Cancer Mortality Among Men in Central Serbia: 1985-2006 Survey Study

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Aim To analyze cancer mortality trends in men in Central Serbia during 1985-2006 period.

Methods Mortality rates and trends for the most frequent cancers in men (lung, stomach, colorectal, pancreatic, and prostate cancer) were calculated. Mortality rates for all cancers were adjusted by direct standardization. Percentage changes of the rates were calculated as the percentage difference between the rates of two successive years and then as a mean of these changes for the entire observed period. Trend lines were estimated using linear regression.

Results Total cancer mortality in men increased, with mean percentage of annual changes being 1.53% (95% confidence interval [CI], -0.09-3.16). Lung, stomach, colorectal, pancreatic, and prostate cancers represented 58.1% and 61.6% of total cancer deaths in 1985 and 2006, respectively. Increasing trends were observed for all investigated cancers: mean annual percentage change for lung cancer was 2.31%(95% CI, 1.03-3.59), for colorectal cancer 2.23% (95% CI, -0.18-4.65), for prostate cancer 3.06% (95% CI, -2.07-8.18), and for pancreatic cancer 1.58% (95% CI, -2.17-5.32). Stomach cancer mortality significantly decreased in age groups 40-49 and 50-59 years.

Conclusion The most frequent cancers in men in Central Serbia, ie, lung, colorectal, prostate, and pancreatic cancer, showed an increasing trend. Only stomach cancer mortality decreased over time.

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Cancer mortality in the European Union (EU) (1) and the United States (2) peaked in the late 1980s and has declined thereafter. Since 1988, the total cancer mortality in men from the EU has leveled off, and declined by an average 1.3% per year over the last 10 years due to the combined effect of early detection and improved treatment (3). The prevention of cancer in the EU was defined by the Code Against Cancer in 1987. The Code was revised in 1994 (4) and again in 2003 (5) as new member states entered the Union.

There are geographic differences in cancer burden between Western and Eastern Europe. According to estimates from 2002, cancer mortality in men was higher in Central-Eastern European countries than in North-Western countries (6). In Serbia, neither prevention activities nor mass screening tests were applied, with the sole exception of the government's effort to implement tobacco control.

The aim of this study was to analyze recent changes in cancer mortality trends for men in Serbia, a country with approximately 5.5 million population (excluding the two autonomous provinces), in the period 1985-2006.

Methods

The source of mortality data for malignant tumors were official death certificates (Federal Institute of Statistics, 1985-2006). During the period under consideration, two revisions of the International Classification of Diseases (ICD) were used, the 9th ICD edition (codes 140-208) and the 10th edition (codes C00-C97). The latter edition has been used in Serbia since 1997. Mortality rates and trends were calculated for the following most frequent cancers in men: stomach cancer (ICD-9: code 151; ICD-10: code C16), colorectal cancer (ICD-9: codes 153-154; ICD-10: codes C18-C21), pancreatic cancer (ICD-9: code 157; ICD-10: code C25), lung cancer (ICD-9: code 162; ICD-10: codes C33-C34), and prostate cancer (ICD-9: code 185; ICD-10: code C61).

For the calculation of mortality rates, the population denominator data were obtained from the 1981, 1991, and 2002 national censuses and from the estimates published by the Federal Institute of Statistics for inter-census years.

Statistical analysis

Age-adjustment of mortality rates was performed by the direct method of standardization using the world population as the standard (7). Percentage changes of mortality rates were calculated as the percentage difference between the adjusted rates of two successive years and then as a mean of these changes for the entire observed period. Age-specific mortality rates were computed for 10-year age groups. Confidence intervals (CI) for the average age-specific rates were assessed with 95% level of probability. Trend lines were estimated using linear regression. Data were processed using the Statistical Package for the Social Sciences, version 8.0 (SPSS Inc, Chicago, IL, USA).

Results

During the 22-year period there were 140 039 cancer deaths in men (Table 1). Mortality rates showed an increasing trend ($y = 119.49 + 2.15x$, $P < 0.001$ for age-adjusted rates). The mean percentage of annual changes was 1.53% (95% CI, -0.09-3.16).

Five most common malignant tumors represented 58.1% of total cancer deaths in 1985 (27.4% lung cancer; 9.6% colorectal cancer; 10.5% stomach cancer; 5.7% prostate cancer, and 4.9% pancreatic cancer). In 2006, they represented 61.6% of total cancer deaths (31.0% lung cancer; 11.6% colorectal cancer;

Table 1. Number of all cancer deaths and crude and standardized mortality rates (per 100 000) in men in Central Serbia in the period 1985-2006

Year	No.	Crude rates	Age-adjusted rates*	Percentage changes of age-adjusted rates
1985	4481	156.6	118.9	0.0
1986	4420	154.0	115.4	-2.9
1987	4785	166.6	122.9	6.5
1988	5313	184.3	134.2	9.2
1989	5041	174.6	125.8	-6.3
1990	5612	194.2	136.5	8.5
1991	5658	197.7	136.0	-0.3
1992	6083	213.0	144.9	6.5
1993	6093	213.0	142.5	-1.6
1994	6146	215.0	141.0	-1.1
1995	6287	220.1	142.8	1.2
1996	6488	227.3	143.7	0.7
1997	6736	236.5	147.7	2.8
1998	6874	241.9	149.3	1.1
1999	6962	258.6	152.8	2.3
2000	7206	268.9	156.8	2.6
2001	7149	267.9	154.7	-1.3
2002	7496	281.7	156.5	1.2
2003	7655	288.5	161.8	3.4
2004	7728	291.9	160.5	-0.8
2005	7858	297.6	163.2	1.7
2006	7968	302.8	163.9	0.4

*Adjusted according to world population.

6.1% stomach cancer; 8.2% prostate cancer; and 4.7% pancreatic cancer).

The analysis of trends of age-adjusted rates for the five most frequent malignant tumors in the population of Central Serbia (Figure 1) showed that the lung cancer mortality in men increased from 32.1 per 100 000 population in 1985 to 52.5 per 100 000 in 2006, with mean annual percentage change of 2.31% (95% CI, 1.03-3.59). Colorectal cancer mortality increased from 11.4 in 1985 to 18.0 in 2006, with mean annual percentage change of 2.23% (95% CI, -0.18-4.65). Prostate cancer mortality increased from 6.3 in 1985 to 10.7 in 2006, with mean annual percentage change of 3.06% (95% CI, -2.07-8.18). Pancreatic cancer mortality increased from 5.9 in 1985 to 7.8 in 2006, with mean annual percentage change of 1.58% (95% CI, -2.17-5.32). There was a considerable decrease in stomach cancer mortality from 14.2 in 1989 to 9.9 in 2006, with mean annual percentage change of -0.83% (95% CI, -3.30-1.64).

Age-specific mortality rates for lung, colorectal, stomach, prostate, and pancreatic cancer are presented in Figures 2-6 and Table 2. During the observed period, a significantly increasing mortality trend was found for lung cancer in all age groups, except in the 30-39 age group (Table 2). Age-specific mortality for colorectal, prostate, and pancreatic cancers increased in 50-59, 60-69, and ≥70 age groups. Stomach cancer mortality significantly decreased in 40-49 and 50-59 age groups.

Table 2. Parameters of linear regression analysis of age-specific mortality rates for the most frequent cancers in men in Central Serbia in the period 1985-2006

Cancer	Age (years)	Trend slope (b)	95% confidence intervals	*P*
Lung	30-39	-0.08	-0.16 to -0.01	0.039
	40-49	0.95	0.70-1.20	<0.001
	50-59	2.19	0.16-2.82	<0.001
	60-69	3.83	2.73-4.92	<0.001
	70+	8.12	7.25-8.99	<0.001
Colorectum	30-39	0.01	-0.06-0.04	0.642
	40-49	0.06	-0.06-0.18	0.333
	50-59	0.47	0.32-0.62	<0.001
	60-69	2.13	1.77-2.46	<0.001
	70+	3.74	3.22-4.27	<0.001
Prostate	30-39	0.003	-0.01-0.12	0.493
	40-49	-0.002	-0.25-0.02	0.888
	50-59	0.08	0.002-0.16	0.045
	60-69	0.69	0.46-0.92	<0.001
	70+	2.63	1.87-3.39	<0.001
Pancreas	30-39	-0.003	-0.03-0.03	0.822
	40-49	0.03	-0.03-0.09	0.295
	50-59	0.37	0.23-0.51	<0.001
	60-69	0.31	0.04-0.57	0.026
	70+	0.67	0.28-1.05	0.002
Stomach	30-39	-0.44	-0.09-0.001	0.057
	40-49	-0.13	-0.22 to -0.30	0.013
	50-59	-0.46	-0.65 to -0.27	<0.001
	60-69	-0.36	-0.85-0.13	0.145
	70+	-0.57	-1.38-0.24	0.159

Discussion

Age-adjusted cancer mortality rates in men in Central Serbia increased during the studied 22 years (1985-2006). In the EU, increasing trend of cancer mortality in men peaked in 1987, with the age-adjusted rate (world population) of 191.1 per 100 000. Afterwards, the rate decreased by 13% from 185.5 per 100 000 in 1992 to 162.3 per 100 000 in 2002 (8). This trend is encouraging and indicates that the forecast of 11% reduction in cancer mortality from 2000 to 2015 is realistic and possible

(9). Unfavorable trend of cancer mortality in men in Central Serbia can be only partially explained by the technological improvements, which allowed the accurate diagnosis of cancer as the cause of death in the initial part of the observed period and by changes in treatment effectiveness during the period of economic sanctions imposed on Serbia during the 1990s (10). The main reason is probably a lack of organized programs for primary and secondary prevention.

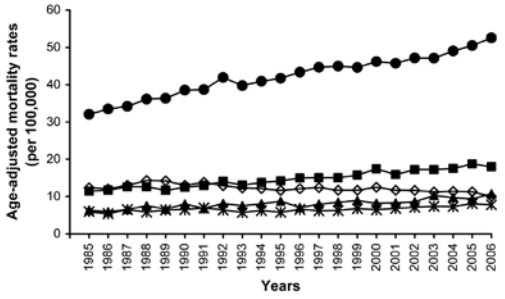

Figure 1. Trends in age-adjusted mortality rates for most frequent cancers in men in Central Serbia, 1985-2006. Circles – lung cancer; squares – colorectal cancer; rhombs – stomach cancer, triangle – prostate cancer; asterisk – pancreas cancer.

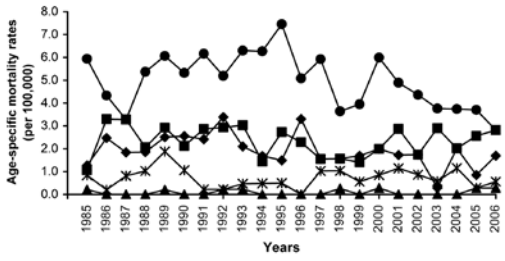

Figure 2. Mortality rates for most frequent cancers in men aged 30-39 years, Central Serbia, 1985-2006. Circles – lung cancer; squares – colorectal cancer; rhombs – stomach cancer, triangle – prostate cancer; asterisk – pancreas cancer.

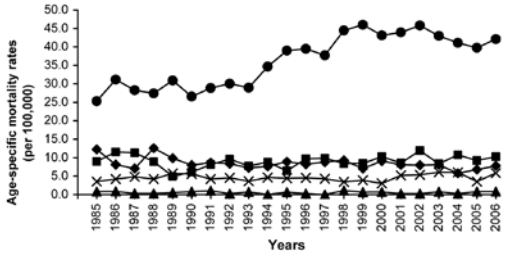

Figure 3. Mortality rates for most frequent cancers in men aged 40-49 years in Central Serbia, 1985-2006. Circles – lung cancer; squares – colorectal cancer; rhombs – stomach cancer, triangle – prostate cancer; asterisk – pancreas cancer.

The age-adjusted mortality rates for all cancers in men in Central Serbia are similar to those in Central and Eastern Europe (predominantly countries from the former socialist block), with the exception of Hungary. The cancer mortality rates among men in Hungary (the highest rate in 1997 was 266.1 per 100 000; the latest available for 2003 was 251.3 per 100 000) are the highest in Europe, higher than those registered in the North-

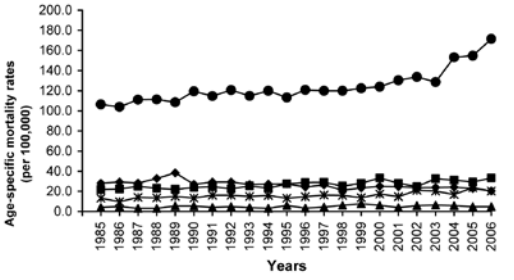

Figure 4. Mortality rates for most frequent cancers in men aged 50-59 years in Central Serbia, 1985-2006. Circles – lung cancer; squares – colorectal cancer; rhombs – stomach cancer, triangle – prostate cancer; asterisk – pancreas cancer.

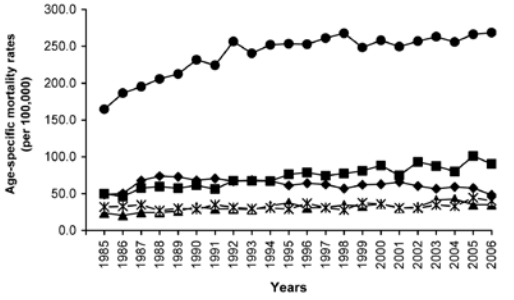

Figure 5. Mortality rates for most frequent cancers in men aged 60-69 years in Central Serbia, 1985-2006. Circles – lung cancer; squares – colorectal cancer; rhombs – stomach cancer, triangle – prostate cancer; asterisk – pancreas cancer.

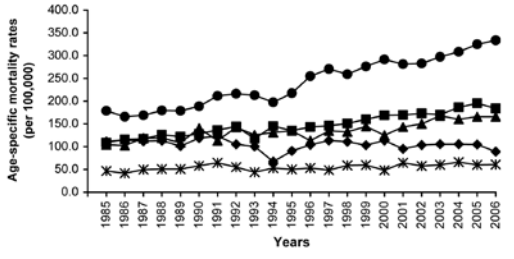

Figure 6. Mortality rates for most frequent cancers in men aged ≥70 years in Central Serbia, 1985-2006. Circles – lung cancer; squares – colorectal cancer; rhombs – stomach cancer, triangle – prostate cancer; asterisk – pancreas cancer.

Western countries, such as France (170.3 per 100 000 population in 2003), the Netherlands (156.6 per 100 000 in 2004); and Denmark (162.9 per 100 000 in 2001) (11). Unless adequate preventive measures are undertaken, the observed cancer mortality rates in Central Serbia will probably continue to increase and would exceed the rates in North-Western countries.

The analysis of individual cancer mortality rates indicated that the overall cancer mortality trends in the EU were largely dependent on the decreasing rates in lung cancer mortality in men and breast cancer mortality in women (9). In the EU overall, lung cancer in men declined from 55.4 per 100 000 in the late 1980s to 49.2 per 100 000 (-11%) in 1997 to 44.4 per 100 000 (-10%) in 2002 (1,3). During the period 1994-2004, the greatest annual lung cancer mortality changes were observed in Italy (-3.9%), Finland (-3.4%), the UK (-3.3%), and the Netherlands (-3.3%) (3). As the tobacco use is the most important risk factor for lung cancer (12), trends in lung cancer incidence and mortality, especially for the squamous cell type, reflect the prevalence of smokers. About 40% of the decline of male cancer mortality in the EU is due to lung cancer alone, and at least an additional 10% to other tobacco-related cancers. Decreasing lung cancer incidence and mortality trends are the result of decreased prevalence of male smokers in Western Europe during the last decades (12). There are no important improvements in lung cancer treatment and survival that could have influenced mortality trends (13).

Lung cancer is still the biggest public health problem in Central-Eastern part of Europe. In the 1990s, lung cancer mortality in men in Eastern Europe was the highest ever registered. Thereafter, downward trends were observed in the Russian Federation and some central and Eastern European countries, such as Estonia, Latvia, Lithuania, and Slovenia, but in Romania lung cancer mortality in men is still increasing (3,14). In Central Serbia, lung cancer mortality in men increased and the increasing trend was seen in all age groups, except in the 30-39 age group, in which the rate slightly decreased. Whether this favorable trend in younger men would continue depends to a great extent on implementation of tobacco control. According to the data for Belgrade population, there were 49% smokers among men in 1976-1977 and 51% in 1988-1989 (15). Measures for tobacco control in Serbia, such as legislative measures, ban on tobacco advertising, and restriction of smoking in public places resulted in a decreasing prevalence of smokers among men in Serbia from 47.9% in 2000 to 38.1% in 2006 (16). Nevertheless, the prevalence of smokers in Serbia, especially among men is one of the highest in Europe. Serbian Action Plan for Tobacco Control for 2007-2011 emphasized the introduction of smoke-free workplaces. A target was to increase the number of smoke-free workplaces by 5% annually. It is estimated that even if the current age-specific rates of lung cancer remain constant, high prevalence of smokers, together with aging of population, would more than double the lung cancer burden by 2030 (17).

Mortality of colorectal cancer, the second major cause of cancer death in Central Serbia, showed increasing tendency, especially in older age groups. This was probably due to unhealthy diet with frequent consumption of meat, fat, and sweets, as well as to insufficient levels of physical activity and obesity (16,18). According to the results of the National Health Survey in 2006, two-thirds of the population of Serbia (67.7%) spent their free time mainly in a sedentary way (16). The upward trend of colorectal cancer mortality in Serbia is comparable with increasing trends of colorectal cancer mortality in Spain, Portugal, Greece, and many Eastern European countries.

On the contrary, in western EU countries, the mortality leveled off since the early 1990s and a subsequent decline was most probably due to modifications in dietary risk factors, early diagnosis, and improvement of treatment (3,19). Survival is related to the stage at which the disease is detected. Five-year survival rate for individuals when colorectal cancer was detected at an early stage is more than 10-fold in comparison with five-year survival of individuals in whom colorectal cancer was diagnosed at an advanced stage (20). Five-year relative survival for patients diagnosed between 1990-1994 and 2000-2002 increased especially in Poland, Slovenia, and the Czech Republic (3). In the last version of the Code Against Cancer (5), screening is proposed for both men and women 50 and more years old. Although there were many controversies about sensitivity of screening for colorectal cancer and type of screening that should be used (fecal occult blood test and/or colonoscopy), it had been shown to be effective (21).

In Central Serbia, prostate cancer mortality increased moderately. However, the rise was higher in persons older than 70, which is in the accordance with the trend in men aged 65 to 84 in Eastern Europe, but contrary to the trend in the EU and the USA (3,8,22). Mortality trend in the EU countries was approximately stable until the early 1990s when it slowly started to decrease, which may be partially attributed to prostate specific antigen testing (1).

The trend of pancreatic cancer in Central Serbia has not decreased, contrary to the findings in both Western and Eastern European countries, where pancreatic cancer mortality in men has shown a decreasing trend since the 1990s (23).

Decreasing trend of stomach cancer mortality in our study is in agreement with the observed trends in other settings, such as Latin America and USA (24), and Europe (3,8,19) The declining trend in Europe is generally attributed to improved food preservation-refrigeration, affluent diet, better control of *Helicobacter pylori* infection, and reduced tobacco smoking (25).

In conclusion, the most frequent cancers in men in Central Serbia – lung, colorectal, prostate, and pancreatic cancer – showed an increasing trend. Only stomach cancer mortality decreased over time. Increasing cancer mortality trends underline the importance of implementing preventive measures that have proved effective in other countries.

Acknowledgment

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