Stroke Mortality Rates and Trends in Romania, 1994-2017

Sorin Ioacara, MD, PhD,*,† Cristina Tiu, MD, PhD,*,‡ Cristina Panea, MD, PhD,*,† Horia Nicolae, MD, PhD,*,† Elisabeta Sava, MD,*,† Sorina Martin, MD, PhD,*,† and Simona Fica, MD, PhD*,†

Background and Aim: Romanian national level stroke mortality data is relatively scarce. The current study investigated stroke mortality rates and trends in Romania. *Methods:* All individual deaths registered in Romania during 1994-2017 were analyzed using an anonymized database, based on death certificates. Stroke crude mortality rates (CMR) and age-standardized mortality rates (ASMR) were calculated and expressed per 100,000 persons-year. *Results:* Between 1994 and 2017, 6,281,873 persons died in Romania, stroke being registered as the underlying cause of death in 959,319 cases. The overall stroke CMR was 188.2 (199.3 for women and 176.5 for men). The CMR for hemorrhagic stroke (HEMS) was 32.4 and for ischemic stroke (ISCS) 10.9. There was a significant decrease in stroke ASMR from 344.4 (95% confidence interval [CI] 343.4-345.4) in 1994 to 192.1 (95% CI 191.5-192.7) in 2017, with an annual percent change (APC) of 2.53% per year (95% CI 2.50-2.55, $P < .001$). Although compared with men, women had higher CMRs, when those rates were age-standardized men had higher ASMR as compared with women. The decline in HEMS ASMR had an APC of 4.65% per year (95% CI 4.59-4.70, $P < .001$). ISCS ASMR showed an initial increase in ASMR during 1994-2005, with APC 6.39% per year (95% CI 6.09-6.70, $P < .001$), followed by a significant decrease until 2017, with APC 2.83% per year (95% CI 2.59-3.07, $P < .001$). *Conclusion:* There was a significant reduction in stroke ASMR during 1994-2017. The decline was slow until 2002 and became steeper after that, with significant differences in gender analysis.

Key Words: Mortality—stroke—life expectancy—age-standardized mortality rates

Introduction

Stroke is a major public health problem, being responsible for approximative 10% of all deaths worldwide.[1,2] It is estimated that 25% of people aged more than or equal to 25 years are affected by stroke during their lifetime.[3] Between 2007 and 2017, the stroke global age-standardized mortality rates (ASMR) decreased by 13.6%, which was paralleled by a 13.8% decrease in the rate of years of life lost due to stroke.[1] Similar results were found for ischemic stroke (ISCS) and hemorrhagic stroke (HEMS).[1] In Romania, between 1990 and 2016, stroke deaths decreased by 27% (95% confidence interval [CI] 19.6-33.8%).[2]

Data addressing stroke mortality at the national level in Romania are mainly registered as stroke, not specified as ischemic or hemorrhagic.[4] While ISCS is more closely related to the atherosclerotic disease, HEMS is to hypertension. Consequently, there is an intricate benefit resulting from the study of ISCS and HEMS mortality trends, as they might reflect different general changes in stroke risk factors. The stroke burden is different in men as compared

From the *"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; †"Elias" University Emergency Hospital, Bucharest, Romania; and ‡University Emergency Hospital, Bucharest, Romania.

Received May 14, 2019; revision received September 15, 2019; accepted September 20, 2019.

Grant support: None.

Address correspondence to Cristina Tiu, MD, PhD, University Hospital Bucharest, Splaiul Independentei 169, sector 6, Bucharest, Romania. E-mail: cristinatiu@yahoo.com.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104431

with women. A gender analysis of stroke mortality rates and trends might reveal important aspects, apprising the public health authorities.

The current study investigated the age and gender-related stroke mortality rates and trends in Romania between 1994 and 2017. The study covers the whole territory of Romania and includes all stroke deaths registered during the study period.

Materials and Methods

Study Population

All individual deaths registered in Romania between 1994 and 2017 were available for analysis using an anonymized database obtained from the National Institute of Statistics (Eurostat microdata). Death related data were collected retrospectively using the information available on the death certificate. Age and sex-specific general population data were available as mean estimates on July 1st, for each year covered by the study.

Outcomes and Confounders

For each deceased person, the following parameters were analyzed: gender, date of birth, year of death, cause and place of death (at home, in hospital, or elsewhere). Causes of death were encoded using a local code system directly derived from International Statistical Classification of Diseases and Related Health Problems (ICD) 9th revision during 1994-1999, and the ICD 10th revision during 2000-2017 (I60-I64). A sensitivity analysis was performed for HEMS (I60-I62) and ischemic stroke (I63). As the day and month of death were not available, we have registered July 1st as the day of death, for all the persons. This date was chosen for minimizing the error of calculation of age at death. Also, the corresponding living general population was measured on July 1st, for every year of the study.

Statistical Analysis

Stroke crude mortality rates (CMR) and ASMR were calculated using the European Standard Population.[5] Patients were distributed in 5-year age groups. The last group included all deaths registered for people aged more than or equal to 85 years. The last age band was chosen based on the availability of the corresponding data for the general population. Although the data were used in overall and age-adjusted mortality analysis, CMRs for age groups below 40 years were not reported in the tables showing detailed analysis due to the low number of encountered deaths. All CMRs are expressed per 100,000 persons per year. Poisson regression was used for the calculation of annual percentage change (APC) in mortality. To predict mortality up to 2030, trend analysis used the APC recurrently applied to the latest available ASMR (year 2017). Life table analysis for the year 2017 was used to calculate the gain in life expectancy at birth possibly obtained by the complete removal of stroke mortality. Statistical analysis was performed using Stata version 13 (www.stata.com).

The study was approved by the local ethics committee. Informed consent was not obtained because this is a retrospective, anonymized, database-driven study. Written consent for data usage was obtained from the Eurostat/National Institute of Statistics.

Results

Between 1994 and 2017, 6,281,873 persons died in Romania, stroke being the underlying cause of death in 959,319 cases (78.2% of all deaths due to cerebrovascular diseases), 520,463 (54.3%) women and 438,856 (45.7%) men. Occlusion and stenosis of precerebral or cerebral arteries, not resulting in cerebral infarction, and other cerebrovascular diseases (ie, aneurysms, hypertensive encephalopathy) were responsible for 11.8% of all cerebrovascular diseases. These stroke deaths were further divided into 165,294 cases of HEMS (17.2%), 55,525 cases of ISCS (5.8%), and 738,500 cases of stroke not specified as hemorrhage or infarction (77.0% of all stroke deaths). The matching alive general population showed a linear decrease from 22.7 million in 1994 to 19.6 million in 2017. The overall stroke CMR per 100,000 person-years was 188.2 (199.3 in women and 176.5 in men). The CMR for HEMS was 32.4 (32.7 in women and 32.2 in men), and for ISCS 10.9 (11.5 in women and 10.2 in men). Stroke overall CMR and age-adjusted mortality rates (ASMR) were summarized in Figure 1, and supplementary appendix Tables e1 and e2. They were further detailed for HEMS and ISCS in supplementary appendix Tables e3-e6. All CMRs increased with age and decreased with the calendar year, in both women (Table 1) and men (Table 2). Life table analysis for the year 2017 showed that complete removal of stroke mortality would result in 0.97 years gain in life expectancy at birth, with similar results in women and men.

There was a significant decrease in stroke ASMR per 100,000 person-years from 344.4 (95% CI 343.4-345.4) in 1994 to 192.1 (95% CI 191.5-192.7) in 2017, see Supplementary appendix Table e2. A similar decrease was found in both men and women, with higher mortality rates in men as compared with women for the entire time covered by the study (Supplementary appendix Table e2). There was a decline in stroke ASMR, with an APC of 2.53% per year (95% CI 2.50-2.55, $P < .001$), with gender analysis showing 2.59% per year (95%CI 2.56-2.63, $P < .001$) in women and 2.43% per year (95% CI 2.41-2.47, $P < .001$) in men.

Death by stroke occurred at home (n = 729,536; 76.0%), in hospital (n = 186,093; 19.4%), and elsewhere (n = 43,690; 4.6%). Deaths from other causes than stroke were less likely to happen at home (69.1%, $P < .001$), and more

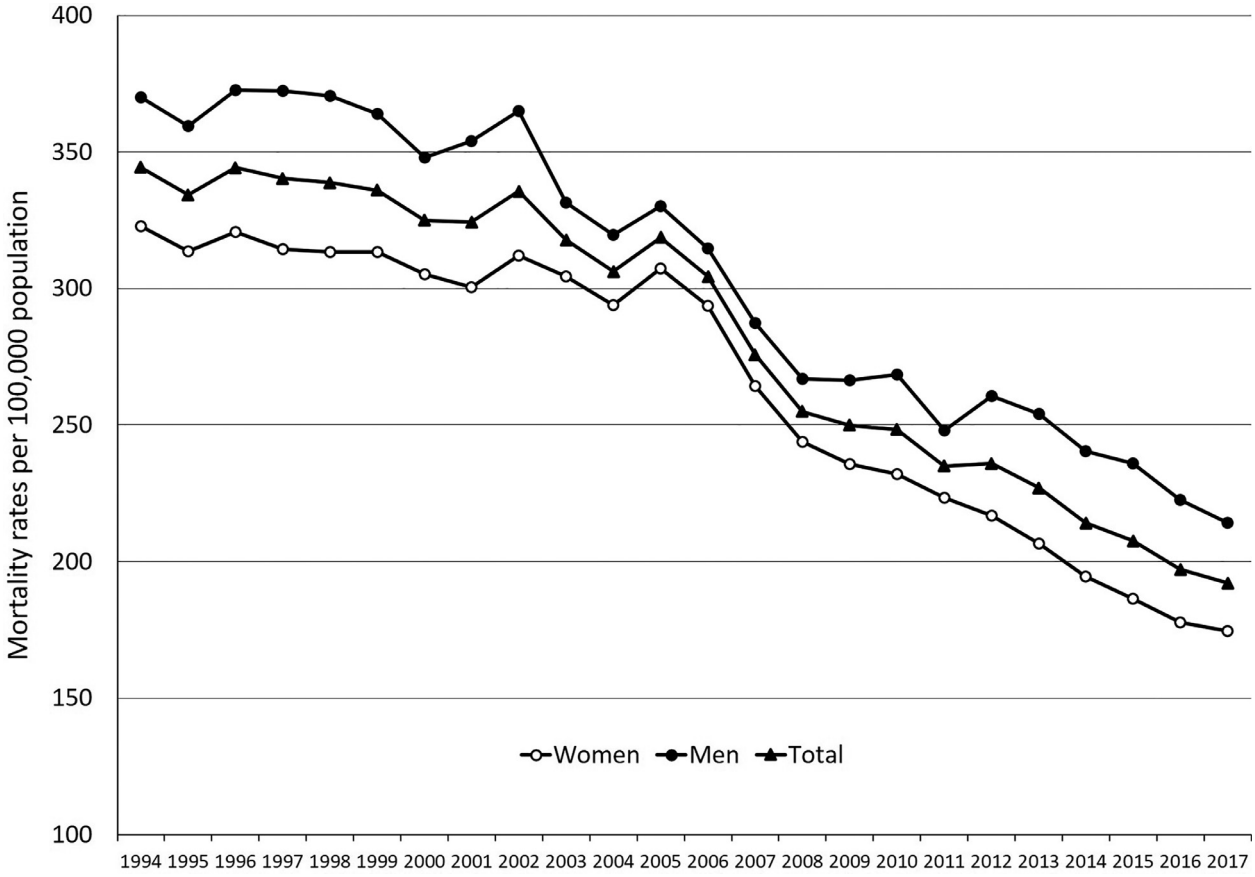

Figure 1. *Stroke age standardized mortality rates in Romania (1994-2017).*

likely in the hospital (22.7%, $P < .001$), and elsewhere (8.2%, $P < .001$). There was a significant increase in the proportion of stroke deaths registered in the hospital, from 15.0% (95% CI 14.6-15.3) in 1994 to 28.1% (95% CI 27.6-28.6, $P < .001$) in 2017, and elsewhere from 3.5% (95% CI 3.3-3.7) in 1994 to 6.7% (95% CI 6.5-7.0, $P < .001$) in 2017. This was accompanied by a corresponding significant decrease in deaths registered at home from 81.5% (95% CI 81.2-81.9) in 1994 to 65.2% in 2017 (95% CI 64.6-65.7, $P < .001$).

Among stroke deaths registered in the hospital, HEMS was registered in 32.8% (48.2% in 1994 versus 23.0% in 2017, $P < .001$) and ISCS in 15.4% (12.1% in 1994 versus 14.4% in 2017, $P < .001$). Among stroke deaths registered at home, HEMS was registered in 13.4% ($P < .001$ versus in hospital) and ISCS in 3.4% ($P < .001$ versus in hospital). HEMS represented 18.9% of all stroke deaths registered at home in 1994 and 7.8% in 2017 ($P < .001$), while ISCS 1.8% in 1994 and 5.2% in 2017 ($P < .001$).

The decline in HEMS ASMR had an APC of 4.65% per year (95% CI 4.59-4.70, $P < .001$), with gender analysis showing 4.86% per year (95% CI 4.77-4.94, $P < .001$) in women and 4.37% per year (95% CI 4.29-4.45, $P < .001$) in men. Stroke mortality rate for ischemic stroke showed an initial increase during 1994-2005, with an annual percentage change (APC) of 6.39% per year (95% CI 6.09-6.70, $P < .001$), women showing an APC of 6.46% per year (95% CI 6.02-6.90, $P < .001$), while men had an APC of 6.36% per year (95% CI 5.95-6.78, $P < .001$). After 2005, there was a significant decrease in ASMR until 2017, with an overall APC of 2.83% per year (95% CI 2.59-3.07, $P < .001$), 3.23% per year for women (95% CI 2.83-3.63, $P < .001$), and 2.0% per year (95% CI 1.62-2.38, $P < .001$) for men.

Based on the 1994-2017 dynamics, predictions for 2030 showed an overall stroke ASMR of 137.7 (95% CI 137.3-138.1), which was 124.1 (95% CI 123.5-124.6) in women and 155.4 (95% CI 154.7-156.1) in men. The HEMS ASMR in 2030 was predicted to be 12.1 (95% CI 12.0-12.2), gender analysis showing 10.0 (95% CI 9.9-10.1) in women and 14.8 (95% CI 14.6-15.0) in men. Overall ISCS ASMR was predicted to reach 10.4 (95% CI 10.1-10.7) by the year 2030, with 9.0 (95% CI 8.6-9.5) in women and 12.8 (95%CI 12.1-12.4) in men.

There was a significant increase of 6.5 years (95% CI 6.3-6.7) of the women's mean age at death by stroke from 74.8 $\pm$ 10.9 years in 1994 to 81.3 $\pm$ 9.4 years in 2017 ($P < .001$). Similarly, the mean age at death by stroke in men increased by 5.7 years (95% CI 5.4-5.9), from 70.6 $\pm$ 11.8 years in 1994 to 76.2 $\pm$ 11.5 years in 2017 ($P < .001$). This was paralleled by a significant increase in mean age at death from causes other than stroke in both women

Table 1. *Stroke crude mortality rates in Romanian women, by age and calendar year*

Women crude mortality rates per 100,000 person-years, by age group (years)										
Year	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	≥85
1994	20.9	44.9	84.8	141.8	247.4	476.1	897.6	1573.8	2386.6	3740.5
1995	21.0	38.3	85.2	139.9	255.3	470.8	870.9	1470.2	2370.7	3618.6
1996	21.0	43.2	86.4	141.0	253.1	447.9	865.5	1477.4	2525.8	3792.2
1997	19.7	43.3	79.6	135.8	249.7	458.1	868.7	1400.1	2451.7	3736.0
1998	19.4	40.9	81.4	135.7	248.8	435.0	821.3	1477.0	2461.9	3715.5
1999	21.6	38.0	75.6	128.0	223.8	436.0	817.6	1476.4	2365.4	3917.1
2000	19.2	37.6	65.3	125.7	212.2	416.5	785.9	1453.6	2349.2	3827.8
2001	18.2	38.2	72.1	121.4	222.9	406.7	793.2	1431.2	2151.3	3850.0
2002	15.2	36.1	72.1	121.2	220.1	424.2	791.3	1442.4	2398.2	4025.4
2003	16.3	33.1	65.8	119.8	202.2	404.3	768.5	1405.8	2350.4	4001.1
2004	13.5	33.7	60.4	105.1	195.4	369.3	707.9	1325.9	2261.2	4071.7
2005	12.9	35.6	60.3	97.4	175.1	366.2	735.6	1346.3	2372.6	4478.8
2006	12.6	24.4	50.0	94.8	167.9	335.2	689.7	1309.4	2321.4	4293.5
2007	11.2	21.0	43.0	76.1	151.0	307.9	605.8	1175.8	2119.6	3893.4
2008	8.4	20.7	38.3	69.1	140.8	270.0	554.3	1089.6	1947.9	3620.4
2009	8.2	21.9	35.6	68.3	128.7	250.0	517.7	1040.4	1965.3	3512.5
2010	8.8	17.8	29.7	52.7	126.2	247.9	507.6	1044.4	1924.3	3500.9
2011	6.4	14.5	30.8	53.1	108.0	211.3	472.8	940.2	1814.6	3636.3
2012	8.0	20.7	32.4	53.5	104.0	199.3	429.5	937.6	1787.9	3499.9
2013	9.6	14.4	27.3	48.8	97.1	203.6	426.8	872.1	1722.6	3313.2
2014	5.2	14.9	26.3	48.4	84.5	178.0	391.0	842.7	1640.2	3130.0
2015	6.9	14.1	26.2	41.1	82.5	165.6	351.3	784.5	1610.6	3066.6
2016	7.4	12.0	22.8	42.2	77.9	154.8	351.6	737.9	1518.8	2929.2
2017	6.5	12.2	20.1	40.6	75.6	146.7	336.5	711.8	1468.1	2970.1

(70.0 ± 19.8 years in 1994, and 77.1 ± 14.3 years in 2017, $P < .001$), and men (62.7 ± 20.2 years in 1994, and 69.9 ± 15.7 years in 2017, $P < .001$). The mean age at death from stroke was significantly higher than the mean age at death from causes other than stroke.

Discussions

There was a significant reduction in age-standardized stroke mortality rates from 1994 to 2017, in both genders. The decline was slow until 2002 and became steeper after that. Although women had higher CMRs as compared with men, when those rates were age-standardized, men had higher ASMR as compared with women. This phenomenon might be explained by the fact that women live longer than men, contributing a higher absolute number of events with increasing age. Stroke has a higher impact on men as compared with women also because it was shown to have higher age-specific mortality rates in men for most of the age groups (except for ≥85 years old).

ISCS and HEMS had a discordant trend until 2005, with HEMS declining, but ISCS rising during 1994-2005. Starting with 2006, both HEMS and ISCS registered a steady decline, which is expected to continue in the next years (as for total stroke).

According to the WHO mortality database, cerebrovascular diseases deaths registered in Romania ranged from 53,480 cases in 1994 (24,881 men and 28,599 women) to 42,875 cases (19,073 men and 23,802 women) in 2016 (last available data).[6] The total population of Romania was 22.7 million in 1994 and 19.7 million in 2016.[5] Consequently, the cerebrovascular CMR per 100,000 was 235 in 1994 (223 in men and 247 in women) and 218 in 2016 (198 in men and 236 in women). All "corresponding" deaths and CMR numbers from the current study are 20%-25% less than those reported by the WHO mortality database. The reason for this apparent discrepancy resides in the strict focus on stroke mortality in the current study (ie, I60-I64 codes) as opposed to the broader category of cerebrovascular diseases (ie, I60-I69) in the WHO mortality database. Indeed, the current study found a stroke prevalence of 75%-80% of cerebrovascular diseases deaths. The Global Burden of Disease Study 2017 uses various data sources, including local registry data, aiming to provide more robust statistical estimates.[1] In the Global Burden of Disease Study 2017, stroke was reported to be responsible for 52,418 deaths in Romania in 1994 (CI 95% 53,532-51,248) and 49,221 deaths in 2016 (CI 95% 51,502-47,746).[7] Again, there the estimated figures were 20%-25% higher as compared with those found in the current study. The same explanation can be easily inferred here, *stroke* being found responsible for all the death due to cerebrovascular diseases. As many other studies which rely on data available on public repositories (ie, WHO mortality database or

Table 2. *Stroke crude mortality rates in Romanian men, by age and calendar year*

Men crude mortality rates per 100,000 person-years, by age group (years)										
Year	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	≥85
1994	37.4	73.4	139.4	253.7	420.3	693.3	1082.6	1719.8	2419.6	3485.4
1995	38.7	79.7	133.5	239.8	392.3	664.9	1069.8	1613.3	2416.4	3431.7
1996	46.2	73.0	144.9	259.4	403.9	658.6	1081.9	1662.5	2559.0	3606.4
1997	39.4	81.6	141.9	255.4	420.7	665.7	1098.4	1648.2	2536.6	3565.8
1998	36.0	70.9	132.0	247.3	416.9	644.5	1073.4	1681.9	2549.6	3627.0
1999	33.6	66.2	122.4	222.5	376.4	642.1	1065.3	1661.3	2507.5	3684.8
2000	29.8	59.1	116.4	212.7	379.7	609.8	1010.8	1638.5	2375.4	3461.7
2001	30.6	64.8	129.5	222.6	381.0	614.2	998.2	1683.7	2281.8	3640.5
2002	31.4	66.4	123.1	219.7	379.1	604.2	1,023.3	1667.9	2499.1	3887.3
2003	28.6	62.0	111.4	205.6	348.3	601.7	992.6	1633.2	2422.7	2910.5
2004	25.4	54.1	106.3	185.0	320.8	570.3	912.3	1527.6	2395.5	3042.2
2005	23.6	55.7	93.1	179.5	321.0	565.0	968.6	1594.2	2396.0	3307.6
2006	23.0	48.6	90.5	175.0	301.6	535.0	884.2	1556.3	2378.1	3084.5
2007	23.2	48.6	86.1	151.8	282.6	499.4	834.2	1344.6	2213.1	2798.4
2008	20.0	40.2	86.5	143.0	253.0	441.5	765.9	1253.4	2107.4	2618.0
2009	17.5	40.7	82.2	139.3	261.4	427.0	751.9	1259.0	2086.1	2693.8
2010	16.4	40.4	73.4	136.1	239.5	433.5	764.3	1306.7	2115.4	2715.4
2011	15.2	39.3	65.8	112.8	211.4	370.7	686.9	1191.7	1971.0	2684.3
2012	12.9	30.2	61.0	112.5	198.3	375.8	621.7	1173.4	1961.1	3415.6
2013	15.7	31.1	63.9	104.5	209.2	359.7	625.8	1162.2	1827.9	3307.6
2014	16.0	33.4	48.6	108.3	188.9	318.4	595.7	1102.8	1832.6	3079.5
2015	14.7	28.0	56.8	101.2	169.2	320.3	566.7	1070.8	1857.0	3043.3
2016	12.7	26.6	51.4	100.0	175.4	299.5	555.9	995.6	1717.6	2854.6
2017	13.9	27.8	49.1	93.5	167.1	294.3	532.1	957.4	1664.8	2723.0

Global Burden of Disease Study), the Stroke Alliance For Europe published valuable stroke mortality data for Romania, but again, stroke was the generic term used for all the deaths due to cerebrovascular diseases (ie, 54,272 deaths due to stroke per year reported for 2015). The only reliable stroke mortality data published so far comes from a local registry expressing a single-center practice.[8] As this is a hospital-based experience, its relevance for the broader outpatient and national stroke population is not straightforward. A recent effort has been done to combine data from some neurological excellence centers, but this also provides data on a short term, in-hospital mortality. According to our best knowledge, the current study is the first to provide national level, granular data on real stroke mortality, further differentiated into ISCS and HEMS, as coded in the death certificates.

The main risk factors for stroke incidence and mortality are age, hypertension, dyslipidemia, diabetes, obesity, smoking, stroke size, acute complications, and other comorbid conditions. A recent cross-sectional study in a national representative sample of Romanian adult population showed a high prevalence of obesity (31.9%), waist circumference (73.9%), metabolic syndrome (38.5%), and diabetes (11.6%).[9,10] SEPHAR III report revealed, on one hand, a mild increase in the prevalence of hypertension (compared with SEPHAR I and II), and on the other hand a significant increase in people's awareness regarding the diagnosis (80.9% versus 69.6%) and treatment of arterial hypertension (72.2% versus 59.2%), with one third of them attaining the blood pressure target (30.8% versus 25%).[11,12] The life expectancy of Romanian diabetes patients increased significantly during the last decade, posing a high public health burden associated with stroke and cardiovascular diseases in general.[13-15]

Smoking prevalence in the general Romanian population aged more than or equal to 15 years was 26.1% (37.4% in men and 16.7% in women), the vast majority being cigarettes daily smokers.[16] More than two thirds of them reported smoking their first cigarette within 30 minutes after getting out of bed in the morning.[16] Starting with 2016, smoking was forbidden in all enclosed public spaces, including restaurants, bars, public transportation, universities or government institutions.

Major healthcare reforms were implemented after the country's admission into the European Union in 2007, improving access to outpatient health care. Consequently, hospitals were able to admit more complex cases, which might explain a nearly doubling in the proportion of stroke deaths registered in the hospital in 2017 as compared with 1994. Despite all efforts, only 1% of strokes were admitted in dedicated stroke units.[17]

Minor differences between the ASMRs reported by this study and some officially reported data might be explained by the overall adjustment for all deaths occurring after the age of 85 years in this study (last age group in the official data was ≥95 years). Another possible explanation could

reside in the measurement error in age at death (see Methods), with a consequent misclassification of the age band for some deaths. However, due to the relatively large number of deaths available for analysis, the positive and negative misclassified cases should efficiently cancel each other.

The generalizability of findings from the current study can be broadly divided into 2 aspects. First, regarding the extrapolation to the whole Romanian population, the current study offers the best possible solution by studying all the deaths caused by stroke in the Romanian population. However, the majority (77%) of stroke cases were not designated as ischemic or hemorrhagic. Given this, the analysis of data related to stroke subtype is likely not generalizable to the population as a whole. Second, extrapolating the results to the Balkan region is not a straightforward process as important differences exist between the cultural background and the healthcare systems in the region.

As a strength, the current study included all deaths due to stroke registered at the national level. The study data were able to discern them from the larger group of cerebrovascular diseases. The deaths due to stroke were further differentiated as ISCS and HEMS. The time covered is more than 2 decades, with an estimated 100% rate of death capture, leading to a very robust trend analysis. Only stroke deaths were analyzed, and this differentiates our study from most previously published data. Having access to case by case analysis allowed very precise measurements of age and gender stroke mortality rates and trends. There are some weaknesses too, starting with the inherent coding errors on the death certificates, in the context of a very low rate of autopsies. Most of the time these errors are systematic, meaning they have little influence on trend analysis. There is no validation study of death certificate data for Romania. Coding outside hospitals resides heavily on general practitioners. They tend to ascribe codes based on known comorbidities, ie HEMS when such an event was recorded in patient's (recent) history. The healthcare information presented in this study is strictly informative, as there is no data to support any causality.

In conclusion, age-standardized stroke mortality in Romania decreased from 1994 to 2017. Age-standardized stroke mortality rates were higher in men compared with women and increased with age in both genders. Predictions for 2030 showed a continued decline in stroke mortality rates.

Conflict of Interest

The authors have no conflict of interest to declare in regard to the current study.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2019.104431.

References

1. Roth GA, Abate D, Abate KH, et al. Causes of death collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980−2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392:1736-1788.
2. Johnson CO, Nguyen M, Roth GA, et al. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18:439-458.
3. Feigin VL, Nguyen G, Cercy K, et al. Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. N Engl J Med 2018;379:2429-2437.
4. Stroke Alliance For Europe (SAFE). The burden of stroke in Europe. Accessed online at: http://strokeeurope.eu/, on March 29th, 2019.
5. United Nations Statistics Division population database (updated on December 31st, 2018), accessed online at: http://data.un.org/Data.aspx?d=POP&f=tableCode%3A22, on January 7th, 2019.
6. WHO mortality database. Accessed online at: http://apps.who.int/healthinfo/statistics/mortality/whodpms/, on April 5th, 2019.
7. Global Burden of Disease Study 2017 (GBD 2017) Data Resources. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2018. Accessed online at: http://ghdx.healthdata.org/gbd-2017, on April 5th, 2019.
8. Szatmári S, Pascu I, Mihálka L, et al. The Mures-Uzhgorod-Debrecen study: a comparison of hospital stroke services in Central-Eastern Europe. Eur J Neurol 2002;9:293-296.
9. Popa S, Moţa M, Popa A, et al. Prevalence of overweight/obesity, abdominal obesity and metabolic syndrome and atypical cardiometabolic phenotypes in the adult Romanian population: PREDATORR study. J Endocrinol Invest 2016;39:1045-1053.
10. Mota M, Popa SG, Mota E, et al. Prevalence of diabetes mellitus and prediabetes in the adult Romanian population: PREDATORR study. J Diabetes 2016;8:336-344.
11. Dorobanţu M, Darabont R, Ghiorghe S, et al. Hypertension prevalence and control in Romania at a seven-year interval. Comparison of SEPHAR I and II surveys. J Hypertens 2014;32:39-47.
12. Dorobantu M, Tautu OF, Dimulescu D, et al. Perspectives on hypertension's prevalence, treatment and control in a high cardiovascular risk East European country: data from the SEPHAR III survey. J Hypertens 2018;36:690-700.
13. Ioacara S, Guja C, Fica S. The dynamics of life expectancy in the last six decades in elder diabetes patients. Diab Res Clin Pract 2013;99:217-222.
14. Ioacara S, Guja C, Ionescu-Tirgoviste C, et al. Rates and causes of death among adult diabetes patients in Romania. Endocr Res 2018:1-6. https://doi.org/10.1080/07435800.2018.1546734.
15. Ioacara S, Sava E, Georgescu O, et al. Recent diabetes-related mortality trends in Romania. Acta Diabetol 2018;55:821-826.
16. Irimie S. Romania 2011 global adult tobacco survey. Bucharest: Ministry of Health; 2012. Accessed online at https://www.who.int/tobacco/surveillance/survey/gats/gats_romania_report_2011.pdf, on April 10th, 2019.
17. Budincevic H, Tiu C, Bereczki D, et al. Management of ischemic stroke in Central and Eastern Europe. Int J Stroke 2015;10:125-127.