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

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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.
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 140039 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;
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.

### 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.

### 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

<table>
<thead>
<tr>
<th>Year</th>
<th>No.</th>
<th>Crude rates</th>
<th>Age-adjusted rates*</th>
<th>Percentage changes of age-adjusted rates</th>
</tr>
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<tbody>
<tr>
<td>1985</td>
<td>4481</td>
<td>156.6</td>
<td>118.9</td>
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</tr>
<tr>
<td>1986</td>
<td>4420</td>
<td>154.0</td>
<td>115.4</td>
<td>-2.9</td>
</tr>
<tr>
<td>1987</td>
<td>4785</td>
<td>166.6</td>
<td>122.9</td>
<td>5.5</td>
</tr>
<tr>
<td>1988</td>
<td>5313</td>
<td>184.3</td>
<td>134.2</td>
<td>3.2</td>
</tr>
<tr>
<td>1989</td>
<td>5041</td>
<td>174.6</td>
<td>125.8</td>
<td>-3.9</td>
</tr>
<tr>
<td>1990</td>
<td>5612</td>
<td>194.2</td>
<td>136.5</td>
<td>8.5</td>
</tr>
<tr>
<td>1991</td>
<td>5658</td>
<td>197.7</td>
<td>136.0</td>
<td>-0.3</td>
</tr>
<tr>
<td>1992</td>
<td>6083</td>
<td>213.0</td>
<td>144.9</td>
<td>6.5</td>
</tr>
<tr>
<td>1993</td>
<td>6093</td>
<td>213.0</td>
<td>142.5</td>
<td>-1.6</td>
</tr>
<tr>
<td>1994</td>
<td>6146</td>
<td>215.0</td>
<td>141.0</td>
<td>-1.1</td>
</tr>
<tr>
<td>1995</td>
<td>6287</td>
<td>220.1</td>
<td>142.8</td>
<td>2.2</td>
</tr>
<tr>
<td>1996</td>
<td>6488</td>
<td>227.3</td>
<td>143.7</td>
<td>0.7</td>
</tr>
<tr>
<td>1997</td>
<td>6736</td>
<td>236.5</td>
<td>147.7</td>
<td>2.8</td>
</tr>
<tr>
<td>1998</td>
<td>6874</td>
<td>241.9</td>
<td>149.3</td>
<td>1.1</td>
</tr>
<tr>
<td>1999</td>
<td>6962</td>
<td>258.6</td>
<td>152.8</td>
<td>2.3</td>
</tr>
<tr>
<td>2000</td>
<td>7206</td>
<td>268.9</td>
<td>156.8</td>
<td>2.6</td>
</tr>
<tr>
<td>2001</td>
<td>7149</td>
<td>267.9</td>
<td>154.7</td>
<td>-1.3</td>
</tr>
<tr>
<td>2002</td>
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<td>281.7</td>
<td>156.5</td>
<td>1.2</td>
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<td>7655</td>
<td>288.6</td>
<td>161.8</td>
<td>3.4</td>
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<td>2004</td>
<td>7728</td>
<td>291.9</td>
<td>160.5</td>
<td>-0.8</td>
</tr>
<tr>
<td>2005</td>
<td>7858</td>
<td>297.6</td>
<td>163.2</td>
<td>1.7</td>
</tr>
<tr>
<td>2006</td>
<td>7968</td>
<td>302.8</td>
<td>163.9</td>
<td>0.4</td>
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</table>

*Adjusted according to world population.

### 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

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Age (years)</th>
<th>Trend slope (b)</th>
<th>95% confidence intervals</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>30-39</td>
<td>-0.08</td>
<td>-0.16 to -0.01</td>
<td>0.039</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>0.95</td>
<td>0.70-1.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>2.19</td>
<td>1.06-3.28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>3.83</td>
<td>2.73-4.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>70+</td>
<td>8.12</td>
<td>7.25-8.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Colorectum</td>
<td>30-39</td>
<td>0.01</td>
<td>-0.06 to 0.04</td>
<td>0.642</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>0.06</td>
<td>-0.06-0.18</td>
<td>0.333</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>0.47</td>
<td>0.32-0.62</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>60-69</td>
<td>2.13</td>
<td>1.77-2.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>70+</td>
<td>3.74</td>
<td>3.22-4.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prostate</td>
<td>30-39</td>
<td>0.003</td>
<td>-0.01-0.12</td>
<td>0.493</td>
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<tr>
<td></td>
<td>40-49</td>
<td>-0.002</td>
<td>-0.25-0.02</td>
<td>0.888</td>
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<tr>
<td></td>
<td>50-59</td>
<td>0.08</td>
<td>0.002-0.16</td>
<td>0.045</td>
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<tr>
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<td>60-69</td>
<td>0.69</td>
<td>0.46-0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>70+</td>
<td>2.63</td>
<td>1.87-3.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pancreas</td>
<td>30-39</td>
<td>-0.003</td>
<td>-0.03-0.03</td>
<td>0.822</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>0.03</td>
<td>0.03-0.09</td>
<td>0.295</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>0.37</td>
<td>0.25-0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>0.31</td>
<td>0.04-0.57</td>
<td>0.026</td>
</tr>
<tr>
<td></td>
<td>70+</td>
<td>0.67</td>
<td>0.28-1.05</td>
<td>0.002</td>
</tr>
<tr>
<td>Stomach</td>
<td>30-39</td>
<td>-0.44</td>
<td>-0.09-0.001</td>
<td>0.057</td>
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<tr>
<td></td>
<td>40-49</td>
<td>-0.13</td>
<td>-0.22 to -0.03</td>
<td>0.013</td>
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<td></td>
<td>50-59</td>
<td>-0.46</td>
<td>-0.65 to -0.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>-0.36</td>
<td>-0.85-0.13</td>
<td>0.145</td>
</tr>
<tr>
<td></td>
<td>70+</td>
<td>-0.57</td>
<td>-1.38-0.24</td>
<td>0.159</td>
</tr>
</tbody>
</table>
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. The main reason is probably a lack of organized programs for primary and secondary prevention.

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-
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 ade-
quately preventive measures are undertaken, the observed cancer mortality rates in Cen-
tral 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 mortal-
ity 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 de-
clined 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 pe-
riod 1994-2004, the greatest annual lung can-
cer 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 Eu-
rope during the last decades (12). There are no
important improvements in lung cancer treat-
ment 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 mortal-
ity 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 coun-
tries, such as Estonia, Latvia, Lithuania, and
Slovenia, but in Romania lung cancer mortal-
ity in men is still increasing (3,14). In Cen-
tral Serbia, lung cancer mortality in men in-
creased and the increasing trend was seen in
all age groups, except in the 30-39 age group,
in which the rate slightly decreased. Wheth-
er this favorable trend in younger men would
continue depends to a great extent on imple-
mentation 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 de-
creasing 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 estimat-
ed 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 bur-
den by 2030 (17).

Mortality of colorectal cancer, the sec-
ond 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 consump-
tion of meat, fat, and sweets, as well as to ins-
sufficient levels of physical activity and obesity
(16,18). According to the results of the Na-
tional 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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References


