

Trends in cancer mortality in Spain: 1975-2004

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ABSTRACT

Aims and background. Total cancer mortality rates in the European Union have declined by about 7% over the period 1982-2002. The aim of the present study was to investigate similar trends in Spain over the period 1975 to 2004 by age, sex, and cancer site.

Patients and methods. Trends in Spanish mortality rates (standardized to the world standard population) for all cancers and for 14 major cancer sites for the years 1975 to 2004 are analyzed. Join point regression analysis was used to identify points where a significant change in trend occurred.

Results. The overall cancer mortality rate in Spain in men and women declined by about 1% a year between 1995 and 2004. For the period 1975 to 2004, declines were observed for several neoplasms: lip, -3.62% in men and -3.39% in women; esophagus, -0.28% in men and -2.73% in women; stomach, -2.99% in men and -3.66% in women; liver, -0.52% in men and -3.77% in women. There was a substantial rise in: colon cancer, 3.72% in men and 1.79% in women; pancreas, 2.21% in men and 2.25% in women; lung cancer rose 1.18% in men and 0.97% in women, and between 1999-2004 it rose 5.23% in women. Most of these are tobacco-related neoplasms.

Conclusions. Cancer mortality in Spain is mainly a tobacco-related problem. More attention needs to be focused on campaigns to decrease and prevent smoking, especially in the young, where smoking rates are higher than in the general population.

Introduction

Total cancer mortality rates in the European Union and other developed countries have seen a steady decline over the past 20 years, with similar trends occurring in Spain. However, cancer remains a major problem in Spain and is the leading cause of death among Spanish men and the second leading cause among Spanish women. For both men and women between the ages of 40 and 79, it is the leading cause of death, exceeding cardiovascular disease and stroke. Therefore, it is important to provide updated information on cancer mortality in Spain and to identify the major tissues contributing to Spanish cancer deaths.

Using official cancer mortality rates in Spain for the years 1975 to 2004, we provide annual mortality rates (adjusted to the world standard population) for all cancers and for 14 major cancer sites. Since long-term trends provide useful information to understand recent patterns and to project most likely future trends, the major aim of the present work is to provide comprehensive documentation on the patterns of cancer mortality trends in Spain.

Materials and methods

Official death-certification numbers for all cancers and for major cancer sites were derived from the official Spanish data base¹. The classification of cancer deaths was recorded for all calendar periods according to the ICD ninth revision. Estimates of the

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resident population, generally based on official censuses, were obtained from the official dates from matrices of certified deaths and resident populations, age-specific rates for each 5-year age group and age-standardized rates per 100,000 population². All ages were computed using the direct method based on the world standard population.

Annual percentage changes in rates were computed using a joinpoint log-linear model³ (Figures 1 and 2). Joinpoint is a statistical software package for the analysis of trends using joinpoint models, that is to say, models where several different straight lines meet at "joinpoints." The program starts with the minimum number of joinpoints and tests whether more joinpoints are statistically significant and must be added to the model. This enables the user to test whether an apparent change in trend is statistically significant. The test of significance uses a Monte Carlo Permutation method. The models may incorporate estimated variation for each point or use a Poisson model of variation. In addition, the models may also be linear on the log of the response (the calculation of annual percentage rate change). The software also enables us to view one graph for each joinpoint model, from the model with the minimum number of joinpoints to the model with the maximum number of joinpoints.

Results

Overall cancer mortality rates in Spain have declined significantly in recent years. After increasing from 1975 to 1995, cancer mortality in men has decreased by about 1% per year since 1995. Cancer mortality in women decreased from 1975 to 1985, remained fairly constant until 1995, and then similar to men, declined at about 1% per year. Table 1 and Figures 1 and 2 provide corresponding changes in rates in both sexes.

Divided into sexes, the following was observed: In men, cancers that decreased the most were, per year, lip cancer (-3.62%), stomach cancer (-2.99%) and testicular cancer (-2.45%). The model enabled us to establish the different percentages of change so that: for lip cancer, whose fall has remained the same for the last 15 years of study, the highest percentage of change corresponded to the period between 1993-2004, with a fall of -5.89%; for stomach cancer, the highest percentage of change occurred between 1975-1981, with a fall of -4.59%, followed by the period between 1981-2004 with -2.77%; for testicular cancer, the most important fall (-3.12%) corresponded to the period between 1987-2004. A slight fall was found in lung cancer and prostate cancer. In previous periods, both underwent important rises (Table 2).

In women, the following decreases in incidence were observed, per year: for lip cancer, -4.17% between 1975-1994; for stomach cancer, -5.84% between 1975-1980 and -3.45% between 1980-2004; for colon cancer, -6.22%

between 1975-1982, and the following years the incidence increased significantly. Rectal cancer decreased throughout the research period, but the most noticeable fall (-1.28%) was between 1996-2004. Liver cancer decreased as well throughout the research period, but mainly between 1975-1987 with a decrease of -5.05%. Laryngeal cancer incidence also dropped during the research period. For lung cancer, of note was a slight fall between 1975-1992, followed by a period of significant increase in incidence. There was a small drop of -0.67% in the incidence of bladder cancer between 1986-2004.

One encouraging result was the 2.46% annual decline in breast cancer between 1993-2004 after having increased by 2.22% per year between 1975-1993. A surprising result was the decrease in uterine cancer between 1975-1981 (-36.7%), followed by a rapid 3.96% annual increase in the years between 1981 and 2004 (Table 3).

Discussion

The overall cancer mortality rate in Spain in 2004 was 156.2 per 100,000 for men and 70.8 per 100,000 for women, representing about 33% and 27% of all deaths annually in Spain for men and women, respectively. The relative cancer mortality rate in Spain can be compared with that of Europe for 2002⁴. In 2002, overall cancer mortality in Spain compared favorably with the average for Europe: 166.0 *vs* 166.5 for men and 70.8 *vs* 95.2 per 100,000 for women in Spain and Europe, respectively. Although cancer mortality in Spain is in the middle range for European countries, it nevertheless takes a large toll in terms of years of life lost due to premature mortality and disability⁵. Cancer is the leading cause of death in Spain for men and women between the ages of 40 and 79. The greatest burden of cancer disease in Spain in terms of premature mortality and disability is due to lung, colorectal, breast, stomach and prostate cancer. Cancer of the lung, colon, prostate, and bladder are the leading causes of mortality in men primarily due to historically high smoking rates in Spanish men. Cancer mortality of the liver, kidney, stomach and brain are also high in men. For Spanish women, cancers of the breast, lung, colon, and stomach are the leading causes of mortality. Although in Spain women started smoking later than men, the rates reached high levels, and it is likely that smoking-related cancers will continue to increase in Spanish women in the near future.

Spain has made considerable progress in recent years in the battle against cancer mortality, primarily due to earlier diagnosis and more effective treatments. Since 1995, cancer mortality in Spain has decreased at a rate of about 1% per year in both men and women (Tables 1 and 2).

Lung cancer is the leading cause of cancer mortality in Spanish men and the third leading cause of cancer mortality in women. In contrast to the EU where lung

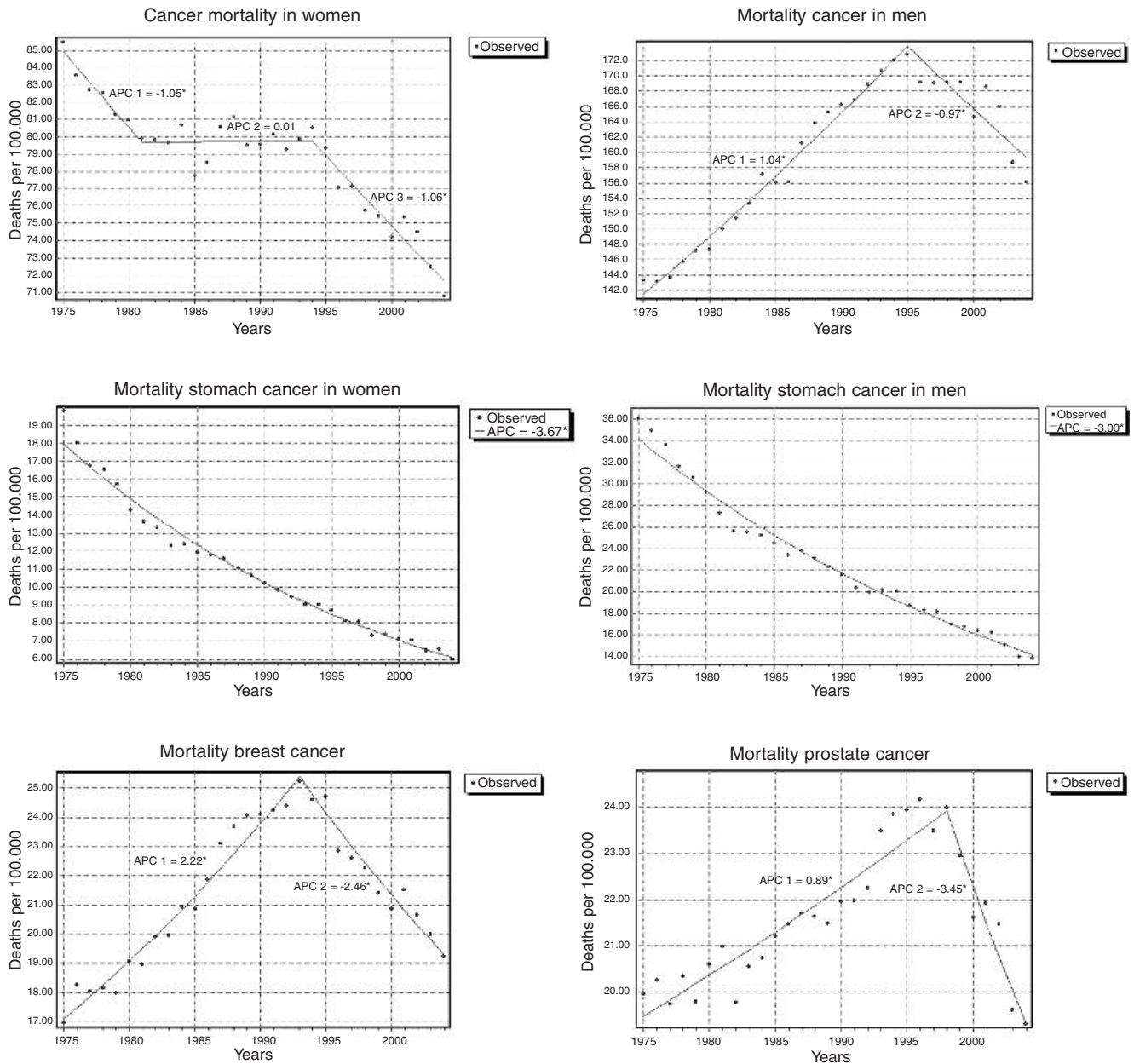


Figure 1 - Cancer mortality trends in Spain, 1975-2004. "Best" joinpoint model estimates for decreasing mortality cancers, for selected cancer sites by gender.

cancer rates have declined by 1.9% per year in men^{6,7} but have increased by 1.7% in women^{8,9}, lung cancer rates in Spain have not declined. Over the period 1975 to 2004, Spanish lung cancer mortality rates increased at an annual rate of 1.18% in men and 0.98% in women. Male lung cancer mortality in Spain appears to have peaked in 1994 and declined by about 5% by 2004. However, the lung cancer mortality rate in Spanish women is still rising.

Despite the persistent rise in female lung cancer in the EU, recent trends in cancer mortality in the EU are encouraging and indicate that an overall 11% reduction

in total EU cancer mortality from 2000 to 2015 may be realistic. This is something that has not yet happened in Spain, where there has been a significant increase (46%) in lung cancer mortality in women under the age of 65 in recent years, for example in Navarre, Spain¹⁰. Reflecting this trend, lung cancer mortality rates in women for the whole of Spain increased at an annual rate of 4.64% between the years 1999 to 2004 (Table 3). In some European countries, lung cancer mortality in females has started to level off, whereas in Spain it is still rising. Lung cancer mortality in women has increased by 62% in the past 15 years and 30% in the past 5 years. In Spain, as in

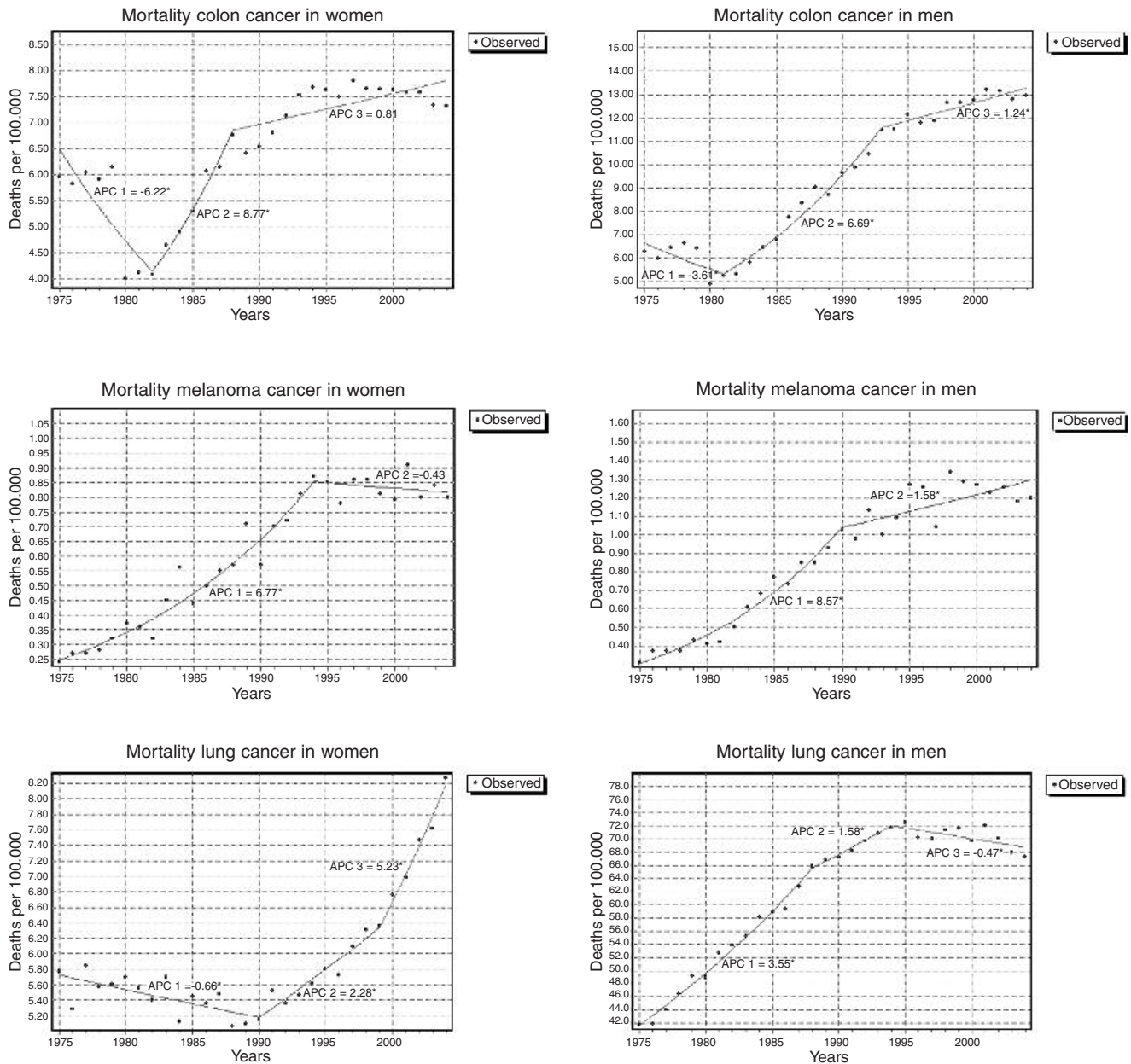


Figure 2 – Cancer mortality trends in Spain, 1975-2004. “Best” joinpoint model estimates for increasing mortality cancers, for selected cancer sites by gender. APC, annual percent change per year.

other countries, lung cancer is the second most common cause of cancer death in women after breast cancer (breast mortality is 13.3 per 100,000, whereas lung cancer mortality in women in Spain is 5.8 per 100,000.) The Spanish female lung cancer mortality rate is still below the average value of 11.4 per 100,000 for Europe in 2002, indicating a potential for continued growth.

Colorectal cancer remains a major cause of cancer mortality in Spain. Between the ages of 40 and 79, it is the second more frequent cause of cancer mortality in Spanish men and women (lung cancer is the first for men and breast cancer is the first for women). Colorectal cancer in Spain accounts for 11% of cancer mortality

in men and 15% in women. This is comparable to Europe, where colorectal cancers are the second most diagnosed form of cancer, accounting for 13% of total cancer incidence, and also rank second in mortality, accounting for 12% of cancer mortality¹¹. Colon cancer mortality has increased steadily in Spanish men from 1981 to the present, increasing at an annual rate of 6.7% from 1981 to 1993 and 1.3% for 1993 to 2004 (Table 2). Spanish women have experienced a similar rise, increasing at an annual rate of 8.6% from 1982 to 1988 and 0.81% from 1988 to 2004 (Table 3). As in many other European countries, colorectal cancer mortality rates in Spanish women are about 60% those of men, a differ-

Table 1 - Cancer mortality in Spain, 1975-2004

Site	Men			Women		
	-APC	95% CL		-APC	95% CL	
All cancers	0.56	0.39,	0.72	-0.41	-0.51,	-0.33
Lip	-3.62	-4.23,	-3.02	-3.39	-4.60,	-2.15
Esophagus	-0.28	-0.48,	-0.28	-2.73	-3.08,	-2.39
Stomach	-2.99	-3.13,	-2.85	-3.67	-3.80,	-3.52
Colon	3.72	3.18,	4.26	1.79	1.17,	2.41
Rectum	0.50	0.30,	0.70	-0.80	-0.10,	-0.70
Liver	-0.52	-0.64,	-0.41	-3.77	-4.00,	-3.52
Pancreas	2.21	1.95,	2.47	2.25	2.03,	2.50
Larynx	0.50	0.30,	0.71	-0.87	-1.04,	-0.77
Lung	1.18	1.47,	2.18	0.97	0.50,	1.37
Melanoma	5.64	4.70,	6.23	4.87	4.14,	5.60
Prostate	0.36	0.10,	0.60	-	-	-
Testicles	-2.45	-3.16,	-1.74	-	-	-
Urinary bladder	0.97	0.78,	1.17	0.32	0.01,	0.63
Kidney	2.65	2.30,	3.00	1.41	1.08,	1.73
Breast	-	-	-	0.66	0.23,	1.09
Ovary	-	-	-	3.69	3.22,	4.16
Uterus (body)	-	-	-	-2.04	-4.90,	0.98
Thyroid	1.13	0.39,	1.88	-0.10	-0.52,	0.30

APC, annual percent change. Per year, in all periods.

ence that may be due to the fact that estrogens appear to be preventive of colon cancer. In many European countries, colon cancer mortality has been decreasing since about 1990. However, since these countries started at a higher colorectal cancer mortality rate than in Spain, colorectal cancer mortality in Spain is currently at about the same level as in Austria, Belgium, France, Italy, and Germany. The US National Cancer Institute estimates that 12% of US colorectal cancer deaths, where smoking rates are about half those in Spain, can be attributed to cigarette smoking¹². Thus high smoking rates in Spain may be a contributing factor in Spanish colorectal cancer mortality. More attention needs to be given to early screening and prevention opportunities, since virtually all colon and rectal cancers can be prevented or cured by early intervention.

Breast cancer is the major cause of cancer mortality in women in most countries. Spain is no exception. Despite increasing attention to breast cancer early detection, breast cancer remains the leading cause of cancer mortality in Spanish women, although there has been a significant decline in mortality in recent years. Breast cancer accounts for 32% of cancer-related deaths in women in the EU and 33% in Spain (our estimate). From 1975 to 1993, breast cancer mortality increased at an annual rate of 2.22% and then decreased at a rate of 2.46% per year until 2004. The recent decline in breast cancer mortality can be attributed to early detection and increased effectiveness of cancer treatment programs. Despite the decline, breast cancer still represents about 24% of the burden of cancer mortality and morbidly in Spanish women. Breast cancer mortality is projected to remain high or increase from 2004 to 2016 in women over 50 due to aging of the population, and thus early

Table 2 - Several periods between 1975-2004 in cancer mortality in men in Spain

Site	Years	APC	95% CL	
All cancers	1975-1995	1.03	0.94,	1.13
	1995-2004	-0.96	-1.27,	-0.65
Lip	1975-1993	-2.50	-3.59,	-1.39
	1993-2004	-5.89	-8.09,	-3.63
	1989-2004	-5.66	-7.11,	-4.19
Esophagus	1975-1984	-5.14	-7.89,	-2.30
	1975-1980	2.52	-3.40,	-1.58
	1980-1999	-0.76	-0.89,	-0.62
	1999-2004	-2.70	-3.63,	-1.76
Stomach	1975-1981	-4.59	-5.75,	-3.42
	1981-2004	-2.77	-2.97,	-2.61
Colon	1975-1981	-3.61	-6.13,	-0.62
	1981-1993	6.69	5.95,	8.02
Rectum	1993-2004	1.24	0.19,	2.49
	1988-2004	0.95	0.42,	1.41
	1975-1983	1.15	0.02,	2.38
	1986-2002	1.27	0.88,	1.67
Liver	1975-2002	-0.46	-0.58,	-0.33
	1975-1987	-0.68	-1.04,	-0.32
	1987-2002	-0.29	-0.58,	-0.09
	1975-1985	4.21	3.56,	4.86
Pancreas	1975-1985	4.16	3.48,	4.89
	1985-2002	1.51	1.19,	1.88
	1993-2004	-5.89	-8.09,	-3.63
	1989-2004	-5.66	-7.11,	-4.19
Melanoma	1975-1990	8.57	7.74,	9.90
	1990-2004	1.58	0.72,	3.00
Larynx	1975-1983	1.15	0.02,	2.39
	1983-1986	-3.06	-12.60,	7.51
	1986-2004	1.04	0.70,	1.38
Lung	1975-1991	3.55	3.13,	3.59
	1988-1994	1.58	0.31,	2.56
	1994-2004	-0.47	-0.82,	-0.05
Prostate	1975-1998	0.89	0.74,	1.04
	1998-2004	-3.45	-4.56,	-2.33
Testicles	1975-1995	-2.20	-3.53,	-0.90
	1987-2004	-3.12	-4.81,	-1.39
Kidney	1975-1996	3.49	3.17,	3.82
Urinary bladder	1975-1993	1.62	1.33,	1.96
	1980-1992	1.90	1.40,	2.42

APC, annual percent change per year. Only significant joinpoints were retained for each site.

detection needs to remain a focus despite recent declines.

Prostate cancer is the second most common cancer in Spanish men and accounts for about 29.4% of cancer mortality in men. Although there has been a huge rise in prostate cancer incidence over the last 20 years, this has not been reflected in mortality rates. Prostate cancer mortality in Spain increased at an annual rate of 0.9% between 1975 and 1998 and then decreased by 3.5% per year until the present. The recent decrease is primarily due to early detection since once prostate cancer has metastasized, it is almost always fatal. Prostate cancer incidence and mortality in Spain are about half those of other European countries such as Austria, Belgium, France, and Germany¹³. Despite this, prostate cancer is the third leading cause of cancer mortality in men in both the EU and in Spain.

Table 3 - Several periods between 1975-2004 in cancer mortality in women in Spain

Site	Years	APC	95% CL	
All cancers	1975-1981	-1.05	-1.59,	-0.50
	1981-1994	0.01	-0.18,	0.19
	1994-2004	-1.06	-1.31,	-0.81
Lip	1975-2000	-3.03	-4.65,	-1.93
	1975-1994	-4.17	-6.50,	-1.79
Stomach	1975-1980	-5.84	-7.24,	-4.41
	1980-2004	-3.45	-3.59,	-3.31
Colon	1975-1982	-6.22	-9.03,	-3.33
	1982-1988	8.77	3.31,	14.30
	1988-2004	0.81	0.07,	1.82
Rectum	1980-2004	-0.90	-1.17,	-0.68
	1980-1993	-1.15	-1.81,	-0.49
	1996-2004	-1.28	-2.33,	-0.21
Liver	1975-1987	-5.04	-5.51,	-4.53
	1987-2004	-3.02	-3.31,	-2.69
Pancreas	1975-1987	3.65	3.04,	4.26
	1987-2004	1.42	1.06,	1.77
Larynx	1975-1990	-0.73	-1.14,	-1.32
	1990-1993	-1.15	-1.81,	-0.49
	1996-2004	-1.28	-2.33,	-0.21
Lung	1975-1992	-0.66	-0.86,	-0.20
	1992-2004	2.28	2.05,	4.12
	1999-2004	5.23	3.16,	7.34
Melanoma	1975-1984	6.77	4.14,	5.60
	1984-1994	-0.43	4.11,	8.54
Urinary bladder	1975-1989	1.37	0.54,	2.20
	1987-2004	-0.67	-1.23,	-0.10
	1986-2004	-0.59	-1.01,	-0.17
Kidney	1975-1999	1.76	1.35,	2.16
	1975-1993	2.22	1.99,	2.44
Breast	1993-2004	-2.46	-2.90,	-2.07
	1975-1981	-36.74	-46.6,	-24.9
	1981-2004	3.96	1.65,	6.32
Cervix	1975-1991	4.15	0.29,	8.16
Ovary	1975-1991	5.28	4.77,	-5.79
	1991-2001	1.15	0.26,	-1.58

APC, annual percent change per year. Only significant joinpoints were retained for each site.

Over the past 30 years, mortality from cutaneous melanoma in Spain has increased by 5.6% in men and 4.9% in women (Table 1). Since 1999, the mortality rate appears to have leveled off and may be falling. Melanoma mortality appears to be decreasing also in other European countries. Age-standardized mortality for cutaneous melanoma in Germany decreased from 1.5 to 0.8 per 100,000 in males and from 2.6 to 0.8 per 100,000 in females, with a significant downward trend for the female population ($P < 0.001$)^{14,15}. Mortality rates in Australia decreased in this period from 3.5 to 2.6 for males and slightly increased for females from 1.2 to 1.6 per 100,000 inhabitants¹⁶. Nevertheless, care must still be taken to continue with primary and secondary prevention, which influences mortality rates.

In summary, joinpoint analysis demonstrated favorable patterns in cancer mortality in recent years in Spain in both sexes. Cancer mortality has decreased significantly over the period 1975 to 2004. Tobacco-related cancers are the major contributor to cancer mortality in

Spain, and despite the fact that smoking is the most significant modifiable risk factor for cancer, Spain continues to have one of the highest smoking rates in Europe. In recent years, tobacco-related cancers appear to have peaked in Spanish men, following a pattern of the rest of Europe. However, smoking continues to take a mortality toll in both Spanish men and women.

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