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ORIGINAL ARTICLE

# Mortality from cancer of the lung in Serbia

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## Summary

***Purpose:*** *To estimate the death rates for lung cancer and their secular trends in the population of Serbia, excluding the autonomous province of Kosovo and Metohia, over the 1991-2009 period.*

***Methods:*** *A descriptive epidemiological method was employed. Trend of the lung cancer mortality rates was estimated using joinpoint linear regression analysis. An average annual percentage of change (AAPC) was computed for trend using linear models assuming a Poisson distribution, and the corresponding 95% confidence interval (CI).*

***Results:*** *The mortality rate from lung cancer in Serbia ranks as the highest in the world, and it has been increasing continuously from 1991 (AAPC = + 1.9; 95% CI=1.7-2.2). A significant increase in mortality was present in both the male population (AAPC = + 1.4; 95% CI=1.2-1.6), and the female population (AAPC = + 3.9; 95% CI=3.6-4.3). However, a significant decline in lung cancer mortality in men was seen in some age groups. In young men (35-39 and 40-44 years age groups), lung cancer death rates decreased continuously from 1991, by – 5.1% and – 2.6% per year, respectively. Among men in the 45-49 years age group, a marked increase of lung cancer mortality was observed from 1991 to 1998 (by + 6.5% per year), followed by significant decrease (- 1.9% per year). Among women, only in the youngest age group (35-39 years) a declining trend was present (- 0.6% per year), yet without significance.*

***Conclusion:*** *Lung cancer mortality rates in Serbia indicate the importance of consistent application of measures of primary and secondary prevention that have been proven effective in other countries.*

***Key words:*** *descriptive epidemiological study, joinpoint analysis, lung cancer, mortality*

## Introduction

Lung cancer was the leading cause of cancer-related deaths in males in 2008 globally, and the second leading cause of cancer-related deaths among females [1]. Lung cancer ranks nearly fifth of all cancer deaths worldwide, with significant geographic variations in frequency and distribution [1-3].

The mortality rate from lung cancer in Serbia for males and females taken together ranks third in the world, after the rates in Hungary and French Polynesia [2]. Lung cancer mortality is more than twice as frequent in men than in women [3,4]. In males, the highest lung cancer death rates are in Central and Eastern Europe, and then North America, Eastern Asia and Western Europe [2]. In females, the highest lung cancer death rates are found in North America, North Europe, and Eastern Asia.

Since the 1980s, lung cancer mortality rates have been declining in most developed countries, but not in all of them [4-6]. Despite the persistent decline of lung cancer in males in the United States of America and the European Union (each by – 1.9% per year), the trends of lung cancer mortality in females continuously rise (by + 0.3% and + 1.7% per year, respectively) [5,7]. It is considered that the major contribution for the decrease in lung cancer mortality rate is attributable to reduction in tobacco smoking [8,9].

The aim of the present study was to estimate death rates for lung cancer in the population of Serbia and their trends during the period 1991-2009.

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**Table 1.** Lung cancer mortality in Serbia by gender, excluding the autonomous province of Kosovo and Metohia, in the 1991-2009 period

| | *Men* | | | *Women* | | |
|---|---|---|---|---|---|---|
| *Year* | *N* | *Crude rate* | *ASR* | *N* | *Crude rate* | *ASR* |
| 1991 | 2537 | 68.27 | 45.63 | 535 | 13.79 | 8.00 |
| 1992 | 2709 | 72.88 | 47.93 | 598 | 15.39 | 8.89 |
| 1993 | 2685 | 72.16 | 46.82 | 585 | 15.03 | 8.66 |
| 1994 | 2692 | 72.29 | 46.32 | 641 | 16.44 | 9.23 |
| 1995 | 2777 | 74.52 | 47.22 | 652 | 16.71 | 9.27 |
| 1996 | 2980 | 80.04 | 50.05 | 676 | 17.34 | 9.45 |
| 1997 | 3075 | 82.71 | 51.02 | 718 | 18.35 | 10.11 |
| 1998 | 3026 | 81.78 | 49.56 | 705 | 18.11 | 9.79 |
| 1999 | 2996 | 81.38 | 48.96 | 764 | 19.61 | 10.52 |
| 2000 | 3151 | 85.62 | 50.85 | 857 | 22.04 | 11.73 |
| 2001 | 3113 | 85.10 | 50.01 | 851 | 21.97 | 11.53 |
| 2002 | 3261 | 88.97 | 52.32 | 907 | 23.49 | 12.33 |
| 2003 | 3295 | 90.03 | 52.08 | 945 | 24.44 | 12.61 |
| 2004 | 3421 | 93.88 | 54.08 | 997 | 25.85 | 13.23 |
| 2005 | 3521 | 96.93 | 55.55 | 1021 | 26.50 | 13.22 |
| 2006 | 3713 | 102.48 | 57.89 | 1142 | 29.83 | 15.12 |
| 2007 | 3686 | 102.48 | 57.51 | 1099 | 28.90 | 14.46 |
| 2008 | 3780 | 105.43 | 58.97 | 1175 | 31.03 | 15.58 |
| 2009 | 3752 | 105.14 | 58.36 | 1303 | 34.46 | 16.80 |

ASR: age standardized rate (per 100 000, using World Standard Population)

## Methods

A descriptive epidemiological method was used. Data on individuals who died of lung cancer (code 162 revision 9 and codes C33-C34 revision 10 of the International Classification of Diseases to classify death, injury and cause of death) were obtained from the Statistical Office of the Republic of Serbia. The research included the entire population of the Republic of Serbia (all ages), excluding the Province of Kosovo and Metohia, from 1991 to 2009. The age groups ≤ 34 years were not included, because there were too few cases to allow for mortality rates calculation and analysis. Data on the number and composition of the population of the Republic of Serbia by gender and age were obtained from the population censuses in the years 1991 and 2002 and, for inter-census years, the estimates published by the Statistical Office of the Republic of Serbia were used. The age-standardized rates (per 100,000 people) were calculated by direct standardization, using the World Standard Population as proposed by Segi et al. [10].

Trends of the lung mortality rates were estimated using joinpoint linear regression analysis. At each line segment, trends in age-standardized rates (ASRs) were measured using the annual percent change (APC) and the corresponding 95% CI. Each joinpoint (if any) marks a significant change in trend, and AAPC was computed for trend using linear models assuming a Poisson distribution. Two-sided p values were considered to indicate statistical significance when they were less than 0.05. Joinpoint regression analyses were performed using Joinpoint regression software (version 3.0), available through the Surveillance Research Program of the US National Cancer Institute.

## Results

Table 1 shows the number of deaths, crude death rates and ASRs of lung cancer by gender in Serbia, during the period 1991-2009. Over this 19-year period, there were 76,341 lung cancer deaths (60,170 men and 16,171 women). The average annual ASRs were 51.64/100,000 for males, and 11.61/100,000 for females (male/female ratio = 4.5).

During the period observed, lung cancer mortality rates increased continuously and significantly (AAPC = + 1.9; 95% CI=1.7-2.2) (Figure 1).

A significant increasing mortality trend was present in both the male population (AAPC = + 1.4; 95% CI=1.2-1.6), and the female population (AAPC = + 3.9; 95% CI=3.6-4.3; Table 2). However, there were some differences in trends of age-specific mortality rates. In young men (35-39 and 40-44 years age groups) lung cancer death rates

**Table 2.** Joinpoint regression analysis of lung cancer mortality in Serbia by gender and age in 1991-2009, excluding the autonomous province of Kosovo and Metohia

| | *1991-2009* | | *Trend 1* | | *Trend 2* | |
|---|---|---|---|---|---|---|
| *Age*[§] | *Average age-specific rates (per 100,000)* | *AAPC (95%CI)* | *Years* | *APC (95%CI)* | *Years* | *APC (95%CI)* |
| **Males** | | | | | | |
| 35-39 | 7.4 | - 5.1* (-7.4 to -2.8) | | | | |
| 40-44 | 24.8 | - 2.6* (-3.8 to -1.4) | | | | |
| 45-49 | 62.7 | + 1.3* (0.4-2.2) | 1991-1998 | + 6.5* (4.5-8.5) | 1998-2009 | -1.9* (-2.8 to -0.9) |
| 50-54 | 120.1 | + 1.1 (-0.8-3.0) | 1991-2007 | + 2.3* (1.7-3.0) | 2007-2009 | - 8.4 (-23.1-9.1) |
| 55-59 | 184.6 | + 2.2* (1.2-3.2) | 1991-1998 | - 0.4 (-2.5-1.7) | 1998-2009 | + 3.9* (2.8-5.0) |
| 60-64 | 260.7 | + 1.0* (0.1-1.9) | 1991-2001 | - 0.8 (-1.9-0.4) | 2001-2009 | + 3.2* (1.5-5.0) |
| 65-69 | 324.5 | + 0.8* (0.5-1.2) | | | | |
| 70-74 | 352.8 | + 2.0* (1.6-2.4) | | | | |
| 75-79 | 322.3 | + 3.0* (2.2-3.8) | | | | |
| 80-84 | 234.6 | + 3.7* (2.6-4.8) | | | | |
| 85+ | 137.8 | + 3.0* (0.7-5.3) | | | | |
| All males | | + 1.4* (1.2-1.6) | | | | |
| **Females** | | | | | | |
| 35-39 | 3.3 | - 0.6 (-4.6-3.7) | | | | |
| 40-44 | 9.6 | + 1.8 (-0.1-3.8) | | | | |
| 45-49 | 17.4 | + 4.3* (2.7-5.9) | | | | |
| 50-54 | 31.0 | + 6.4* (5.4-7.3) | | | | |
| 55-59 | 40.3 | + 5.2* (3.7-6.9) | | | | |
| 60-64 | 48.7 | + 4.1* (3.3-5.0) | | | | |
| 65-69 | 45.2 | + 3.0* (2.1-3.8) | | | | |
| 70-74 | 71.8 | + 3.6* (2.7-4.4) | | | | |
| 75-79 | 74.5 | + 3.3* (2.4-4.1) | | | | |
| 80-84 | 65.0 | + 3.6* (2.1-5.2) | | | | |
| 85+ | 46.4 | + 1.9 (-0.3-4.2) | | | | |
| All females | | + 3.9* (3.6-4.3) | | | | |

* Joinpoint significantly different from zero at alpha = 0.05; [§] Joinpoint results are not shown for the age subgroup ≤ 34, because there were less than 10 cases in any year.
AAPC: average annual percent change, APC: annual percent change, CI: confidence interval

decreased continuously from 1991, by – 5.1% and – 2.6% per year, respectively. In men 65 years and older, age specific mortality rates increased continuously over the entire study period. In middle-aged men (45-64 ages) two patterns of changes in lung cancer mortality were observed. Among men in the 45-49 age group, a marked increase of lung cancer mortality from 1991 to 1998 (by + 6.5% per year) was followed by significant decrease (- 1.9% per year). In men 50-54 years old, after a significant increase from 1991 to 2007 (+ 2.3 % per year), lung cancer death rates began to decline in the last 3 years of the period observed, but not significantly (– 8.4 % per year). In men 55-59 and 60-64 years old nonsignificant decline of mortality rates (by - 0.4% and – 0.8% per year, respectively) were followed by significant increase from 1998 (+ 3.8% per year), and 2001, respectively (+ 3.2% per year).

Among women, in all age groups from 45 to 84 years, a significant rise in lung cancer death rates was observed continuously from 1991. Only in the youngest age group (35-39 years) a declining trend was present (- 0.6% per year), but without significance.

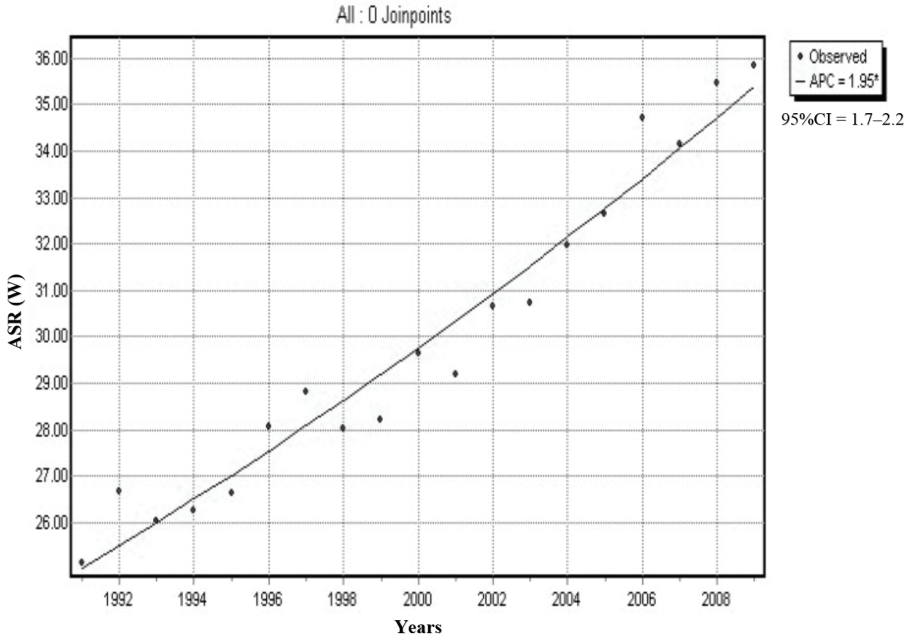


**Figure 1.** Joinpoint regression analysis of lung cancer mortality in Serbia, excluding the autonomous province of Kosovo and Metohia, in the 1991-2009 period. ASR (W): age standardized rate (per 100 000, using World Standard Population); APC: annual percent change; CI: confidence interval; * The APC change is statistically significantly different from 0 (two-sided p < 0.05).

## Discussion

Death rates from lung cancer in Serbia, excluding the Autonomous Province of Kosovo and Metohia, are among the highest in the world and with increasing tendency. The mortality rates for lung cancer in Serbia (37.3 per 100,000) in 2008 are similar to those in Central and Eastern European countries (such as Hungary – 46.0, Armenia – 35.8, Poland – 34.9) [2]. Far less rates were observed in most of European countries (such as United Kingdom – 25.9, Russian Federation - 22.4, Finland – 16.9, Portugal – 15.7), and Asian countries (China – 28.7, Japan – 17.4, India – 5.9). In the last years of the period observed, the mortality rates from lung cancer in Serbia were similar to those in United States of America registered in 1970s [2], and to the mortality rates in the European Union as a whole, in the late 1980s when they reached the peak [11].

The mortality rate from lung cancer in Serbia increased markedly in the last two decades, both in males and females. Our results are in contrast to the pattern seen in men in developed countries, such as the most of European countries (lung cancer rates declined by – 0.95% per year from 1987 to 1997, and thereafter declined substantially by –2.67% per year) and the United States of America (by –2.0% per year for males of all races/ethnicities) [5,12]. Among men in 36 European countries in the 1970-2007 period, only two countries recorded a significant increase in mortality rates from lung cancer (Romania by + 0.9% per year, and Portugal by + 0.5%) [6]. At the same time, in women, increasing lung cancer mortality trend was found in all Western and Northern European countries, and in most Eastern and Southern European countries. Different patterns were only observed for lung cancer death rates in women in four European countries. Continuous decreasing trend in women was observed during the 1970-2007 period in Ukraine (- 2.8% per year), Belarus (– 2.4%), Russian Federation (– 1.7%), and Bulgaria (- 1.0%) [6].

As already stated, the total lung cancer mortality rates in Serbia increased significantly in both men and women. However, in men 35-44 and 45-49 years old significant decreasing trends were detected during longer or shorter periods of time. Our results are similar to the lung cancer mortality trends among younger age groups for males in Russian Federation and Ukraine [13], and Spain [14]. In women in Serbia, only in the 35-39 years age group a modest, not significant decreasing trend was found. During the period 1980-2001, in several European countries (Russian Federation, Ukraine, Lithuania and United Kingdom), a decline in lung cancer mortality in young women (20-44 years) was observed [15]. However, lung cancer mortality continuously increased among women of the same age groups in France, Germany, Hungary, Italy, the Netherlands and Norway,

as well as in the European Union as a whole [15].

About 90% of lung cancers in men and 83% in women in developed countries are caused by smoking [16]. In Serbia, 82.8% of the lung cancer burden for men and 90.2% for women was attributable to smoking [17]. Levels and changes in the prevalence of smoking may explain both differences in lung cancer morbidity and mortality among countries and between men and women, and decreasing and increasing trend of lung cancer rates. The tobacco exposure in Serbia is still higher than in developed countries. According to data for the Belgrade population there were 49% male and 25% female smokers in the years 1976-1977, and 51% male and 37% female smokers in the years 1988-1989 [18]. Thanks to antismoking campaign which was intensified from 2000, in 2006 in Serbia 33.6% of the population were smokers (38.1 males vs 29.9% females), suggesting a reduction of the smoking rate by 6.9% in comparison with 2000, when the habit was 47.9% among men and 38.1% among women [19]. The highest percentage of smokers (46.9%) was recorded in the 35 to 44 years age group. In comparison to 2000, the number of young people aged 15-19 who have never tried to smoke was increased by 7.3%. Serbia joined World Health Organization convention on tobacco control and this convention became effective in June 2006. Taking into account the period of latency, one could expect that lung cancer mortality rates, especially in Serbian women, will continue to increase in the following years. Providing successful tobacco control strategy, the decreasing trend could be expected to begin in about 10 years. The already seen decline in lung cancer mortality rates in young men are promising.

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