of prostate cancer. On the one hand, an actual increase in the incidence occurs due to increased exposure to one or more risk factors. On the other hand, an increase in the detection of existing tumours occurs due to the introduction of new diagnostic and therapeutic techniques such as transurethral resection (TUR) and, above all, PSA test [75]). The use of PSA has had a dramatic impact on incidence trends in many countries, but has also produced undesirable effects like overdiagnosis. The speed in the spread of PSA test in Spain was slower than that in other countries and it is impossible to know its impact on age-stage-specific incidence rates trends.

Haematology neoplasms

Non-Hodgkin lymphomas

It is estimated that in Spain a total of 7670 new cases of non-Hodgkin lymphoma (NHL) were diagnosed in 2015, 4190 in men and 3480 in women. In men, it occupied seventh place and sixth in women (Tables 1, 2). In 2012, NHL was the tenth most incident cancer globally (385,500 new cases) and the ninth in the EU-27 (79,000 new cases) [7, 22].

During the period 2003–2007 in Spanish cancer registries, the ASIRw in men fluctuated from 6.5 in Ciudad Real to 13.5 in the Canary Islands. In women, rates varied from 4.6 in Ciudad Real to 9.0 in Canary Islands [18]. Variability in Europe was even wider. In men, ASIRe estimated for 2012 in the EU-27 varied from 3.4 (Greece) to 18.6 (Finland), while in Spain it was 14.6 standing at an intermediate-high position. In women, the highest rate was in Finland (13.1) and the lowest in Greece (2.2) while that of Spain (9.6) was placed in an intermediate position [22]. NHL was more common in men than in women (Tables 1, 2).

Alterations in the immune system such as immunosuppression present in AIDS or in patients with immunosuppressive therapy have been associated with an increased risk for NHL. The infection by Epstein–Barr virus (EBV) also increases the risk, in a similar way to HIV infection. Another infectious agent, the human T-lymphotropic virus type 1 (HTLV-1), causes a rare variety of NHL, the adult T cell lymphoma. Also noteworthy is the role of Helicobacter pylori in increasing the risk of another type of NHL, the gastric lymphoma. On the other hand, infection by hepatitis C virus (HCV) increases the risk of some types of NHL, especially B cell types [29]. Some autoimmune disorders increase the risk of this cancer [76]. Finally, occupational exposure to benzene, or diagnostic or therapeutic exposures to ionizing radiation also increase the risk of this cancer [24, 77].

The NHLs are a heterogeneous group of tumours in their aetiology and their clinico-pathological features. So, incidence patterns can vary according to the morphological distribution of NHL in the population.

In Spain, the incidence of NHL rose until 1996 probably due, at least in part, to diagnostic improvements and to the increase of AIDS-related lymphomas among young adults [78]. Since the mid-1990s, incidence rates have remained very similar despite the decrease in cases attributable to AIDS (Tables 4, 5).

Leukaemia

In 2012, leukaemia was the eleventh most incident type of cancer in the world (352,000 new cases) and the twelfth in the EU-27 (62,000 new cases) [7, 22]. It is estimated that in 2015 in Spain a total of 6518 new cases of leukaemia were diagnosed, 3782 in men and 2736 in women. In men it occupied the ninth place and in women the tenth one (Tables 1, 2).

During the period 2003–2007 in Spanish cancer registries, the ASIRw in men fluctuated from 6.1 in Ciudad Real to 11.6 in Murcia. In women, rates ranged from 4.5 in Ciudad Real to 9.5 in Cuenca [18]. It is a slightly more common cancer in men than in women (Tables 1, 2).

Only risk factors for some specific subtypes of leukaemia are known. Diagnostic, therapeutic and occupational exposures to ionizing radiation increase the risk for any subtypes of leukaemia excluding chronic lymphocytic leukaemia [24]. Occupational exposure to benzene increases the risk of acute myeloid leukaemia (AML). Another known occupational exposure that increases the risk of this cancer is formaldehyde, with twice the risk in the exposed population versus the unexposed [77]. Fanconi anaemia determines an increased risk of AML in affected persons. Similarly, Down's syndrome is also associated with an increased risk for the acute megakaryocytic leukaemia [79, 80]. Treatments with Phosphorus-32 radioisotope or MOPP chemotherapy also increase the risk of AML [66, 81]. Tobacco smoking increases the probability of developing myeloid leukaemia. There is also sufficient evidence of the relationship between prenatal tobacco exposure and increased risk of childhood leukaemia, especially acute lymphoblastic leukaemia [51].

Due to the variety of factors involved which, at the same time, explain only a low proportion of incident cases, it is difficult to interpret the stability in the incidence of these tumours.

Skin

Skin melanoma

In 2015, 4890 new estimated cases of skin melanoma (2577 in men and 2313 in women) were diagnosed in Spain. This cancer ranks the fifteenth place in both, men and women (Tables 1, 2). In 2012, skin melanoma was the 19th most incident type of cancer in the world (232,000 new cases) and the seventh in the EU-27 (82,000 new cases) [7, 22]. Among Spanish cancer registries, the ASIRw of the period 2003–2007 fluctuated from 3.6 in Cuenca to 7.3 in Granada in men and from 4.2 in Ciudad Real to 8.9 in Granada in women [18].

Skin melanoma is a particularly common tumour in fair-skinned white populations. The highest incidence rates are observed in Caucasian origin populations of Australia, New Zealand and South Africa followed by North America and Northern Europe. Spain presents one of Europe's lowest incidence rates [18]. In European countries, melanoma incidence is higher among women than men, but in other predominantly Caucasian populations such as Australia and the US this malignancy is more common among men [82]. In Spain, as in the majority of Caucasian populations, the most frequent primary site for skin melanoma is the torso or upper body in men and the lower extremities in women [83, 84]. Apart from the characteristics of the skin, the risk of developing skin melanoma is related to intense and intermittent exposure to natural and artificial UV-exposure [81] and a history of sunburn particularly during childhood [85].

During the past several decades, there has been a substantial increase in the incidence of skin melanoma among all Caucasian populations with the majority annual percentage changes between 3 and 7% in these populations [86]. In Spain, from 1993–1997 to 2003–2007, skin melanoma incidence ASRe increased among females from 4 to 7.9 with an estimated annual percentage of change (APC) of 2.6% whereas in men, incidence was 4.7 in 1993–1997 and 7.2 in 2003–2007 (APC: 4.9%) (Tables 5, 6). This higher increase in men compared with women observed in recent years explains the similarity of the present incidence numbers and rates in men and women (8.6 vs 7.3).

Limitations

Although the coverage of Spanish PBCRs of this study is less than 30%, these estimates have been made with data from the most quantity of PBCRs to date. The projected numbers and rates of new cancer cases should be interpreted with caution because they are model-based estimates that may vary considerably from year to year for reasons other than changes in cancer occurrence. For instance, the model is sometimes oversensitive or undersensitive to abrupt or large changes in observed data. However, the methods and the strategy used in these estimates direct to minimize as much as possible the errors and, as consequence, these estimates of new cancer cases provide a reasonably accurate estimate of the current cancer incidence in Spain. Caution in the interpretation of results should be applied above all in some specific cancers. For breast and prostate cancers, incidence trends are very influenced by the different intensity and calendar screening activities among the areas covered by the registries. In these two cases, we used the strategy already used in other studies, that is, to assign to the year 2015 the same rates as those in the model estimated for 2007. International comparisons of urinary bladder tumours are difficult because of the differences in their definition and inclusion criteria. The estimations of REDECAN were not comparable with those of EUCAN-2012, and for this type of cancer, European incidence was compared with that estimated by EUCAN-2012 for Spain.

Conclusions

In 2015, nearly a quarter of a million new cancer cases were diagnosed in Spain. In recent years, cancer incidence in men seems to have stabilized due to the fact that the decrease in tobacco-related cancers compensates for the increase in other types of cancer like those of colon and prostate. In women, despite the stabilization of breast cancer incidence (probably due to the saturation of screening), increased incidence is due, above all, to the rise of colorectal and tobacco-related cancers. Improvement of smoking control policies and extension of colorectal cancer screening should be the two priorities in cancer prevention for the next years.

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Compliance with ethical standards

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