Original Article

The lung cancer epidemic in Spanish women: an analysis of mortality rates over a 37-year period

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Background: Lung cancer continues to be the leading cause of cancer-related mortality in the European Union (EU) and deaths from lung cancer have been projected to escalate to epidemic proportions amongst females over the next years. We examined lung cancer mortality rates in men and women from Andalusia (Spain) over a 37-year period [1975-2012].

Methods: Longitudinal epidemiological study analyzing lung cancer mortality trends in males and females. Data on lung cancer mortality in Andalusia for the period 1975-2012 were obtained from the official cause-of-death publications of the Institute of Statistics of Andalusia. For each sex, age-standardized (European standard population) mortality rates (ASR) from lung cancer were calculated for all ages and truncated at 30-64, 65-74, and >75 years using the direct method. Standardized rate trends by age and sex were estimated by joinpoint regression analysis.

Results: In men, the ASR steadily increased through the period 1993-1995, reaching a peak of 145.72 deaths/100,000 people. Subsequently, lung cancer deaths decreased to a rate of 125.47 in the 2011-2012 period. A moderate increase was seen in women until the late 1990s and early 2000s. Thereafter, a very notable rise was observed in females for all age groups, the only exception being older subjects. The sex differences decreased from 8.6:1 in the 1975-1977 period to 6.8:1 in the 2011-2012 period.

Conclusions: Lung cancer mortality rates decreased significantly in Andalusian men from 1975 to 2012. More importantly, we demonstrate for the first time the beginning of the lung cancer epidemics in Andalusian women as previously predicted for this area.

Keywords: Lung cancer; mortality; males; females; epidemics

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Introduction

Lung cancer continues to be the leading cause of cancer-related death in the European Union (EU). An estimated 334,800 European people died of lung cancer in 2006, representing 19.7% of all cancer deaths (1). In the EU as a whole, mortality from lung cancer in men reached a peak of 53.3/100,000 in the late 1980s but declined thereafter to reach 44.0/100,000 in the early 2000s. In contrast, lung cancer mortality tended to rise in women from 9.0 to 11.4/100,000 over the same calendar period (2) and it has been hypothesized that deaths from lung cancer in females will escalate to epidemic proportions over the next years (3).

The trends of lung cancer mortality in Spain are similar to those observed in the EU as a whole. Starting in the nineties, age-specific death rates in males decreased for each age group under 85 years old. However, a statistically significant annual increase of 6.3% in truncated mortality rates has been observed in women since 1992 (4). Consequently, lung cancer age-standardized mortality rates

for females doubled from 5.6 in 1980 to 11.3 in 2005 in all regions of the country (5) and are also projected to increase over the next years (6).

Lung cancer mortality trends have been thoroughly examined in Andalusia (7-9), the second largest Spanish region with a surface area of 87,268 km² and over 8 million inhabitants. In the mid-nineties, there has been a convergence in lung cancer deaths for Andalusian men and women (8) with a decrease in the male-to-female mortality ratio (9). However, previous series describing mortality trends until the year 2000 did not observe the projected epidemic rise of lung cancer deaths in women (8).

The present study extends the comparison of lung cancer mortality rates in Andalusian men and women over a longer period of time [1975-2012]; herein, the projected epidemic in female lung mortality rates is being demonstrated for the first time in Andalusia. These enhanced data will improve the utility and quality of cancer surveillance activities and are the key to improving cancer prevention strategies.

Methods

Data on lung cancer mortality in Andalusia for the period 1975-2012 were obtained from the official cause-of-death publications of the Institute of Statistics of Andalusia. Population estimates referred to the population as of July 1 of each year based on official census information. Lung cancer corresponds to codes 162 in the International Classification of Diseases (ICD) 8th and 9th revisions (1975-1979 and 1980-1998, respectively) and C33-C34 in the 10th revision [1999-2012]. For each sex, age-standardized (European standard population) mortality rates (ASR) from lung cancer were calculated for all ages and truncated at 30-64, 65-74, and >75 years using the direct method. The results were expressed as rates per 100,000 person-years.

The standardized rate trends by age and sex were estimated by joinpoint regression analysis (10). Specifically, we used joinpoint regression analysis to identify the changes in the slope of mortality trends. We selected the best fitting points (the "joinpoints") where the rate changed significantly. This approach has two major advantages. First, it allows the precise identification of significant trend changes. Second, it provides a framework for estimating the increase or decrease occurring in each time interval using the percentage of annual change (PAC). We used the Surveillance Epidemiology and End Results (SEER) Stat software (Joinpoint Regression Program, Version 4.0.4., Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD, USA, 2011) for calculations. We also fitted segmented Poisson regression models to estimate the changes of trends over time. Standardized rates were used as the dependent variable, whereas the year of death was entered in the model as the independent variable (11). In all analyses, a two-tailed P value <0.05 was considered statistically significant.

Results

In men, the ASR steadily increased through the period 1993-1995, reaching a peak of 145.72 deaths/100,000 people. Subsequently, lung cancer deaths decreased to a rate of 125.47 in the 2011-2012 period. Truncated rates at 30-64, 65-74, and >75 years showed similar patterns, although less evident amongst older age groups (*Figure 1*, *Table 1*). Joinpoint regression analysis unambiguously identified the inflexion points at which there was a significant change in the trends (i.e., a striking rise was observed until 1993 which was followed by a decrease thereafter; *Figure 1*, *Table 2*).

However, opposite trends in lung cancer death rates were observed in women. A moderate increase was seen until the late 1990s and early 2000s. Thereafter, a very notable rise was observed for all age groups, albeit to lesser extent in the 65-74 years age group and without clear trends in older age groups (*Figure 1*, *Table 1*). Joinpoint regression analysis successfully identified the timing and extent of mortality increase (*Figure 1*, *Table 2*).

The combined analysis of mortality rates in men and women showed a specular pattern with a marked reduction in sex difference (from 8.6:1 for the period 1975-1977 to 6.8:1 for the period 2011-2012) which became more evident as of the late 1990s.

Discussion

Vital statistics of lung cancer provide valuable information on the occurrence of lung cancer because the highly aggressive nature of the disease makes its incidence and mortality rates nearly identical (12). The present study shows that lung cancer mortality rates decreased significantly in Andalusian men from 1975 to 2012. More importantly, we show for the first time the beginning of the lung cancer epidemics in Andalusian women as previously predicted for this area (8).

Our results should be interpreted in light of the evolving smoking patterns in our area. As of 1993, tobacco consumption in Andalusia has been constantly decreasing

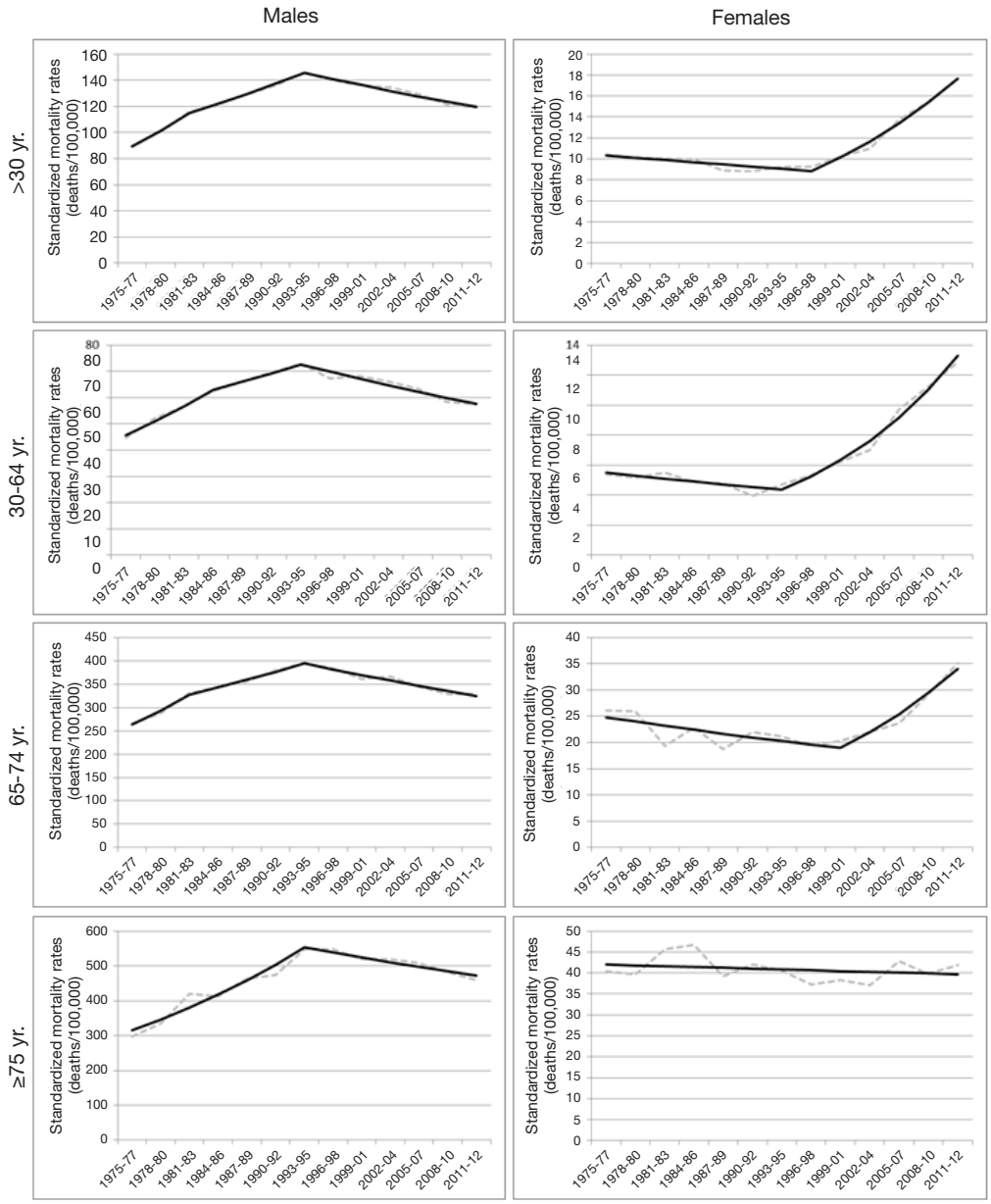

Figure 1 Age-standardized mortality and joinpoint regression trends of lung cancer deaths in Andalusia, 1975-2012. Solid lines represent the joinpoint regression lines, whereas dashed lines indicate age-standardized mortality.

in most—but not all—of the age groups (6). In particular, teen smoking patterns do not show marked sex differences in Spain. Interestingly, the results of the 2006 Spanish National Health Survey have shown for the first time that the smoking prevalence was significantly higher in females than in males aged between 16 and 24 years. The last 2011/2012 Spanish National Health Survey confirmed the declining trend regarding sex differences in smoking, with a prevalence of 27.9% in males and of 20.2% in females aged ≥15 years (13).

The lung cancer mortality data used in our study were based on death certificates. Obviously, the accuracy of our findings substantially depends on the quality of cause-of-death information in death certificates, especially for older age groups. Because death certification in Andalusia is performed according to international standards and is subjected to quality controls, we are reasonably confident that our data are internally valid (14). Previous studies have supported the validity of death certification for the most

Table 1 Age-standardized mortality trends from lung cancer in Andalusia, 1975-2012

Period	Deaths		Crude		ASR		ASR 30-64		ASR 65-74		ASR ≥75	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
1975-1977	3,335	515	82.54	11.26	89.52	10.39	44.71	5.39	265.55	26.13	296.78	40.39
1978-1980	3,981	538	95.47	11.43	101.08	10.16	52.18	5.19	288.30	25.97	335.72	39.61
1981-1983	4,868	557	112.16	11.43	115.97	10.04	56.78	5.51	330.83	19.36	420.63	45.73
1984-1986	5,487	608	120.12	11.93	121.51	9.99	62.49	4.86	343.30	22.78	412.15	46.69
1987-1989	6,220	563	130.15	10.60	129.52	8.91	66.14	4.79	355.22	18.71	463.45	39.14
1990-1992	6,899	599	137.75	10.80	136.11	8.85	69.58	3.96	379.82	22.00	474.74	42.01
1993-1995	7,852	656	146.94	11.12	145.72	9.25	72.87	4.71	394.76	21.19	547.66	40.48
1996-1998	8,004	685	140.89	10.95	140.02	9.28	67.35	5.32	384.20	19.39	548.42	37.18
1999-2001	8,200	783	137.20	11.93	135.92	10.22	68.20	6.24	361.51	20.35	519.96	38.33
2002-2004	8,644	871	137.60	12.66	134.64	10.98	66.06	7.03	365.68	22.03	518.97	37.03
2005-2007	8,777	1,129	133.00	15.65	129.14	13.76	63.45	9.72	344.14	23.67	508.31	42.80
2008-2010	8,768	1,292	126.82	17.13	121.34	15.44	58.38	11.24	329.10	29.12	481.77	39.79
2011-2012	5,974	1,015	125.47	19.58	119.10	17.64	57.36	12.89	329.88	35.04	460.23	41.84

ASR, age-standardized mortality rates.

Table 2 Trend changes according to joinpoint regression analysis

Groups	Period	PAC	Period 1	PAC	Period 2	PAC	Period 3	PAC
Males								
ASR	1975-1977; 2011-2012	1.27	1975-1977; 1981-1983	13.5*	1981-1983; 1993-1995	6.1*	1993-1995; 2011-2012	–3.2*
ASR 30-64	1975-1977; 2011-2012	0.99	1975-1977; 1984-1986	11.3*	1984-1986; 1993-1995	4.8	1993-1995; 2011-2012	–3.8*
ASR 65-74	1975-1977; 2011-2012	1.13	1975-1977; 1984-1986	11.6*	1984-1986; 1993-1995	4.8*	1993-1995; 2011-2012	–3.2*
ASR ≥75	1975-1977; 2011-2012	2.12	1975-1977; 1993-1995	9.8*	1993-1995; 2011-1912	–2.6*		
Females								
ASR	1975-1977; 2011-2012	4.76*	1975-1977; 1999-2001	–2.2*	1999-2001; 2011-2012	14.8*		
ASR 30-64	1975-1977; 2011-2012	9.03*	1975-1977; 1993-1995	–3.8	1993-1995; 2011-2012	20.3*		
ASR 65-74	1975-1977; 2011-2012	2.4	1975-1977; 1999-2001	–3.3*	1999-2001; 2011-2012	15.8*		
ASR ≥75	1975-1977; 2011-2012	–0.47						

*, P<0.05. PAC, percentage of annual change; ASR, age-standardized mortality rates.

common malignancies occurring in Spain (15). Despite a modest risk of underreporting cancer deaths, certificates are generally considered a valid source for population-based cancer registries (15).

In most EU countries, there has been an increase in deaths from lung cancer in female subjects (3). However, more favorable trends in young women over recent years have been observed (16), suggesting that effective tobacco control measures have been implemented when the outbreak was recognized (17). Unfortunately, the Spanish national and regional anti-tobacco regulations have not been able to impede the expected lung cancer epidemics amongst Andalusian women. Accordingly, factors other than smoking may also influence the incidence of lung cancer in women. Although there have been reports suggesting the onset of lung cancer epidemics in Spain (5), to our knowledge, the outbreak occurring in Andalusia has not been previously reported (8). A previous study has shown that lung cancer mortality increased significantly in Andalusian women aged between 35 and 64 years, although the mortality rates remained very low until the year 2000 (8). Thereafter, there was a steady and substantial increase that can be explained by the growth of tobacco use during the last decades (18). Collectively, the current data extend our previous findings up to the year 2012 and unequivocally demonstrate that a lung cancer epidemic swept through the female Andalusian population.

Cancer mortality trends in 33 European countries between 1970 and 2009 have been recently analyzed and the projected EU rates for the year 2015 estimated according to the World Health Organization data (3). The authors demonstrated that lung cancer death rates for women have been increasing up to recent years in most European countries, although a few notable exceptions exist (Eastern EU nations). Our current findings in Andalusia corroborate the occurrence of an unfavorable mortality trend in lung cancer mortality observed in women living in Southern Europe.

Evidence-based strategies for prevention are eagerly required to reverse the rising trend of lung cancer mortality. Besides anti-tobacco policy measures, low-dose computed tomography may be useful to detect early stages of lung cancer (19). Further studies are needed to examine the usefulness of lung cancer screening programs from the perspectives of cost-effectiveness and survival benefit.

In summary, there are two principal findings in this study. First, we have shown that lung cancer mortality rates decreased significantly in Andalusian men from 1975 to 2012. Second, we demonstrate the beginning of the lung cancer epidemics in Andalusian women as previously predicted for this area. Local anti-tobacco regulations have not demonstrated an effect in reversing the predicted mortality increase. Our results suggest imposing more effective tobacco use control policies and designing region-specific programs to reduce lung cancer mortality risks.

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References

1. Ferlay J, Autier P, Boniol M, et al. Estimates of the cancer incidence and mortality in Europe in 2006. Ann Oncol 2007;18:581-92.
2. La Vecchia C, Bosetti C, Lucchini F, et al. Cancer mortality in Europe, 2000-2004, and an overview of trends since 1975. Ann Oncol 2010;21:1323-60.
3. Bosetti C, Malvezzi M, Rosso T, et al. Lung cancer mortality in European women: trends and predictions. Lung Cancer 2012;78:171-8.
4. Cayuela A, Rodríguez-Domínguez S, et al. Lung cancer mortality trends in Spain between 1980 and 2005. Arch Bronconeumol 2008;44:70-4.
5. Cayuela A, Rodríguez-Domínguez S, López-Campos JL, et al. Lung cancer mortality trends by geographical area in Spanish women, 1980-2005. Int J Tuberc Lung Dis 2008;12:453-7.
6. Cayuela A, Rodríguez-Dominguez S, López-Campos JL, et al. Lung cancer mortality in Spain: estimating the future burden to the year 2028. Int J Tuberc Lung Dis 2011;15:1117-21.
7. Ruiz Ramos M, Viciana Fernández F, Canto Casasola V, et al. Evolution of mortality due to lung cancer in Andalusia between 1975 and 1977. Aten Primaria 2000;25:220-5.
8. Cayuela A, Rodríguez-Domínguez S, López-Campos JL, et al. Joinpoint regression analysis of lung cancer mortality, Andalusia 1975-2000. Ann Oncol 2004;15:793-6.
9. Cayuela A, Rodríguez-Domínguez S, Jara-Palomares L, et al. Gender differences in lung cancer mortality trends in Andalusia 1975-2008: a joinpoint regression analysis. Med Oncol 2012;29:1593-8.
10. Kim HJ, Fay MP, Feuer EJ, et al. Permutation tests for

joinpoint regression with applications to cancer rates. Stat Med 2000;19:335-51.
11. National Cancer Institute. Surveillance Research Cancer Control and Population Sciences. Joinpoint Regression Program. Available online: http://surveillance.cancer.gov/joinpoint/
12. Malvezzi M, Bosetti C, Rosso T, et al. Lung cancer mortality in European men: trends and predictions. Lung Cancer 2013;80:138-45.
13. Instituto Nacional de Estadística. Encuesta Nacional de Salud 2011 – 2012. Last accessed: 04/07/2013. Available online: http://www.msssi.gob.es/estadEstudios/estadisticas/encuestaNacional/encuestaNac2011/NotaTecnica2011-12.pdf
14. Glasser JH. The quality and utility of death certificate data. Am J Public Health 1981;71:231-3.
15. Cáffaro Rovira M, Garau Llinás I, Cabeza Irigoyen E, et al. Validity of death certificates for cancer in Mallorca. Gac Sanit 1995;9:166-73.
16. Didkowska J, Manczuk M, McNeill A, et al. Lung cancer mortality at ages 35-54 in the European Union: ecological study of evolving tobacco epidemics. BMJ 2005;331:189-91.
17. Levi F, Lucchini F, Negri E, et al. Continuing declines in cancer mortality in the European Union. Ann Oncol 2007;18:593-5.
18. Solano-Reina S, De Granda-Orive JI, Jiménez-Ruiz CA. Smoking cessation: an essential component in the treatment of lung cancer patients. Arch Bronconeumol 2011;47:477.
19. Infante M, Cavuto S, Lutman FR, et al. A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial. Am J Respir Crit Care Med 2009;180:445-53.

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