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Diabetes mortality in Serbia, 1991–2015 (a nationwide study): A joinpoint regression analysis

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ABSTRACT

Purpose: The aim of this study was to analyze the mortality trends of diabetes mellitus in Serbia (excluding the Autonomous Province of Kosovo and Metohia).
Methods: A population-based cross sectional study analyzing diabetes mortality in Serbia in the period 1991–2015 was carried out based on official data. The age-standardized mortality rates (per 100,000) were calculated by direct standardization, using the European Standard Population. Average annual percentage of change (AAPC) and the corresponding 95% confidence interval (CI) were computed using the joinpoint regression analysis.
Results: More than 63,000 (about 27,000 of men and 36,000 of women) diabetes deaths occurred in Serbia from 1991 to 2015. Death rates from diabetes were almost equal in men and in women (about 24.0 per 100,000) and places Serbia among the countries with the highest diabetes mortality rates in Europe. Since 1991, mortality from diabetes in men significantly increased by +1.2% per year (95% CI 0.7–1.7), but non-significantly increased in women by +0.2% per year (95% CI −0.4 to 0.7). Increased trends in diabetes type 1 mortality rates were significant in both genders in Serbia. Trends in mortality for diabetes type 2 showed a significant decrease in both genders since 2010.
Conclusion: Given that diabetes mortality trends showed different patterns during the studied period, our results imply that further observation of trend is needed.

1. Introduction

Diabetes is an increasing global health problem in the world during the last decades [1–3]. Based on the World Health Organization (WHO) 2012 estimates, diabetes directly caused 1.5 million of deaths in the world in 2012 (this represents about 2.7% of all deaths globally), up from 1.0 million (2.0%) deaths in 2000 [1]. More than 80% of diabetes deaths occur in low- and middle-income countries [1]. Diabetes alone is the third most common cause of death in low- and middle-income countries in WHO Region of the Americas, accounting for nearly 0.2 million deaths each year: approximately 6.5% of all deaths in both genders are from diabetes [1]. In Europe, diabetes caused nearly 35,000 deaths in 2012 (accounts for 1.3% of all deaths).

Although the number of deaths from diabetes is almost the same in both developed and developing regions, the death rates from diabetes vary by more than 50 times around the world [4]. The death rates from diabetes were high in the predominantly islands population (Trinidad and Tobago—128.2

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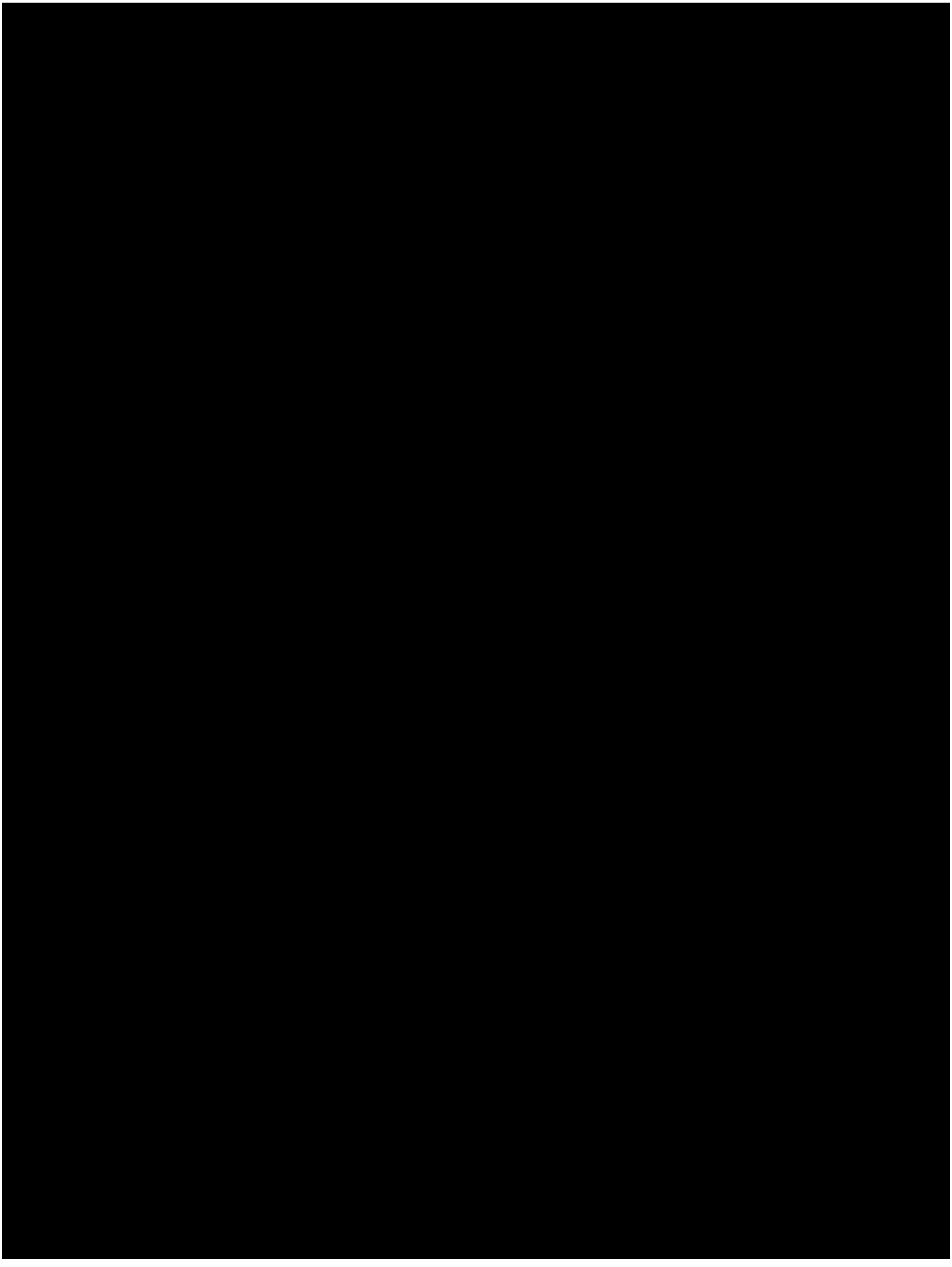

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not shown for age groups <30 for diabetes type 1 and for age groups <40 for diabetes type 2, because count of diabetes deaths that occurred in each of the decennium in any year was zero. The analysis began with the minimum number of joinpoints (e.g., 0 joinpoint, representing a straight line), and tested whether one or more joinpoints were significant. The joinpoint analysis provided average annual percentage change (AAPC)—a summary measure over a fixed interval, with the corresponding 95% confidence interval (95%CI) [15]. For zero joinpoints, APC and AAPC are identical. In describing trends, the term "increase" was used when the slope (positive APC or AAPC) of the trend was statistically significant. Significant differences by genders were detected using a specific procedure—comparability test [16]. The test is applied to compare diabetes mortality rates between two age groups using tests of parallelism and coincidence of time trends. Test determines whether the two regression mean functions are parallel allowing different intercepts (test of parallelism) or whether two joinpoint regression functions are identical (test of coincidence). Two-sided *P* values were considered to indicate statistical significance when they were less than 0.05.

2.4. *Ethical considerations*

This study is approved by the Ethics Committee of the Faculty of Medical Sciences, University of Kragujevac (Ref. No.: 01-1176).

3. Results

More than 63,000 (about 27,000 of men and 36,000 of women) diabetes deaths occurred in Serbia (excluding the Autonomous Province of Kosovo and Metohia) during the observed period, with the average annual ASRs being 24.2 per 100,000 (Table 1). Mortality rates from diabetes were almost equal in men and in women (23.9 per 100,000 men and 24.0 per 100,000 women).

Mortality from diabetes significantly increased since 1991 by +1.2% (95% CI 0.7–1.7) yearly in men, but non-significantly increased by +0.2% (95% CI −0.4 to 0.7) yearly in women (Fig. 1). However, for mortality from diabetes in women, there was one joinpoint at 2010: ASRs significantly increased by +0.9% (95% CI 0.3–1.5) yearly from 1991 to 2010, and then rapidly decreased by −4.8% (95% CI −9.3 to −0.2) yearly from 2010 to 2015. According to the comparability test, mortality trends from diabetes in men and women differed significantly (final selected model rejected parallelism, $P = 0.0002$). Overall mortality rates from diabetes significantly increased by 0.6% (95% CI 0.1–1.1) in Serbia in the whole observed period (data not shown).

Changes in diabetes type 1 mortality rates were large and significant in both genders in Serbia (Fig. 2). Trends in ASRs for diabetes type 1 mortality showed a similar pattern in men and women: two joinpoints were detected for men (a significant decrease by 12.1% from 1997 to 2002, and then a significant increase by 22.8% from 2002 to 2006, followed by a significant increase by 3.8% from 2006 to onwards) and in women (a significant decrease by 11.5% from 1997 to 2002 and a significant increase by 11.4% from 2002 to 2011, and then a non-significant decline by −6.7% per year from 2011 to onwards). According to the comparability test, mortality trends from diabetes type 1 in men and women were parallel (final selected model failed to reject parallelism, $P > 0.05$).

Table 1 – Diabetes mellitus mortality in Serbia, excluding the Autonomous Province of Kosovo and Metohia, in 1991–2015 period.

Year	No.	Crude rates	ASRs
1991	1904	25.1	22.9
1992	1952	25.7	23.0
1993	1769	23.2	20.3
1994	1759	23.1	19.4
1995	2104	27.6	23.0
1996	2181	28.6	23.6
1997	2209	29.1	23.2
1998	2232	29.5	23.1
1999	2514	33.3	25.8
2000	2506	33.3	25.4
2001	2336	31.1	23.0
2002	2553	34.0	24.8
2003	2660	35.6	25.3
2004	2571	34.5	24.0
2005	2575	34.6	23.8
2006	2541	34.3	23.2
2007	3005	40.7	27.3
2008	3113	42.4	28.0
2009	3066	41.9	27.0
2010	3195	43.8	28.1
2011	3135	43.2	27.2
2012	2998	41.6	25.5
2013	2802	39.1	23.8
2014	2513	35.2	20.7
2015	3027	42.5	24.8
Overall	63,220	34.1	24.2

ASR = age standardized rate (per 100,000 persons, using European standard population).

Trends in ASRs for diabetes type 2 mortality showed a significant decrease in both genders since 2010 (Fig. 3). One joinpoint was detected for men (a non-significant increased trend was observed from 1997 to 2010, but then a significantly decreased trend by 8.3% was recorded from 2010 to onwards) and in women (a non-significant change was observed from 1997 to 2010, but from 2010 to onwards a significantly decreasing trend by 9.8% was recorded). According to the comparability test, mortality trends from diabetes type 2 in men and women were not parallel (final selected model rejected parallelism, $P = 0.0129$).

Since the 2000s, a significant increase in mortality rates from diabetes type 1 was identified in almost all age groups in both genders, except in one age group (50–59 years) in women where a significant decrease was present (Table 2). Non-significant trends in both genders were observed in the age groups of 30–49 years (increased trends in men and decreased trends in women).

Trends in age-specific mortality rates from diabetes type 2 showed a similar pattern in men and women (Table 3). Declines in mortality rates from diabetes type 2 were identified in almost all age groups, except in the oldest age group in both genders where a significant increase was present during the whole period. Significant declining trends in type 2

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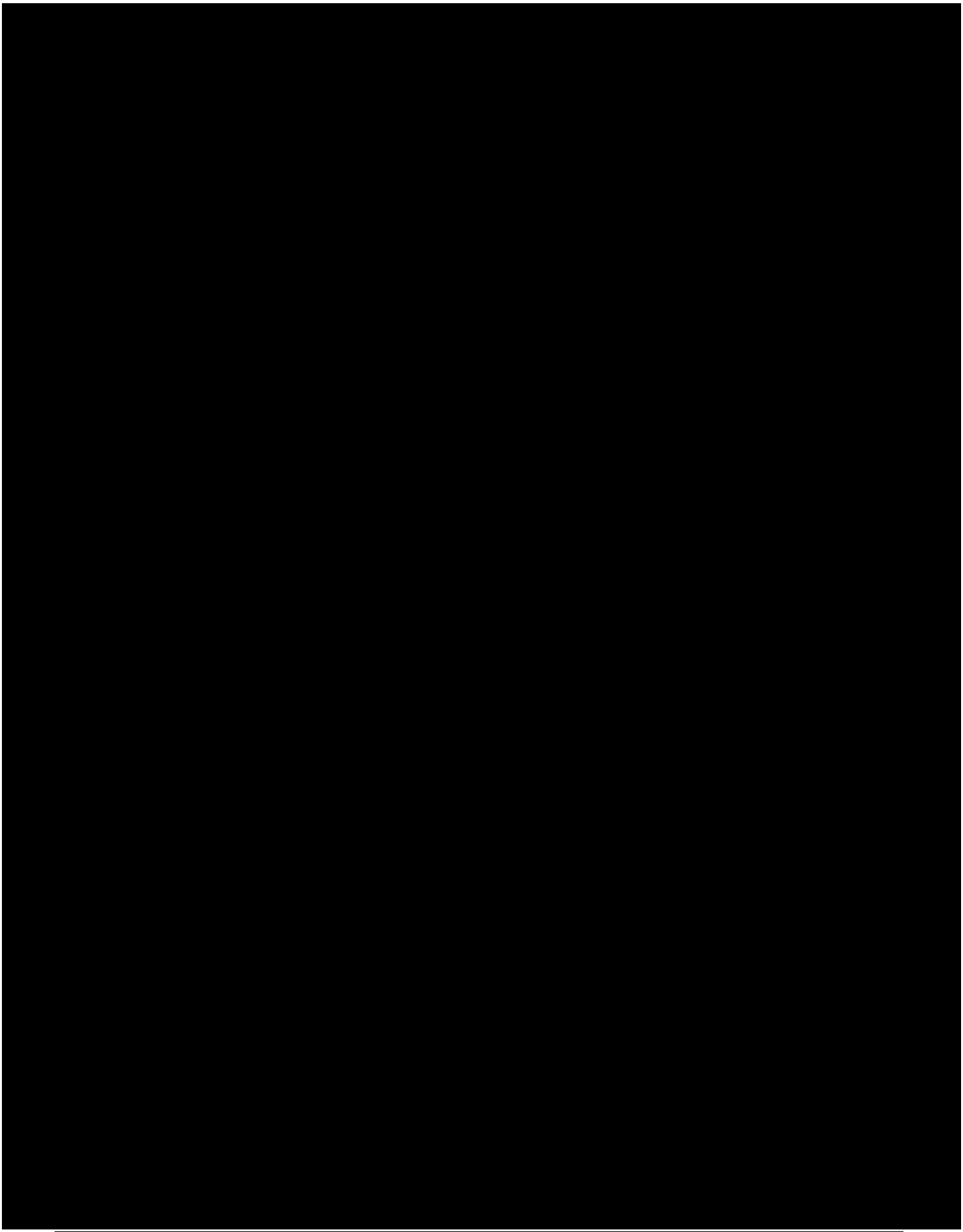

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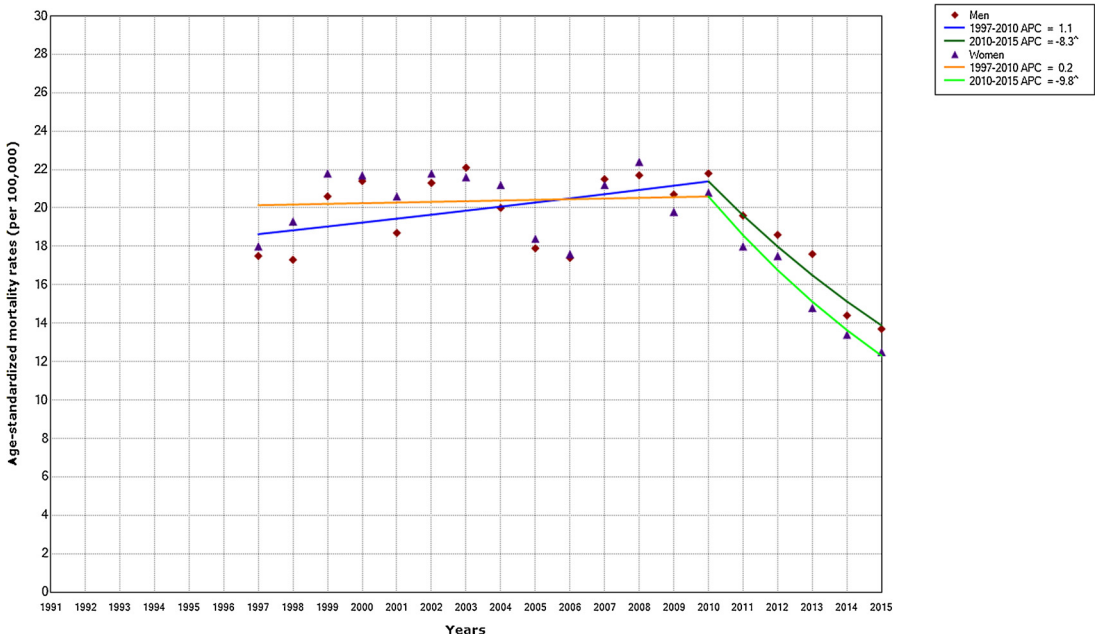

Fig. 3 – Diabetes mellitus type 2 mortality trends, men and women in Serbia, in 1997–2015 period: a joinpoint regression analysis.
***Statistically significant trend; APC—annual percent change.**

in men. The exception was a decreased trend in diabetes type 2 mortality rates both in men and women.

The ASR of diabetes (25.5 per 100,000) in Serbia was two times higher than the average ASR in countries of European region (12.9 per 100,000) in 2012 [5]. In 2012, in Europe, high rates have been observed in Armenia (41.5 per 100.000) and the Mediterranean countries (Cyprus—32.8, Turkey—30.8, Israel—26.5, Portugal—23.0); the lowest rate (approximately—5.5) in United Kingdom, Finland and Greece [5]. Finally, the above mentioned mortality rate puts Serbia on the fifth place among the countries with the highest diabetes mortality rates in Europe. Some unfavorable changes (economic crisis, poverty, civil wars, refugees, unemployment, disintegration of the country, NATO bombing) occurred in Serbia in the last decades, that have had a considerable impact on lifestyle as well as on the functioning of the health services in Serbia during the studied period (lack of drugs, public health weakness) [17,18]. The National Health Survey revealed that 18.3% of adult male population in Serbia were obese (body mass index ≥30) in 2006, significantly more

Table 2 – Trends[a] in age-specific diabetes type 1 mortality rates, men and women in Serbia, in 1997–2015 period: a joinpoint regression analysis.

Age[b]	AAPC (95% CI)	Trend 1	APC (95% CI)	Trend 2	APC (95% CI)	Trend 3	APC (95% CI)
Men							
30–40	0.9 (−3.7 to 5.6)						
40–49	0.7 (−1.1 to 2.5)						
50–59	3.1[a] (0.7–5.6)	1997–2001	−13.4 (−28.4 to 4.8)	2001–2015	6.1[a] (3.2–9.2)		
60–69	5.3[a] (2.5–8.3)	1997–2001	−13.5 (−30.3 to 7.4)	2001–2015	8.8[a] (5.4–12.3)		
70–79	6.8[a] (4.4–9.2)	1997–2001	−10.5 (−25.2 to 7.1)	2001–2015	9.9[a] (7.0–12.8)		
80+	11.9[a] (9.4–14.5)						
Women							
30–40	−3.0 (−7.7 to 1.9)						
40–49	−1.8 (−5.5 to 2.1)						
50–59	−2.6[a] (−5.1 to −0.2)						
60–69	1.1 (−1.5 to 3.7)	1997–2000	−23.8 (−45.6 to 6.6)	2000–2015	3.9[a] (1.0–6.9)		
70–79	5.5[a] (3.4–7.6)	1997–2001	−11.3 (−23.4 to 2.6)	2001–2011	11.4[a] (6.8–16.2)	2011–2015	−4.8 (−17.7 to 10.1)
80+	13.3[a] (9.4–17.3)						

AAPC = average annual percent change; APC = annual percent change; CI = confidence interval.
[a] Statistically significant trend.
[b] Joinpoint results are not shown for age subgroups <30, because count of diabetes type 1 deaths occurred in each of the decennium in any year was zero.

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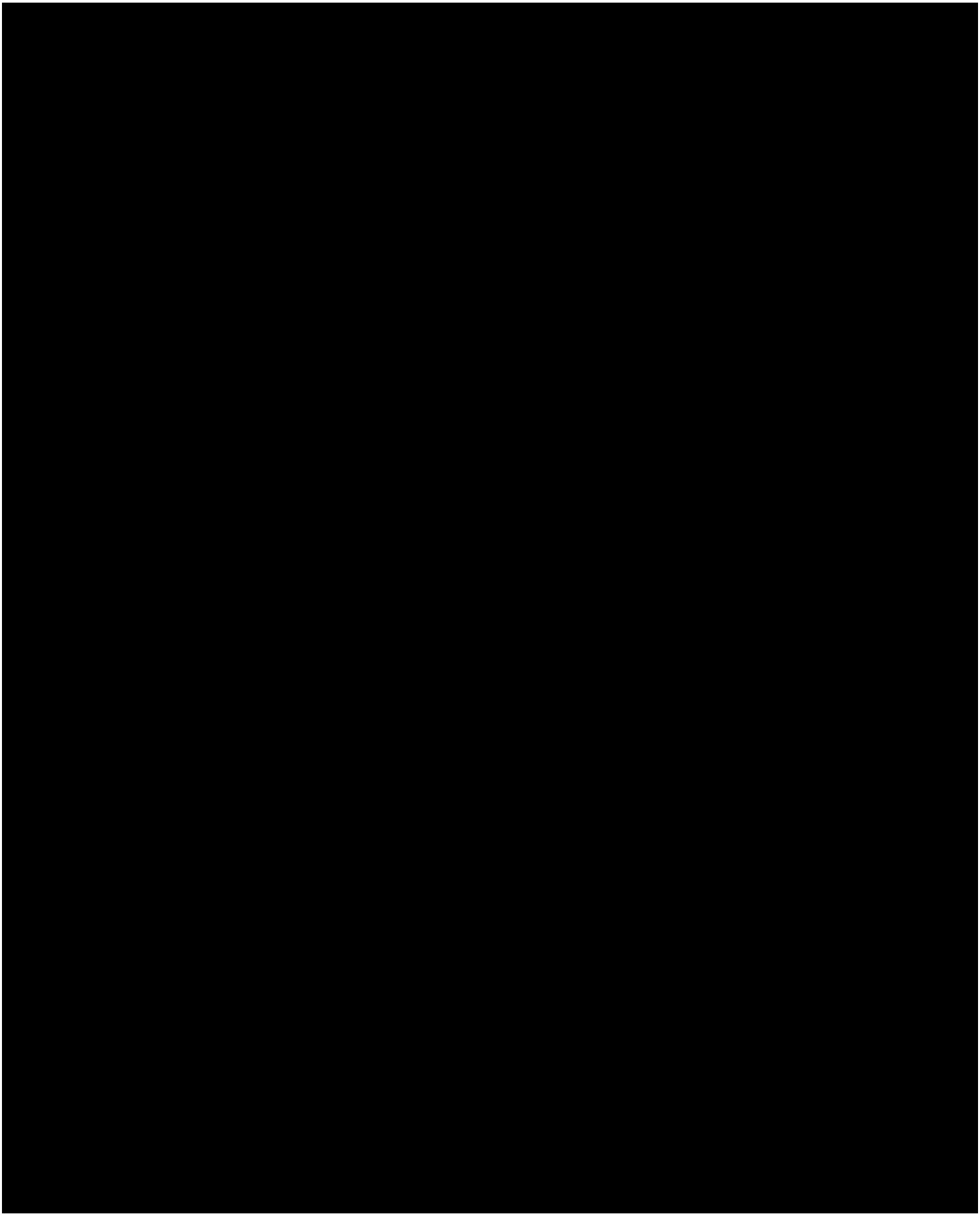

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or in insulin sensitivity, but involves complex social and cultural issues of gender [23]. Type 1 diabetes includes those cases currently ascribable to an autoimmune process and those for which etiology is unknown, while type 2 diabetes is caused by both environmental (such as physical inactivity, drugs and toxic agents, obesity, viral infection) and genetic factors [39]. The increased rates of deaths from diabetes type 1 might have been a consequence of unfavorable circumstances in Serbia in the observed period: the general standard was poor, the quality of health services was unsatisfactory (including the lack of vaccines, drugs, medical equipment, a large number of wounded as well as refugees, decreasing hospitalization rates, particularly for people aged 60 years and older), social disintegration, aging of the population, etc. [9].

Relatively favorable trend in mortality from diabetes type 2 may be attributed to the implementation of mass preventive programs (tobacco control, etc.) and improvements in diabetes treatment in Serbia [19]. Paradoxically, the decline trend in diabetes mortality in women in Serbia coincided with the global economic crisis. Therefore, these results should encourage the launching of epidemiological studies in order to identify future trends in diabetes mortality and to plan for health care delivery, especially in developing countries.

4.1. *Strengths and limitations of this study*

This study provides the first nationwide estimates of diabetes mortality in Serbia over 25 years. The strength of our study lies in the fact that it is a population-based study, using quality death data with comprehensive coverage, completeness and comparability, with temporal trends assessed by joinpoint analysis. Thanks to the WHO assessment of the quality of data on the cause of death in Serbia as intermediate [12], we could give a good assessment of national mortality trend for diabetes and carry out a comparison with the pattern of diabetes mortality in other countries. Also, our study implies the need for effective measures of diabetes prevention and treatment in Serbia.

However, there were several sources of limitations in this paper. We acknowledge that a longer study period may be better to more accurately assess mortality time-trends, but in Serbia there was no available data for this. Also, a limitation is that there are no separate data on diabetes deaths among refugees that can possibly confound the diabetes mortality pattern in Serbia: for internally displaced persons and refugees data were included in the Serbian population and could not be set aside as a special contingent. Certainly, a better quality deaths registration system, which is available in high-income countries, is needed in Serbia. Namely, mortality rates from diabetes may have been underestimated, because of the errors in coding the causes of death and recording the diabetes as antecedent, instead of underlying main cause of death, particularly in those who died from infarction, stroke, and renal diseases [40]. Also, there are no data of diabetes incidence for the entire study period to be used for explanation of temporal mortality trends (Diabetes Registry was implemented since 2006). The available literature does not have enough relevant information about the presence of risk factors for diabetes in the Serbian population. In the applied log-linear model in this study, dropping a particular year observations with count of diabetes deaths being zero from the analysis may shift or affect the detection or locations of joinpoints affecting the analysis. Despite these limitations, this study helped to elucidate diabetes death trends in Serbia, which still need to be clarified in analytical epidemiological studies in the future.

Conflict of Interest

The authors state that they have no conflict of interest.

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