

Malignant Melanoma of Skin Mortality in Serbia, 1991–2019; A Joinpoint Analysis [†]

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Abstract: This is a nation-wide descriptive epidemiological study. Joinpoint analysis was applied. Average annual ASR of malignant melanoma of skin mortality in men was higher than in women (11.2 per 100,000 and 3.3 per 100,000, respectively). Overall, a significantly decreasing trend for malignant melanoma of skin mortality was observed, but one joinpoint was observed: a significant decrease of malignant melanoma mortality from 1991 to 2012 (by -1.6% per year, 95% CI = -2.0 to -1.2) was followed by a significant decrease to onwards (by -4.0% per year, 95% CI = -5.9 to -2.2). Further research will allow a clarification of trends and help in future cancer control.

Keywords: malignant melanoma of skin; mortality; trends

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1. Introduction

In 2020 worldwide, according to the GLOBOCAN estimates, there were 57,043 malignant melanoma deaths (0.6% of the total cancer death) [1,2]. Almost 50% of deaths (26,360 cases) occurred in Europe (about 14,500 in men, 11,500 in women). The estimated 5-year survival rates for malignant melanoma are relatively low ($\leq 20\%$ for metastatic disease), while for localized disease are about 90% [3,4].

The world regions with the greatest mortality rates from malignant melanoma are Europe, North America, and Europe at ≥ 1.3 per 100,000 [2]. In contrast, regions like the South-Central Asia, Micronesia, and Northern Africa reported the lowest rates at 0.2 per 100,000. In the world, malignant melanoma mortality was greater in males than in females (0.7 vs. 0.4 per 100,000). Globally, overall decreasing trend in malignant melanoma mortality was observed across a large number of different populations over the past decades [1–4].

For malignant melanoma of skin, one of the most aggressive skin cancers, great differences in mortality across the world have been observed during the last decades. The purpose of this study was to assess the mortality of malignant melanoma of skin in Serbia in 1991–2019.

2. Materials and Methods

For this descriptive epidemiological study, we used annual underlying cause of death data from Serbia to describe trends in mortality from malignant melanoma for the period 1991–2019. Data on persons who died of malignant melanoma (site code 172 revision 9 and C43 revision 10 of the International Classification of Diseases to classify death, injury and cause of death—ICD) were obtained from the Statistical Office of the Republic of Serbia (unpublished data). In Serbia, from 1991 to 1996 data about the main cause of death were classified by the ICD 9th Revision. Since 1997, the data processing of mortality

statistics is based on the ICD 10th Revision. Based on the indicators of mortality statistics, the WHO assessed the registration of death data in Serbia as having medium quality [5].

The study comprised the entire population of the Republic of Serbia (all ages). The entire population of Serbia comprised about 7 million inhabitants in 2019. Data on the number and composition of the Serbian population by gender and age were presented according to 1991, 2002 and 2011 censuses.

Three types of death rates were calculated: crude, specific (age-, and sex-specific) and age-standardized (expressed per 100,000 persons). The age standardized rate (ASR) was calculated by direct method (World population was used as the standard population, stratified by 5-year age strata).

Mortality trends from suicides were assessed using the joinpoint regression analysis (Joinpoint regression software, available through the Surveillance Research Program of the US National Cancer Institute). The results are presented as straight lines connected at change points, on a log scale, and these trends in the annual age-standardized mortality rates are characterized with an annual percentage change (APC) between successive change points, with 95% confidence intervals (CI). The goal of the comparability test was to answer whether the two regression mean functions were identical (test of coincidence) or parallel (test of parallelism). A *p* value of < 0.05 was considered statistically significant for all tests.

3. Results

Nearly 6500 (about 3600 men and 2700 women) malignant melanoma deaths occurred in Serbia during the observed period, with the average annual age-standardized mortality rate being 7.0 per 100,000 inhabitants (Table 1). Average annual ASR of malignant melanoma of skin mortality in men was higher than in women (11.2 per 100,000 and 3.3 per 100,000, respectively).

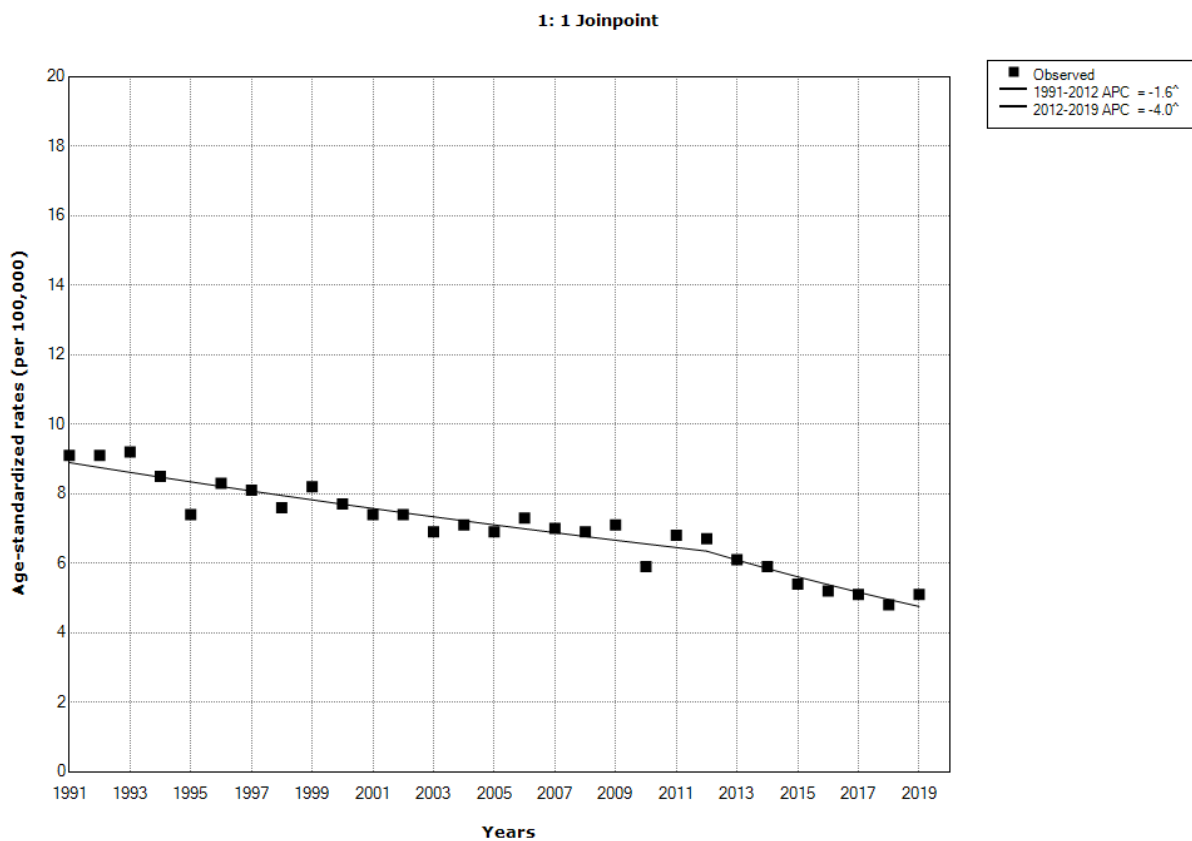
Overall, a significantly decreasing trend for malignant melanoma of skin mortality was observed (AAPC = -2.0% per year, 95%CI = -2.3 to -1.7), but one joinpoint was observed: a significant decrease of malignant melanoma mortality from 1991 to 2012 (by -1.6% per year, 95%CI = -2.0 to -1.2) was followed by a significant decrease to onwards (by -4.0% per year, 95%CI = -5.9 to -2.2) (Figure 1).

Table 1. Malignant melanoma mortality in Serbia, 1991–2019.

Year	Total			Men			Women		
	Number	Crude Rates	ASRs	Number	Crude Rates	ASRs	Number	Crude Rates	ASRs
1991	133	12.9	9.1	76	18.6	14.1	57	7.4	4.7
1992	134	13.3	9.1	79	18.8	13.7	55	8.1	5.0
1993	142	13.6	9.2	88	18.5	13.6	54	8.8	5.4
1994	149	12.4	8.5	80	18.2	13.3	69	6.9	4.3
1995	176	10.9	7.4	86	15.8	11.4	90	6.2	4.0
1996	173	11.9	8.3	92	17.1	12.6	81	7.0	4.5
1997	156	11.9	8.1	96	17.5	12.6	60	6.6	4.0
1998	176	11.3	7.6	103	16.1	11.6	73	6.8	4.2
1999	185	12.6	8.2	93	18.0	12.7	92	7.4	4.3
2000	181	12.2	7.7	105	17.7	12.1	76	7.1	3.9
2001	207	11.5	7.4	120	16.6	11.4	87	6.6	3.9
2002	194	11.7	7.4	98	17.7	12.0	96	6.0	3.3
2003	182	10.8	6.9	101	16.5	11.5	81	5.4	2.9
2004	206	11.2	7.1	111	17.2	11.6	95	5.6	3.2
2005	223	11.5	6.9	127	16.8	11.0	96	6.5	3.2
2006	208	11.9	7.3	114	17.8	11.7	94	6.3	3.3
2007	238	11.4	7.0	130	17.0	11.1	108	6.1	3.3

2008	258	10.9	6.9	160	16.0	10.6	98	6.1	3.4
2009	259	11.4	7.1	151	17.7	11.6	108	5.5	3.1
2010	253	10.2	5.9	150	15.8	9.7	103	4.9	2.4
2011	232	11.3	6.8	145	17.1	10.9	87	5.8	3.1
2012	273	11.2	6.7	157	17.6	11.1	116	5.2	2.7
2013	247	10.2	6.1	153	16.1	10.1	94	4.7	2.5
2014	264	10.1	5.9	149	16.1	9.9	115	4.4	2.2
2015	300	9.1	5.4	190	14.5	9.0	110	4.0	2.1
2016	271	8.5	5.2	159	13.1	8.4	112	4.2	2.2
2017	274	8.7	5.1	166	14.1	8.7	108	3.7	1.9
2018	269	8.4	4.8	159	13.7	8.2	110	3.4	1.7
2019	283	8.4	5.1	175	13.4	8.5	108	3.7	1.9
Overall	6246	11.1	7.0	3613	16.6	11.2	2633	5.9	3.3

ASR—Age Standardized Rate (using World standard population, per 100,000).

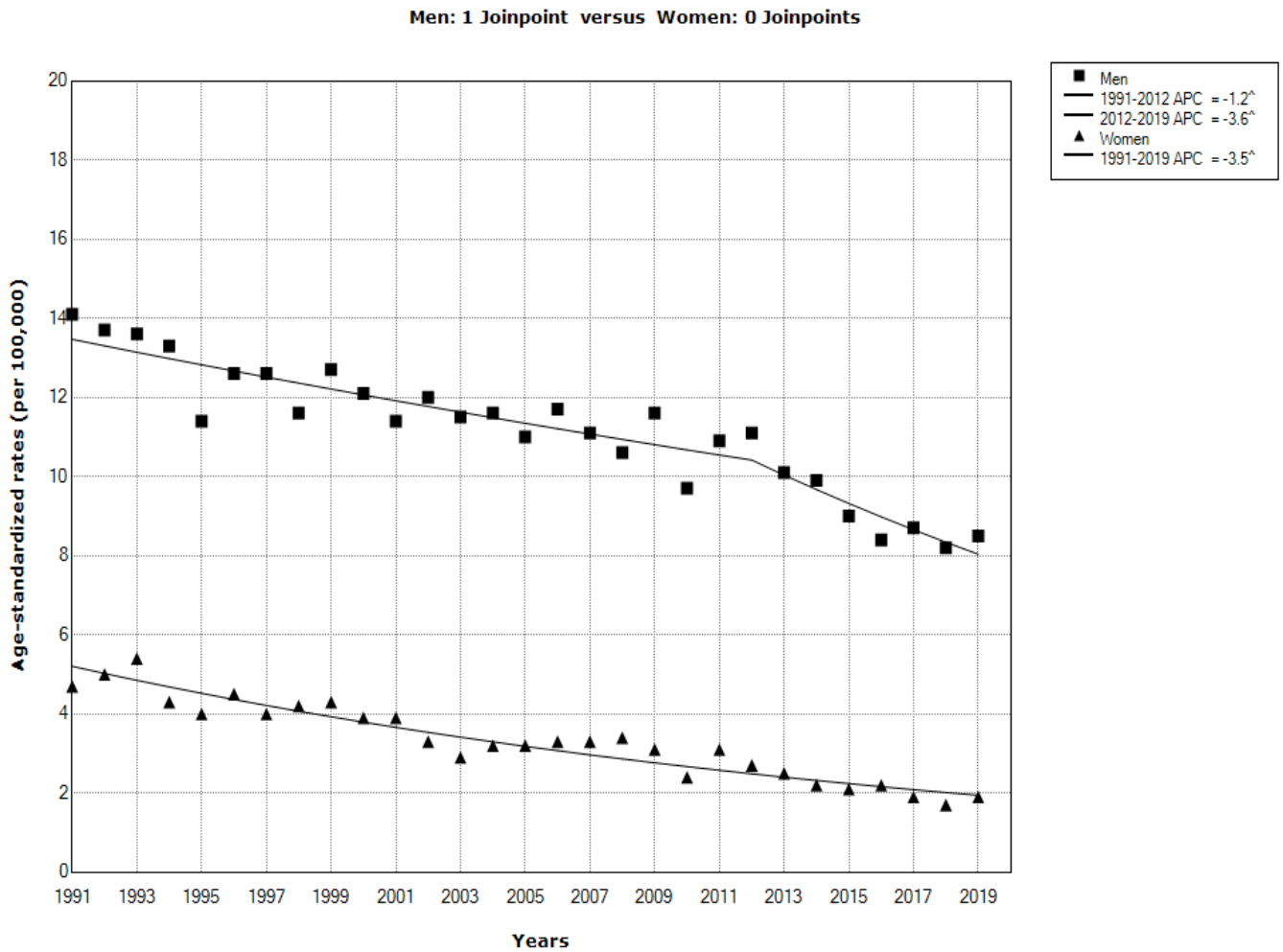


^ Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 1 Joinpoint.

Figure 1. Malignant melanoma mortality in Serbia, 1991–2019; a joinpoint analysis.

Trends from malignant melanoma of skin mortality rates significantly decreased both in men (AAPC = -1.6% per year; 95%CI = -1.9 to -1.4 ; but one joinpoint was observed: a significant decrease of malignant melanoma mortality from 1991 to 2012 (by -1.2% per year, 95%CI = -1.6 to -0.9) was followed by a significant decrease to onwards (by -3.6% per year, 95%CI = -5.4 to -1.8) and women (AAPC = -3.5% per year; 95%CI = -3.9 to -3.0) (Figure 2). Mortality trends in men and women were not parallel (final selected model rejected parallelism, $p = 0.0002$) and not coincident (final selected model rejected coincidence, $p = 0.0002$).

Malignant melanoma mortality rates in both sexes increased with age and were higher among men than among women in all age groups (Figure 3).



^ Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
 Final Selected Model: Men - 1 Joinpoint, Women - 0 Joinpoints. Rejected Coincidence.

Figure 2. Malignant melanoma mortality in Serbia, both sexes, 1991–2019; a joinpoint analysis.

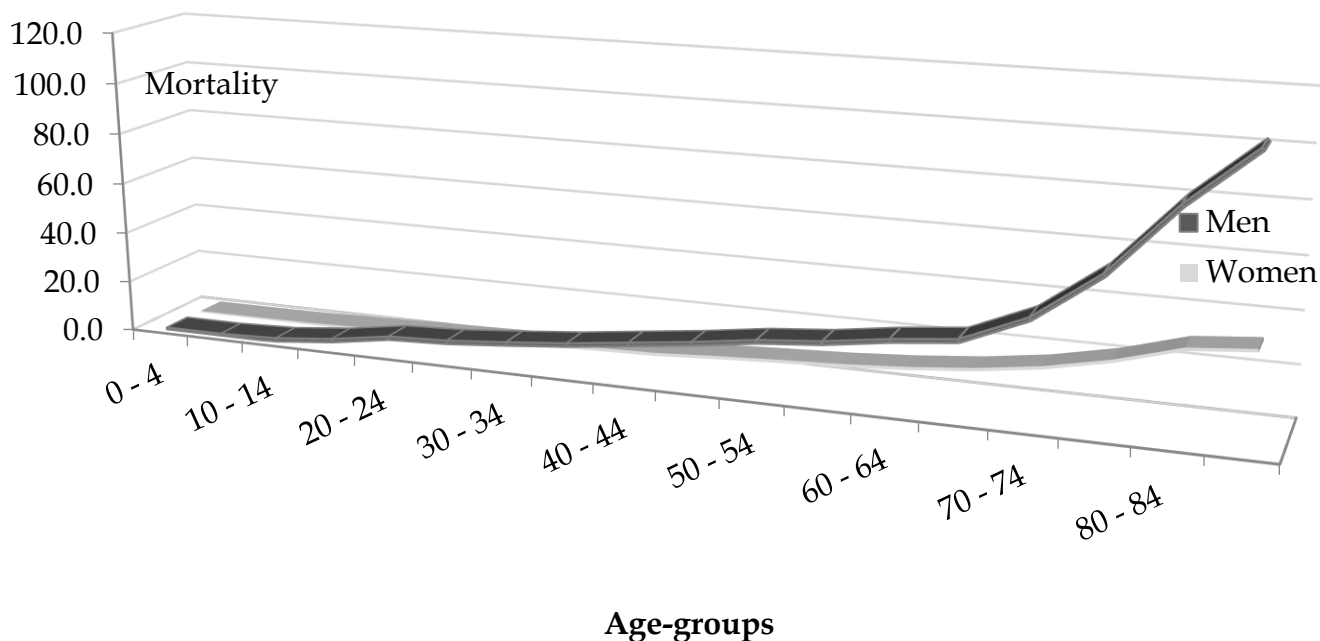


Figure 3. Age-specific malignant melanoma mortality rates (per 100,000) in Serbia, by sexes, 1991–2019.

4. Discussion

The trend in malignant melanoma of skin mortality has been decreasing in Serbia in the last decades, both in men and women. Despite decreasing trends, mortality rates for malignant melanoma in Serbia remain among the highest in the world.

Mortality rates for malignant melanoma among men in the world in 2020 vary between 6.7 per 100,000 in New Zealand, 4.0 in Montenegro, 3.8 in Norway and Slovakia, followed by 3.4 in Slovenia, 3.3 in Croatia, 3.2 in Australia and 3.1 in Serbia [2]. Contrary, the lowest rates (≤ 0.2 per 100,000) are found in China, Ethiopia, Nepal, Nigeria, Viet Nam, Barbados, Jordan, Saudi Arabia. Mortality rates among women in the world in 2020 vary between 2.8 per 100,000 in New Zealand, 2.6 in Norway, followed by 2.3 in Montenegro, 2.2 in Slovakia, 2.1 in Denmark, 1.9 in Slovenia, and 1.7 in Serbia, Croatia, Australia, and Ireland equally [2].

According to Yang et al. [8], continuously increasing malignant melanoma mortality for both sexes between 1985 and 2015 was reported in Belgium, Croatia, Germany, Ireland, Italy, Norway, Republic of Korea, Serbia and United Kingdom. Also, continuously decreasing malignant melanoma mortality for both sexes between 1985 and 2015 was reported in Czech Republic only. Besides, continuously decreasing malignant melanoma mortality for females between 1985 and 2015 was reported in Australia only. Denmark, Estonia, Finland, Hungary, Lithuania, Netherlands, Moldova, Slovakia, Slovenia and Sweden reported continuously decreasing malignant melanoma mortality for males only between 1985 and 2015.

The large geographic variations in malignant melanoma mortality could be attributed to differences in practice of diagnosis and treatment, life-style habits [6–8]. Some differences by sexes could be due to the fact that men protect themselves less from the sun [9]. On the other hand, men are more likely to have outdoor occupations and thus experience more exposure to ultraviolet radiation. Additionally, although women are more likely to practice sun protection, they are also more likely to engage in intentional sun tanning behavior. Some other factors that may be the reasons underlying the sex disparity in malignant melanoma mortality in different countries include differences in alcohol intake and diet, as well as biological factors.

5. Conclusions

The trend in malignant melanoma of skin mortality has been decreasing in Serbia in the last decades, both in men and women. Despite decreasing trends, mortality rates for malignant melanoma in Serbia remain among the highest in the world. Future epidemiological studies are needed in order to elucidate the reasons of malignant melanoma burden in Serbia.

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