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Pancreatic cancer mortality in Serbia from 1991-2010 – a joinpoint analysis

Aim To analyze the trends of pancreatic cancer mortality in Serbia.

Methods The study covered the population of Serbia in the period 1991 to 2010. Mortality trends were assessed by the joinpoint regression analysis by age and sex.

Results Age-standardized mortality rates ranged from 5.93 to 8.57 per 100 000 in men and from 3.51 to 5.79 per 100 000 in women. Pancreatic cancer mortality in all age groups was higher among men than among women. It was continuously increasing since 1991 by 1.6% (95% confidence interval [CI] 1.1 to 2.0) yearly in men and by 2.2% (95% CI 1.7 to 2.7) yearly in women. Changes in mortality were not significant in younger age groups for both sexes. In older men (≥ 55 years), mortality was increasing, although in age groups 70-74 and 80-84 the increase was not significant. In 65-69 years old men, the increase in mortality was significant only in the period 2004 to 2010. In ≥ 50 years old women, mortality significantly increased from 1991 onward. In 75-79 years old women, a non-significant decrease in the period 1991 to 2000 was followed by a significant increase from 2000 to 2010.

Conclusion Serbia is one of the countries with the highest pancreatic cancer mortality in the world, with increasing mortality trend in both sexes and in most age groups.

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represented by joinpoint regression. Specific interests were to test (i) whether two joinpoint regression functions were identical (test of coincidence) or (ii) whether two regression mean functions were parallel (test of parallelism) (17).

RESULTS

In Serbia from 1991 to 2010, more than 16 000 inhabitants died from pancreatic cancer (approximately 9000 men and 7000 women) (Table 1). Age-standardized mortality rates ranged from 5.93 to 8.57 per 100 000 in men and from 3.51 to 5.79 per 100 000 in women. In both sexes the highest rates were recorded in 2010.

Pancreatic cancer mortality was continuously increasing since 1991 by 1.6% (95% confidence interval [CI] 1.1 to 2.0) yearly in men and by 2.2% (95% CI 1.7 to 2.7) yearly in women (Figure 1, Table 1). According to comparability test, pancreatic mortality trends in men and women were parallel (final selected model failed to reject parallelism, $P=0.243$).

Mortality from pancreatic cancer was higher among men than among women in all age groups (Table 2). There

TABLE 1. Pancreatic cancer mortality in Serbia, excluding the Autonomous Province of Kosovo and Metohia, in the period 1991-2010, by sex. Number of cases, crude rate, and age standardized rate (ASR, per 100 000, using world standard population)

Year	Men			Women		
	N	crude rate	ASR	N	crude rate	ASR
1991	392	10.55	7.03	246	6.34	3.50
1992	366	9.85	6.41	265	6.82	3.76
1993	335	9.00	5.93	261	6.70	3.51
1994	356	9.56	6.17	273	7.00	3.65
1995	354	9.50	6.01	307	7.87	4.10
1996	412	11.06	6.87	296	7.59	3.80
1997	396	10.68	6.64	343	8.82	4.42
1998	416	11.28	6.77	337	8.68	4.28
1999	438	11.94	7.11	344	8.86	4.28
2000	401	10.97	6.48	346	8.96	4.28
2001	445	12.20	7.04	327	8.48	4.00
2002	466	12.78	7.22	369	9.58	4.49
2003	451	12.40	6.98	404	10.51	4.88
2004	476	13.12	7.32	376	9.78	4.29
2005	518	14.32	8.07	470	12.29	5.31
2006	520	14.43	7.99	390	10.24	4.54
2007	491	13.68	7.42	475	12.52	5.13
2008	561	15.70	8.29	473	12.53	5.17
2009	546	15.34	8.19	474	12.60	5.01
2010	566	15.96	8.57	522	13.94	5.79

were some sex differences in time trends by age. Among men, changes in mortality were small and not significant in younger age groups (<55 years), but in participants 55 years and older mortality was increasing, although in the age groups 70-74 and 80-84 the increase was not significant. In 65-69 years old men, the increase in mortality was significant only in the period from 2004 to 2010. Among women, changes in mortality in younger age groups (40-44 and 45-49 years) were not significant, but in older age groups mortality significantly increased from 1991 onward. The exception were 75-79 years old women, in whom a non-significant decreasing trend in the period 1991 to 2000 was followed by a significant increase from 2000 to 2010. According to comparability test, mortality trend in 50-54 years old men and 75-79 and 85+ years old women

TABLE 2. Joinpoint regression analysis of pancreatic cancer mortality in Serbia, excluding the Autonomous Province of Kosovo and Metohia, by sex and age, from 1991-2010

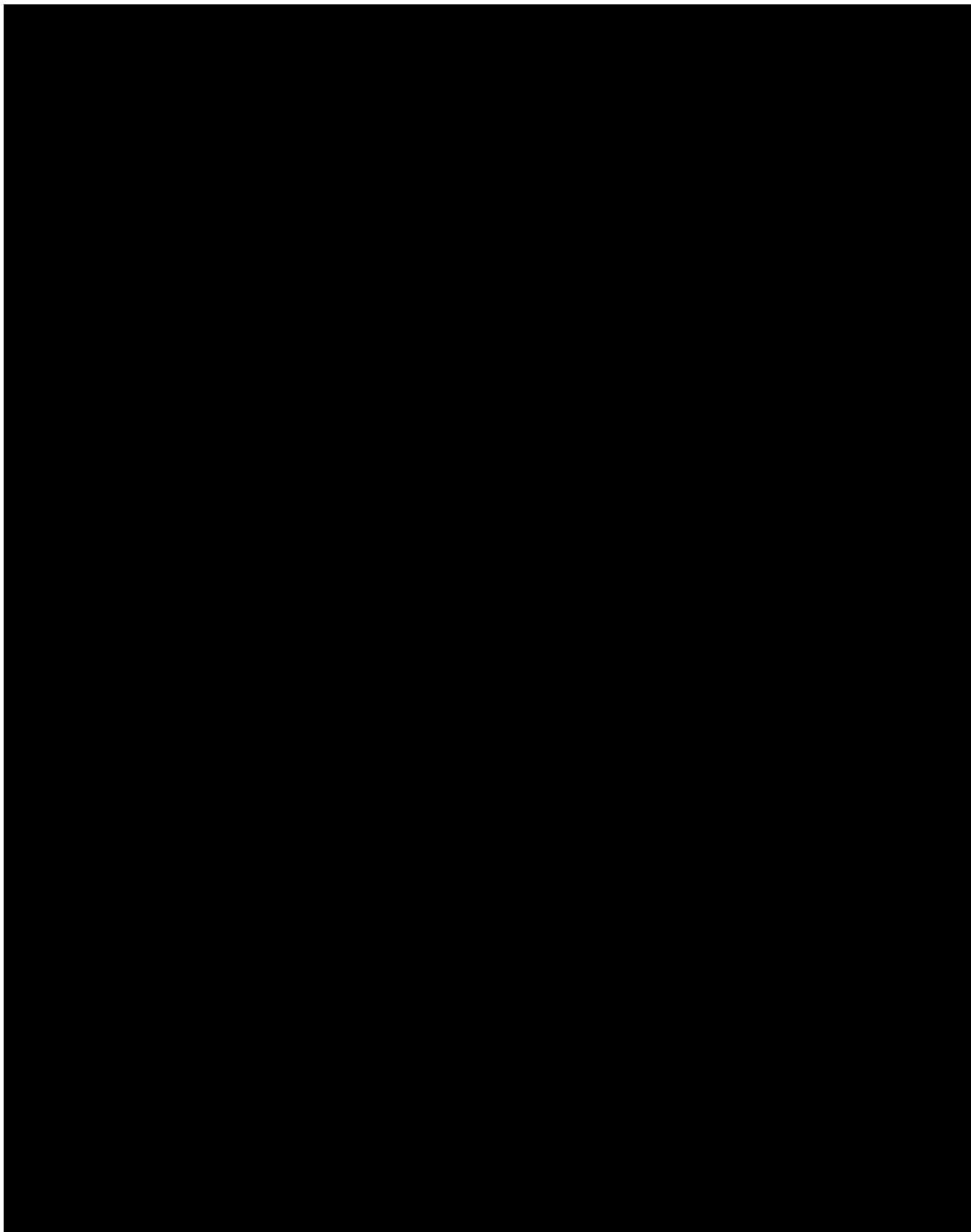
Age*	Average age-specific rate	
	rate (per 100 000)	average annual percent change (95% confidence interval [CI])
Men		
40-44	3.15	+ 0.4 (-3.1 to 4.0)
45-49	6.26	+ 0.9 (-0.9 to 2.8)
50-54	13.03	- 0.3 (-1.3 to 0.8)
55-59	23.36	+ 2.6 [‡] (1.4 to 3.8)
60-64	30.39	+ 2.1 [‡] (0.7 to 3.4)
65-69 [†]	43.00	+ 2.6 [‡] (1.1 to 4.2)
70-74	55.71	+ 1.0 (-0.1 to 2.2)
75-79	60.62	+ 1.6 [‡] (0.7 to 2.6)
80-84	72.15	+ 1.0 (-1.2 to 3.1)
85+	55.37	+ 2.6 [‡] (0.6 to 4.7)
All men		+ 1.6 [‡] (1.1 to 2.0)
Women		
40-44	1.51	- 2.0 (-6.1 to 2.3)
45-49	3.34	+ 1.0 (-2.0 to 4.0)
50-54	6.85	+ 2.9 [‡] (0.8 to 5.0)
55-59	11.22	+ 2.4 [‡] (0.9 to 3.8)
60-64	18.95	+ 1.9 [‡] (0.8 to 3.0)
65-69	26.43	+ 1.5 [‡] (0.4 to 2.5)
70-74	37.39	+ 2.5 [‡] (1.7 to 3.3)
75-79 [§]	46.07	+ 3.0 [‡] (1.0 to 5.0)
80-84	51.88	+ 3.1 [‡] (1.4 to 4.8)
85+	44.83	+ 4.3 [‡] (2.6 to 5.9)
All women		+ 2.2 [‡] (1.7 to 2.7)

*Joinpoint results are not shown for the age subgroups <40, because there were fewer than 5 cases in any year.

†Trend 1 (1991-2004): annual percent change (APC) (95% CI) = +0.9 (-0.4 to 2.2); Trend 2 (2004-2010): APC (95% CI) = +6.6[‡] (2.2 to 11.2).

‡Joinpoint is significantly different from zero at $\alpha=0.05$.

§Trend 1 (1991-2000): APC (95% CI) = -0.3 (-3.4 to 3.0); Trend 2 (2000-2010): APC (95% CI) = 5.9[‡] (3.1 to 8.9).



pends mainly on its incidence. International differences in mortality rates and temporal trends suggest that etiology of pancreatic cancer is influenced by environmental factors, especially smoking, but also by nutritional and dietary factors, obesity, alcohol use, and diabetes mellitus (26-29).

The strongest environmental risk factor for pancreatic cancer is smoking. For example, the relative risk of pancreatic cancer in smokers compared to non-smokers was 2.0 (29,30) and the proportion of pancreatic cancer attributable to cigarette smoking in US African-Americans was 29% and 26% in Caucasians (31). As for other tobacco-related malignant tumors, international disparities in mortality trends most likely reflect different rates of tobacco use (30-34). Tobacco exposure in Serbia is high. The percentage of male and female smokers in Belgrade in 1976 and 1977 was 49% and 25%, respectively; in 1988 and 1989, 51% and 37% (35), and in 2000, 48% and 38% (32). The antismoking campaign, which was intensified from 2000, contributed to a decrease in the number of smokers (38% of men and 30% of women in 2006) (36). Serbian joining of the World Health Organization Convention on Tobacco Control in June 2006 is expected to bring about a further reduction in the number of smokers.

However, there are also other important risk factors for pancreatic cancer; according to the data for 2006, 3.4% of the adult population of Serbia consumed alcohol on a daily basis, which is an increase of 0.1% compared with 2000 (3.3%) (36). As in many other countries, the frequency of obesity and diabetes in Serbia has been increasing, and the increase is estimated to continue (37,38). In 2000 as in 2006, one in two adults was overweight, 18.3% were obese, and 36.2% were pre-obese, and the number of overweight and obese 7-19 years old children increased from 12.6% to 18.0% (36). In 2006, about 6.8% of adults in Serbia had diabetes mellitus (6.2% of men and 7.5% of women), which is significantly higher than 4.8% in 2000 (4.5% of men and 5.0% of women) (39,40). Taking all this into account, it seems very difficult to predict the future pancreatic cancer mortality trend, although moderate and insignificant mortality changes in younger age groups are promising.

A limitation of the present study is related to the reliability and validity of death certificates. The World Health Organization assessed the quality of Serbian data on the cause of death as moderate (41). Besides that, pancreatic cancer is difficult to diagnose and the increasing mortality trends may be related to greater diagnostic accuracy (20). It can be assumed that diagnostics of pancreatic cancer was

worse during the first half of the observed period (from 1991 to 2000) than during the second half, because of the war and economic crisis in the country. The proportion of cases with uncertain death cause (revision 9 codes 780-799 and revision 10 codes R00-R99) in the observed period was on average 6.8%, with a non-significant decreasing trend ($P=0.137$). In the majority of developed countries, the quality of death certification is better than in Serbia. For example, the proportion of uncertain causes of death in Nordic countries is 1% (42) and 5% in China (43). We have no data on changes in the autopsy rate during the studied period, which could influence the mortality coding. Registration of autopsies in Serbia began in 2006. From 2006 to 2010, autopsy was performed in 2.1% of all deaths and 2.6% of pancreatic cancers diagnosed at autopsy were missing on the death certificate. We also have no data on possible changes in survival of pancreatic cancer patients, but it is not probable that survival deteriorated during the observed period since the treatment progress has been negligible (44-46). During the study period, there was a change from ICD9 to ICD10, but it seems not to have had an effect on the overall rates of pancreatic cancer. There are no data on pancreatic cancer incidence for the entire Serbia without Kosovo and Metohia (Central Serbia and Vojvodina). For the period 1999 to 2010, there are only data for Central Serbia, showing a non-significant increasing trend of age-standardized pancreatic cancer incidence in both sexes ($P=0.338$ in men and $P=0.679$ in women) (47).

Serbia is among the countries with the highest pancreatic cancer mortality in the world. An increasing mortality trend was present in both sexes and in most age groups. Pancreatic cancer is one of the leading causes of cancer death in Serbia and therefore further effort should be made to clarify its etiology and risk factors.

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Declaration of authorship MI conceived and designed the study, took part in data collection, data analysis, interpretation of the results, and manuscript preparation, editing, and review. HV performed data analysis, interpretation of the results, manuscript editing, and manuscript review. JM performed data analysis, interpretation of the results, manuscript editing, and manuscript review. NK performed data analysis and manuscript editing and review. All authors took part in editing of the final version and gave approval for submission.

Competing interests All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

References

- 1 Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin*. 2011;61:69-90. [Medline:21296855](#) [doi:10.3322/caac.20107](#)
- 2 Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin D. M. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010;127:2893-917. [Medline:21351269](#) [doi:10.1002/ijc.25516](#)
- 3 Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10. Lyon: International Agency for Research on Cancer; 2010. Available from: <http://globocan.iarc.fr>. Accessed: July 4, 2013.
- 4 Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin*. 2005;55:74-108. [Medline:15761078](#) [doi:10.3322/canjclin.55.2.74](#)
- 5 Fesinmeyer MD, Austin MA, Li CI, De Roos AJ, Bowen DJ. Differences in survival by histologic type of pancreatic cancer. *Cancer Epidemiol Biomarkers Prev*. 2005;14:1766-73. [Medline:16030115](#) [doi:10.1158/1055-9965.EPI-05-0120](#)
- 6 Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Altekruse SF, et al, editors. SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations). Bethesda, MD: National Cancer Institute; Available from: http://seer.cancer.gov/csr/1975_2009_pops09/. Accessed: July 4, 2013.
- 7 Qiu D, Katanoda K, Marugame T, Sobue T. A joinpoint regression analysis of long-term trends in cancer mortality in Japan (1958-2004). *Int J Cancer*. 2009;124:443-8. [Medline:18844218](#) [doi:10.1002/ijc.23911](#)
- 8 La Vecchia C, Bosetti C, Lucchini F, Bertuccio P, Negri E, Boyle P, et al. Cancer mortality in Europe, 2000-2004, and an overview of trends since 1975. *Ann Oncol*. 2010;21:1323-60. [Medline:19948741](#) [doi:10.1093/annonc/mdp530](#)
- 9 World Health Organisation. International classification of diseases, ninth revision (ICD-9). Geneva (Switzerland): World Health Organization; 1977.
- 10 World Health Organisation. International statistical classification of diseases and related health problems, tenth revision (ICD-10). Geneva (Switzerland): World Health Organization; 1992.
- 11 The By-law document of emission and form of certificate of death [in Serbian]. Official Gazette SR Serbia 8/2005.
- 12 Statistical Office of the Republic of Serbia. Demographic yearbook in the Republic of Serbia, 1991-2010. Belgrade: Statistical Office of the Republic of Serbia; 2011.
- 13 Jensen OM, Parkin DM, Lennan R, Muir CS, Skeet RG. Cancer registration. Principles and methods. Lyon: International Agency for Research on Cancer; 1991.
- 14 Clegg LX, Hankey BF, Tiwari R, Feuer EJ, Edwards BK. Estimating average annual per cent change in trend analysis. *Stat Med*. 2009;28:3670-82. [Medline:19856324](#) [doi:10.1002/sim.3733](#)
- 15 Lerman PM. Fitting segmented regression models by grid search. *Appl Stat*. 1980;29:77-84. [doi:10.2307/2346413](#)
- 16 Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*. 2000;19:335-51. [Medline:10649300](#) [doi:10.1002/\(SICI\)1097-0258\(20000215\)19:3<335::AID-SIM336>3.0.CO;2-Z](#)
- 17 Kim HJ, Fay MP, Yu B, Barrett MJ, Feuer EJ. Comparability of segmented line regression models. *Biometrics*. 2004;60:1005-14. [Medline:15606421](#) [doi:10.1111/j.0006-341X.2004.00256.x](#)
- 18 Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from major cancers in the European Union, including acceding countries, in 2004. *Cancer*. 2004;101:2843-50. [Medline:15526321](#) [doi:10.1002/cncr.20666](#)
- 19 Levi F, Lucchini F, Negri E, Boyle P, La Vecchia C. Cancer mortality in Europe, 1995-1999, and an overview of trends since 1960. *Int J Cancer*. 2004;110:155-69. [Medline:15069676](#) [doi:10.1002/ijc.20097](#)
- 20 Wingo PA, Cardinez CJ, Landis SH, Greenlee RT, Ries LA, Anderson RN, et al. Long-term trends in cancer mortality in the United States, 1930-1998. *Cancer*. 2003;97(12 Suppl):3133-275. [Medline:12784323](#) [doi:10.1002/cncr.11380](#)
- 21 Fernandez E, La Vecchia C, Porta M, Negri E, Lucchini F, Levi F. Trends in pancreatic cancer mortality in Europe, 1955-89. *Int J Cancer*. 1994;57:786-92. [Medline:8206673](#) [doi:10.1002/ijc.2910570605](#)
- 22 Wood HE, Gupta S, Kang JY, Quinn MJ, Maxwell JD, Mudan S, et al. Pancreatic cancer in England and Wales 1975-2000: patterns and trends in incidence, survival and mortality. *Aliment Pharmacol Ther*. 2006;23:1205-14. [Medline:16611282](#) [doi:10.1111/j.1365-2036.2006.02860.x](#)
- 23 Yang L, Fujimoto J, Qiu D, Sakamoto N. Trends in cancer mortality in the elderly in Japan, 1970-2007. *Ann Oncol*. 2010;21:389-96. [Medline:19622594](#) [doi:10.1093/annonc/mdp303](#)
- 24 Ries LAG, Melbert D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, et al, editors. SEER Cancer Statistics Review, 1975-2004, National Cancer Institute. Bethesda, MD. Available from: http://seer.cancer.gov/csr/1975_2004. Accessed: July 4, 2013.
- 25 Vanderveen KA, Chen SL, Yin D, Cress RD, Bold RJ. Benefit of postoperative adjuvant therapy for pancreatic cancer. *Cancer*. 2009;115:2420-9. [Medline:19301434](#) [doi:10.1002/cncr.24269](#)
- 26 Iodice S, Gandini S, Maisonneuve P, Lowenfels AB. Tobacco and the risk of pancreatic cancer: a review and meta-analysis. *Langenbecks Arch Surg*. 2008;393:535-45. [Medline:18193270](#) [doi:10.1007/s00423-007-0266-2](#)
- 27 Larsson SC, Permert J, Håkansson N, Näslund I, Bergkvist L, Wolk A. Overall obesity, abdominal adiposity, diabetes and cigarette smoking in relation to the risk of pancreatic cancer in two Swedish population-based cohorts. *Br J Cancer*. 2005;93:1310-5. [Medline:16288300](#) [doi:10.1038/sj.bjc.6602868](#)
- 28 Michaud DS, Vrieling A, Jiao L, Mendelsohn JB, Stepilowski E, Lynch SM, et al. Alcohol intake and pancreatic cancer: a pooled analysis

- from the pancreatic cancer cohort consortium (PanScan). *Cancer Causes Control*. 2010;21:1213-25. [Medline:20373013](#) [doi:10.1007/s10552-010-9548-z](#)
- 29 Lowenfels AB, Maisonneuve P. Epidemiology and prevention of pancreatic cancer. *Jpn J Clin Oncol*. 2004;34:238-44. [Medline:15231857](#) [doi:10.1093/jjco/hyh045](#)
 - 30 International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans. Vol. 83. Tobacco Smoke and Involuntary Smoking. Lyon, France: IARC 2004. Available from: <http://globocan.iarc.fr>. Accessed: July 4, 2013.
 - 31 Silverman DT, Dunn JA, Hoover RN, Schiffman M, Lillemoe KD, Schoenberg JB, et al. Cigarette smoking and pancreas cancer: a case-control study based on direct interviews. *J Natl Cancer Inst*. 1994;86:1510-6. [Medline:7932805](#) [doi:10.1093/jnci/86.20.1510](#)
 - 32 Potter JD. Pancreas cancer – we know about smoking, but do we know anything else? *Am J Epidemiol*. 2002;155:793-5. [Medline:11978581](#) [doi:10.1093/aje/155.9.793](#)
 - 33 Weiss W, Benarde MA. The temporal relation between cigarette smoking and pancreatic cancer. *Am J Public Health*. 1983;73:1403-4. [Medline:6638239](#) [doi:10.2105/AJPH.73.12.1403](#)
 - 34 Weiderpass E, Partanen T, Kaaks R, Vainio H, Porta M, Kauppinen T, et al. Occurrence, trends and environment etiology of pancreatic cancer. *Scand J Work Environ Health*. 1998;24:165-74. [Medline:9710368](#) [doi:10.5271/sjweh.295](#)
 - 35 Vlajinac H, Adanja B, Jarebinski M. Smoking habits of urban population of Belgrade [in Serbian]. *Medicinska istraživanja*. 1990;23:73-6.
 - 36 Ministry of Health. Republic of Serbia. National Health Survey, Serbia 2006. Key findings. Belgrade: Ministry of Health, Republic of Serbia; 2007.
 - 37 von Ruesten A, Steffen A, Floegel A, van der A DL, Masala G, Tjønneland A, et al. Trend in obesity prevalence in European adult cohort populations during follow-up since 1996 and their predictions to 2015. *PLoS ONE*. 2011;6:e27455. [Medline:22102897](#) [doi:10.1371/journal.pone.0027455](#)
 - 38 Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract*. 2010;87:4-14. [Medline:19896746](#) [doi:10.1016/j.diabres.2009.10.007](#)
 - 39 Vuković D, Bjegović V, Vuković G. Prevalence of chronic diseases according to socioeconomic status measured by wealth index: health survey in Serbia. *Croat Med J*. 2008;49:832-41. [Medline:19090609](#) [doi:10.3325/cmj.2008.49.832](#)
 - 40 Bjegović V, Terzić Z, Marinković J, Lalić N, Sipetić S, Laaser U. The burden of type 2 diabetes in Serbia and the cost-effectiveness of its management. *Eur J Health Econ*. 2007;8:97-103. [Medline:17221182](#) [doi:10.1007/s10198-006-0012-7](#)
 - 41 Mathers CD, Fat DM, Inoue M, Rao C, Lopez AD. Counting the dead and what they died from: an assessment of the global status of cause of death data. *Bull World Health Organ*. 2005;83:171-7. [Medline:15798840](#)
 - 42 Nagenthiraja K, Ewertz M, Engholm G, Storm HH. Incidence and mortality of pancreatic cancer in the Nordic countries 1971-2000. *Acta Oncol*. 2007;46:1064-9. [Medline:17952708](#) [doi:10.1080/02841860701381234](#)
 - 43 Wang L, Yang GH, Lu XH, Huang ZJ, Li H. Pancreatic cancer mortality in China (1991-2000). *World J Gastroenterol*. 2003;9:1819-23. [Medline:12918128](#)
 - 44 Klint A, Engholm G, Storm HH, Tryggvadóttir L, Gislum M, Hakulinen T, et al. Trends in survival of patients diagnosed with cancer of the digestive organs in the Nordic countries 1964-2003 followed up to the end of 2006. *Acta Oncol*. 2010;49:578-607. [Medline:20491524](#) [doi:10.3109/02841861003739330](#)
 - 45 Sharma C, Eltawil KM, Renfrew PD, Walsh MJ, Molinari M. Advances in diagnosis, treatment and palliation of pancreatic carcinoma: 1990-2010. *World J Gastroenterol*. 2011;17:867-97. [Medline:21412497](#) [doi:10.3748/wjg.v17.i7.867](#)
 - 46 Bosetti C, Bertuccio P, Negri E, La Vecchia C, Zeegers MP, Boffetta P. Pancreatic cancer: overview of descriptive epidemiology. *Mol Carcinog*. 2012;51:3-13. [Medline:22162227](#) [doi:10.1002/mc.20785](#)
 - 47 Center for prevention and control of noncommunicable diseases. Cancer incidence and mortality in Central Serbia, 1999-2010. Belgrade: Institute of Public Health of Serbia "Dr. Milan Jovanovic Batut"; 2003-2010.