ANNUAL AND SEASONAL TRENDS IN MORTALITY RATES FROM CARDIOVASCULAR DISEASES IN HUNGARY BETWEEN 1984 AND 2013

Katalin Virág[1], Tibor András Nyári[2]
[1]Bolyai Institute, University of Szeged, Szeged, Hungary
[2]Department of Medical Physics and Informatics, University of Szeged, Szeged, Hungary

SUMMARY

Objectives: The aim of this study was to investigate annual and seasonal trends in mortality rates from cardiovascular diseases in Hungary between 1984 and 2013.

Methods: Annual and monthly mortality and population data were obtained from the Hungarian Central Statistical Office. The annual mortality data by gender and age were available for the following disease classifications of the circulatory system: all cardiovascular diseases, all diseases of the heart, hypertension, coronary heart disease, and cerebrovascular diseases. Six age groups were defined for both sexes. Negative binomial regression was carried out to analyse annual trends in age-standardized mortality rates. The Walter-Elwood method was used to identify seasonal variation using monthly numbers of deaths.

Results: Significant decreases in annual mortality rates for all cardiovascular diseases were found, but not for hypertension. Age-standardized death rates were higher for men for all causes, except for hypertension. The greatest sex difference in the average risk of death was observed in the middle-aged groups. The greatest percentage decrease in death rates during the study period was seen for both sexes in the under 35 age group. The lowest percentage change was observed among people aged over 75. Significant seasonality was found in monthly death rates from all causes, with a peak in February.

Conclusions: In spite of a decreasing trend in the annual mortality rates for cardiovascular diseases, the Hungarian mortality rate is still high. Moreover, this study demonstrated a significant winter peak in mortality from cardiovascular diseases over a thirty-year period.

Key words: cardiovascular mortality, annual trend, seasonal trend, epidemiology, Hungary

Address for correspondence: T. A. Nyári, Department of Medical Physics and Informatics, University of Szeged, Korányi fasor 9, H-6720 Szeged, Hungary. E-mail: nyari.tibor@med.u-szeged.hu

https://doi.org/10.21101/cejph.a4928

INTRODUCTION

Despite declines in mortality rates in most European countries, cardiovascular diseases are still the most common causes of death in Europe and are responsible for 45% of all deaths (1). Similarly, cardiovascular diseases are the leading causes of death in Hungary in spite of the fact that decreasing death rates have been seen for the last three decades. Hungarian cardiovascular mortality rates are ranked high among countries in the European Union (1). In 2013, 49.7% of deaths were caused by cardiovascular diseases (2). Of the total number of 62,979 deaths from all cardiovascular diseases, 73.7% were caused by heart disease and 20.4% by cerebrovascular disease. The most common types of heart disease are ischaemic heart disease and hypertension (69.1% and 16.4% of all diseases of the heart, respectively). The aim of this study was to describe the seasonal and annual trends in age-standardized death rates from cardiovascular diseases over the last thirty years in Hungary.

MATERIALS AND METHODS

The Hungarian monthly and annual mortality data for cardiovascular diseases and the annual mid-year population estimates for the 1984–2013 period were provided by the Hungarian Central Statistical Office (2). The underlying causes of death were classified according to the International Classification of Diseases, Ninth and Tenth Revisions. The ICD-10 codes used were I00-I99 for all diseases of the circulatory system, I00-I51 for all diseases of the heart, I10-I15 for hypertension, I20-I25 for coronary heart disease, and I60-I69 for cerebrovascular diseases.

Annual Trends

Death rates are expressed per 100,000 population using the annual mid-year population estimates for the relevant year. Age-standardized death rates were calculated for all causes by direct standardization to the European standard population

(3). Time trends in annual age-standardized death rates from 1984 to 2013 were assessed by negative binomial regression analysis. Twelve age- and sex-specific groups were defined: ages under 35, 35–44, 45–54, 55–64, 65–74, and over 75. Annual percentage changes (APC), standardized rate ratios and 95% confidence intervals (CI) associated with gender and age were estimated (4, 5). Interaction terms were included in the negative binomial regression models to obtain age- and sex-specific mortality estimates.

Seasonal Trends

Cyclic trends in aggregated monthly data on deaths from cardiovascular diseases were investigated with the Walter-Elwood method, which takes into account the underlying population at risk (6, 7). Monthly deaths were adjusted for month length. Monthly population estimates were calculated based on the monthly number of births and deaths provided by the Hungarian Central Statistical Office. Winter-to-summer ratios for all causes of death were calculated as the total deaths in January, February

Table 1. *Age-standardized mortality rates (per 100,000 population) for cardiovascular diseases by gender in Hungary between 1984 and 2013*

	Men (95% CI)	Women (95% CI)	Men to women standardized rate ratio (95% CI)
All cardiovascular diseases [a]			
1984–1988	775.97 (772.45–779.51)	514.52 (512.23–516.82)	1.51 (1.50–1.52)
1989–1993	764.84 (761.33–768.35)	496.83 (494.60–499.06)	1.54 (1.53–1.55)
1994–1998	721.65 (718.23–725.08)	472.85 (470.71–474.99)	1.53 (1.52–1.54)
1999–2003	629.38 (626.29–632.48)	407.86 (405.96–409.77)	1.54 (1.53–1.55)
2004–2008	576.17 (573.29–579.06)	362.10 (360.38–363.84)	1.59 (1.58–1.60)
2009–2013	506.80 (504.17–509.44)	331.20 (329.60–332.80)	1.53 (1.52–1.54)
All diseases of the heart [b]			
1984–1988	429.98 (427.36–432.61)	253.80 (252.17–255.43)	1.69 (1.68–1.71)
1989–1993	441.66 (439.00–444.33)	258.86 (257.24–260.49)	1.71 (1.69–1.72)
1994–1998	435.05 (432.40–437.71)	262.50 (260.90–264.11)	1.66 (1.64–1.67)
1999–2003	388.21 (385.79–390.65)	235.28 (233.83–236.73)	1.65 (1.64–1.66)
2004–2008	408.14 (405.72–410.58)	248.45 (247.02–249.88)	1.64 (1.63–1.66)
2009–2013	374.36 (372.10–376.63)	240.45 (239.09–241.81)	1.56 (1.54–1.57)
Coronary heart disease [c]			
1984–1988	321.78 (319.51–324.06)	160.90 (159.61–162.21)	2.00 (1.98–2.02)
1989–1993	330.13 (327.83–332.44)	169.52 (168.21–170.84)	1.95 (1.93–1.97)
1994–1998	331.60 (329.28–333.92)	184.13 (182.79–185.47)	1.80 (1.78–1.82)
1999–2003	294.00 (291.89–296.12)	170.44 (169.21–171.67)	1.72 (1.71–1.74)
2004–2008	301.45 (299.37–303.54)	176.74 (175.54–177.94)	1.71 (1.69–1.72)
2009–2013	268.44 (266.52–270.36)	164.16 (163.05–165.28)	1.64 (1.62–1.65)
Hypertension [d]			
1984–1988	39.16 (38.37–39.95)	44.36 (43.70–45.03)	0.88 (0.86–0.91)
1989–1993	41.50 (40.69–42.33)	43.41 (42.76–44.07)	0.96 (0.93–0.98)
1994–1998	33.96 (33.22–34.71)	35.58 (35.00–36.17)	0.95 (0.93–0.98)
1999–2003	32.71 (32.01–33.42)	30.39 (29.88–30.91)	1.08 (1.05–1.11)
2004–2008	41.49 (40.72–42.27)	35.85 (35.31–36.39)	1.16 (1.13–1.19)
2009–2013	44.50 (43.72–45.28)	40.12 (39.57–40.67)	1.11 (1.08–1.13)
Cerebrovascular diseases [e]			
1984–1988	211.59 (209.76–213.44)	159.97 (158.69–161.26)	1.32 (1.31–1.34)
1989–1993	198.55 (196.77–200.35)	144.39 (143.19–145.60)	1.38 (1.36–1.39)
1994–1998	184.49 (182.76–186.22)	132.39 (131.25–133.53)	1.39 (1.38–1.41)
1999–2003	165.72 (164.14–167.31)	114.59 (113.58–115.60)	1.45 (1.43–1.47)
2004–2008	125.61 (124.27–126.96)	85.03 (84.19–85.88)	1.48 (1.46–1.50)
2009–2013	102.86 (101.68–104.05)	71.45 (70.70–72.20)	1.44 (1.42–1.46)

[a] ICD-10 codes I00-I99, [b] ICD-10 codes I00-I51, [c] ICD-10 codes I20-I25, [d] ICD-10 codes I10-I13, [e] ICD-10 codes I60-I69

and March divided by the total number of deaths in July, August and September.

Values of p less than 0.05 were considered statistically significant. All analyses were performed with the Stata 13 software (8).

RESULTS

Overall Annual Trends

Between 1984 and 2013, the age-standardized death rate (per 100,000 population) from all cardiovascular diseases in Hungary decreased by 40.6% from 675 to 401 based on the European standard population. The greatest percentage decreases during this interval were in death rates from cerebrovascular disease (59.3% from 199 to 81). Death rates decreased by 16.1% from 353 to 296 for heart diseases, dropped by 15.6% from 244 to 206 for ischaemic heart disease, and increased by 11.1% from 41 to 45 for hypertension.

The age-standardized death rates from all causes were higher for men from 1984 to 1998 except for hypertension (Table 1).

When age-standardized annual mortality rates were examined using negative binomial regression analyses, significantly decreasing trends were observed for all causes but hypertension.

Annual Trends by Gender

When death rates were examined by gender, negative binomial regression analyses showed significantly decreasing trends for both males and females for all cardiovascular diseases (Table 2). Similarly, significantly declining trends were observed for all heart diseases and for cerebrovascular diseases. For coronary heart disease, annual mortality rates decreased significantly for men and increased non-significantly for women. Mortality rates from hypertension increased non-significantly for males and decreased significantly for females.

The average risk of death for males was 1.54 times higher (95% CI = 1.534–1.545) than for females for cardiovascular diseases, 1.65 times higher (95% CI = 1.636–1.668) for heart diseases, 1.80 times higher (95% CI = 1.755–1.849) for coronary heart disease, 1.02 times higher (95% CI = 0.983–1.058) for hypertension, and 1.41 times higher (95% CI = 1.391–1.429) for cerebrovascular diseases.

Annual Trends by Gender and Age

Age-standardized death rates increased with age among both men and women for all cardiovascular diseases under examination. For all causes other than hypertension, significantly decreasing trends were observed in annual mortality rates for both sexes and for most age groups (Fig. 1). The greatest percentage decrease

Table 2. *Annual trends for all cardiovascular diseases, all heart diseases, coronary heart disease, hypertension, and cerebrovascular diseases by gender in Hungary between 1984 and 2013*

	Men			Women		
	APC	95% CI	p-value	APC (%)	95% CI	p-value
All cardiovascular diseases	−1.73%	−1.91, −1.55	< 0.001	−1.84	−2.05–1.63	< 0.001
All heart diseases	−0.59%	−0.79, −0.39	< 0.001	−0.29	−0.55–0.03	0.029
Cerebrovascular diseases	−2.70%	−3.01, −2.38	< 0.001	−3.09	−3.47,−2.71	0.001
Coronary heart disease	−0.73%	−0.96, −0.49	< 0.001	0.07	−0.25–0.38	0.679
Hypertension	0.38%	−0.28, −1.05	0.261	−0.74	−1.40–0.07	0.029

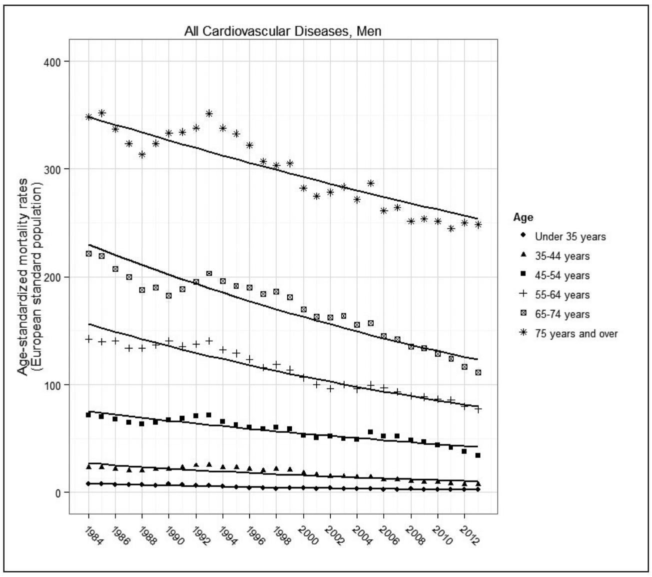

Fig. 1a *All cardiovascular diseases, men.*

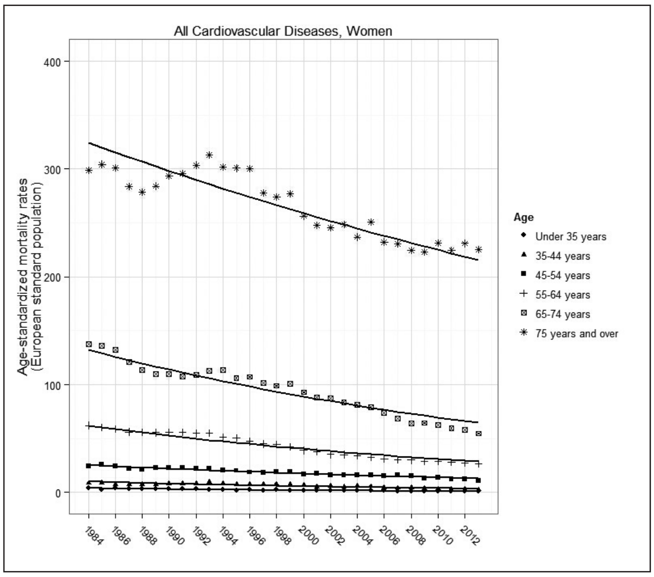

Fig. 1b *All cardiovascular diseases, women.*

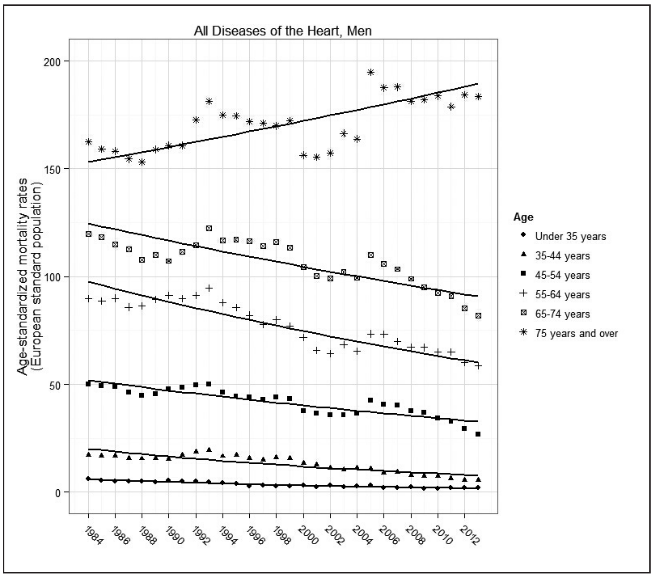

Fig. 1c *All diseases of the heart, men.*

Fig. 1d *All diseases of the heart, women.*

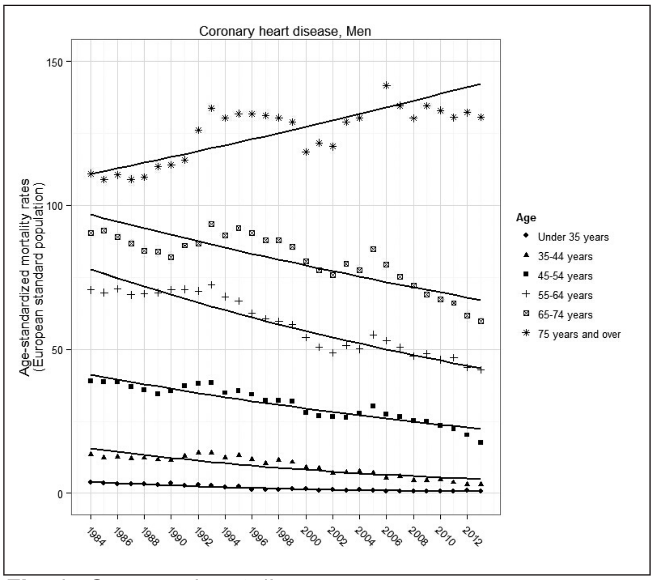

Fig. 1e *Coronary heart disease, men.*

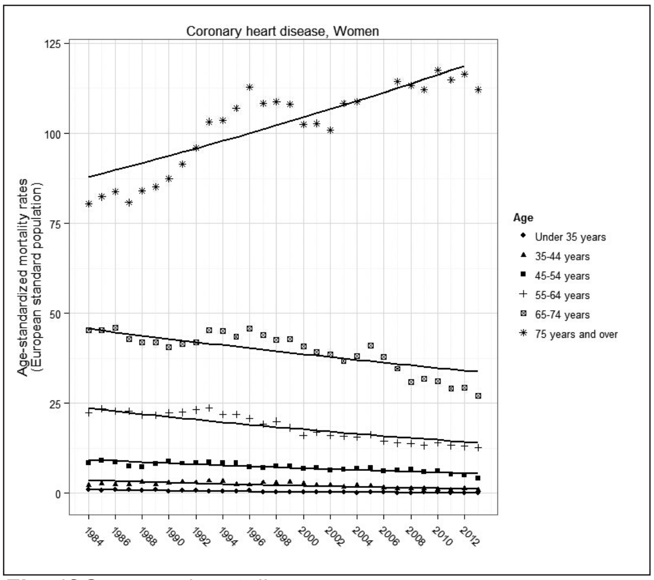

Fig. 1f *Coronary heart disease, women.*

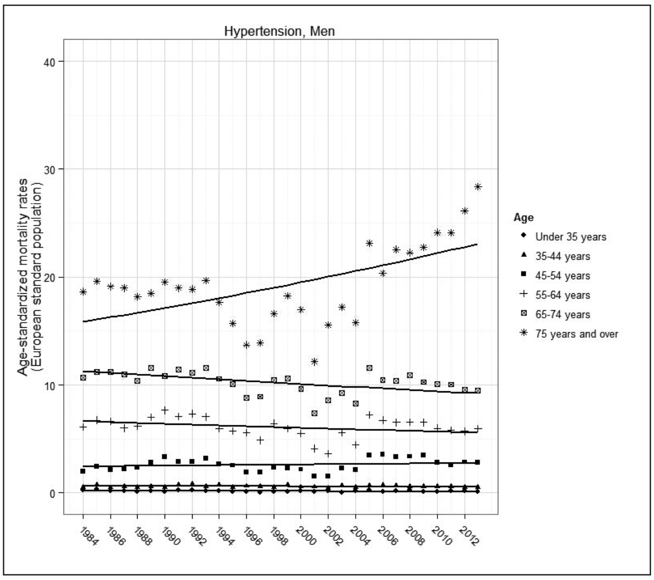

Fig. 1g *Hypertension, men.*

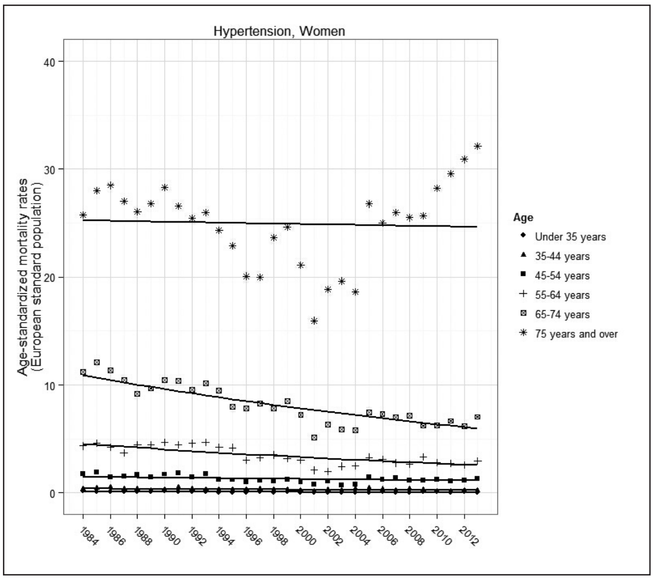

Fig. 1h *Hypertension, women.*

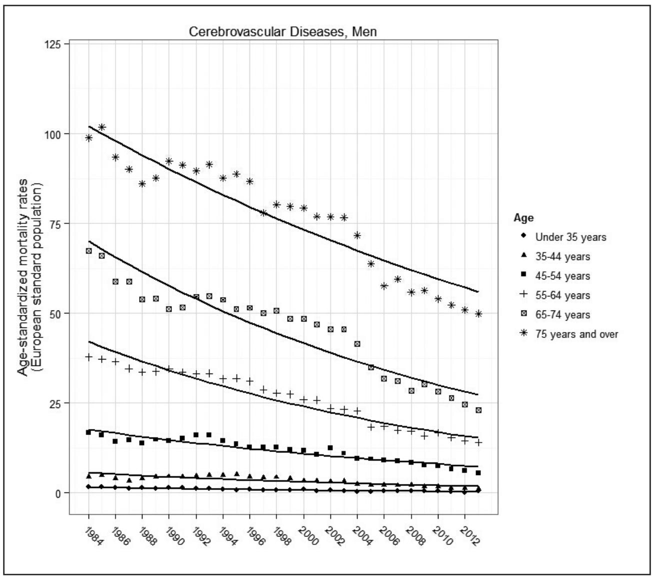

Fig. 1i Cerebrovascular diseases, men.

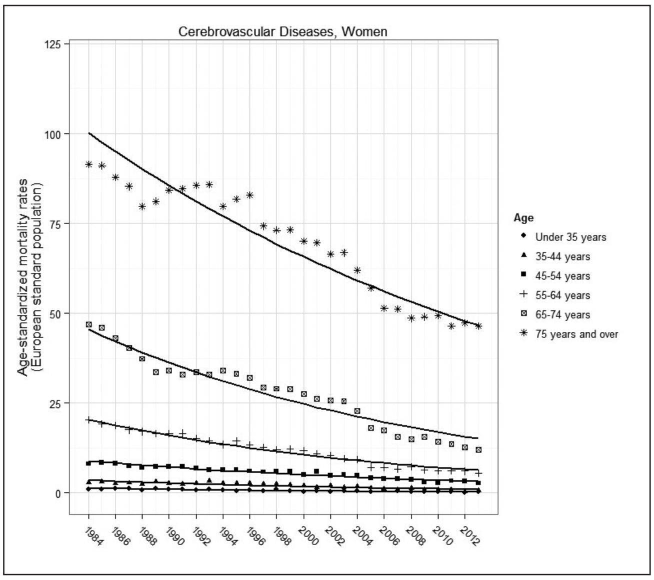

Fig. 1j Cerebrovascular diseases, women.

Fig. 1. *Annual trends in standardized mortality rates for all cardiovascular diseases, all heart diseases, coronary heart disease, hypertension and cerebrovascular diseases in Hungary between 1984 and 2013.*

during the study period was seen in the under 35 age group for both men and women, with a percentage decrease of 4.30% (95% CI = −5.88, −2.70; p < 0.001) and 4.60% (95% CI = −6.18, −3.00; p < 0.001) for cardiovascular diseases; 4.20% (95% CI = −6.06, −2.29; p < 0.001) and 4.35% (95% CI = −6.23, −2.44; p < 0.001) for heart diseases; 6.66% (95% CI = −9.47, −3.77; p < 0.001) and 6.46% (95% CI = −9.29, −3.54; p < 0.001) for coronary heart disease; and 5.00% (95% CI = −8.35, −1.54; p = 0.005) and 5.54% (95% CI = −8.86, −2.09; p = 0.002) for cerebrovascular diseases. The lowest percentage change was observed for both men and women in the over 75 age group, with a percentage decrease of 1.09% (95% CI = −1.30, −0.88; p < 0.001) and 1.40% (95% CI = −1.62, −1.18; p < 0.001) for cardiovascular diseases; and 2.05% (95% CI = −2.46, −1.64; p < 0.001) and 2.60% (95% CI = −3.02, −2.17; p < 0.001) for cerebrovascular diseases; as well as percentage increase of 0.73% (95% CI = 0.45–1.02; p < 0.001) and 0.57% (95% CI = 0.27–0.86; p < 0.001) for heart diseases; and 0.86% (95% CI = 0.53–1.20; p < 0.001) and 1.08% (95% CI = 0.73–1.44; p < 0.001) for coronary heart disease. Trends in hypertension mortality data were not significant except for men over 75 (APC = 1.30%, 95% CI = 0.47–2.14, p = 0.002) and women aged 55–64 (APC = −1.97%, 95% CI = −3.41, −0.51, p = 0.008) and 65–74 (APC = −2.05%, 95% CI = −3.12, −0.96; p < 0.001).

On average, the risk of death from hypertension for males was higher than that for females in all age categories, except for the oldest group. For cardiovascular diseases, heart diseases and coronary heart diseases, the lowest rate was seen among people aged over 75 years, and the highest was observed in the 45–54 age group. The average ratio of men to women varied from 1.13 (95% CI = 1.113–1.137) to 3.11 (95% CI = 3.078– 3.143) for cardiovascular diseases; from 1.14 (95% CI = 1.130–1.143) to 3.65 (95% CI = 3.625–3.665) for heart disease; and from 1.22 (95% CI = 1.214–1.232) to 4.27 (95% CI = 4.242–4.303) for coronary heart disease. For hypertension, the ratio of men to women ranged from 0.77 (95% CI = 0.738–0.808, aged over 75 years) to 2.14 (95% CI = 2.042–2.236, aged under 35 years). The average men-to-women risk ratio for cerebrovascular death is the largest for those aged 55–64 (2.24, 95% CI = 2.203–2.286) and the lowest in the oldest age group with a value of 1.11 (95% CI = 1.087–1.128).

Seasonal Trends

The Walter-Elwood tests on aggregated monthly mortality data indicate significant evidence of seasonality for all cardiovascular diseases under examination (p < 0.001). Mortality rates are highest during winter (in January and February) and lowest during late summer (in August and September). The winter-to-summer ratio varied from 1.24 (cerebrovascular diseases) to 1.28 (hypertension). The Walter-Elwood tests showed a maximum estimated mortality rate in February for all diseases (Fig. 2).

DISCUSSION

Main Findings

Significant decreases in annual mortality rates for all cardiovascular, heart and cerebrovascular diseases were found in Hungary between 1984 and 2013. However, age-standardized death rates for hypertension did not show a clear trend during this period. Similar trends were observed among male and female annual mortality rates for all cardiovascular and cerebrovascular diseases, but not for all heart diseases, ischaemic heart disease and hypertension. Annual mortality rates did not change significantly for ischaemic heart disease among women and for hypertension among men. The greatest percentage decrease in death rates during the study period was seen for both sexes in the under 35 age group. The lowest percentage change was observed among those aged over 75. The greatest sex difference in the average risk of death was detected in the middle-aged groups. Significant seasonality was found in monthly death rates from all causes, with a peak in February.

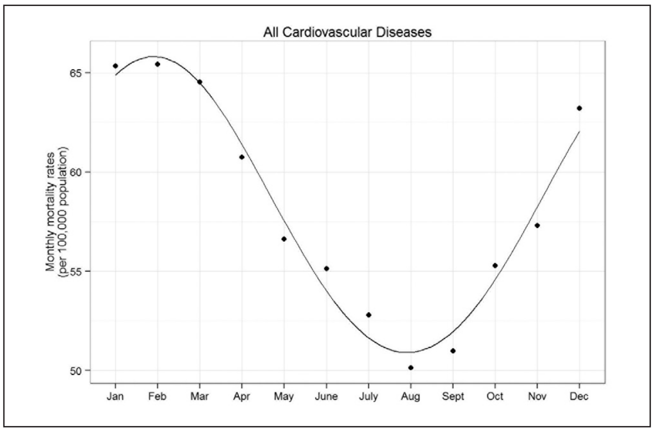

Fig. 2a *All cardiovascular diseases.*

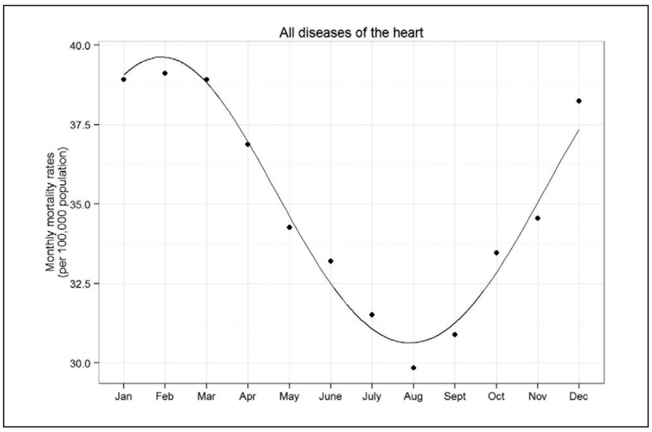

Fig. 2b *All diseases of the heart.*

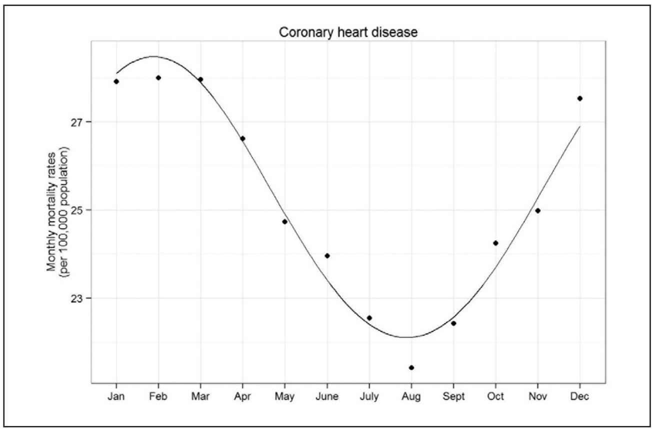

Fig. 2c *Coronary heart disease.*

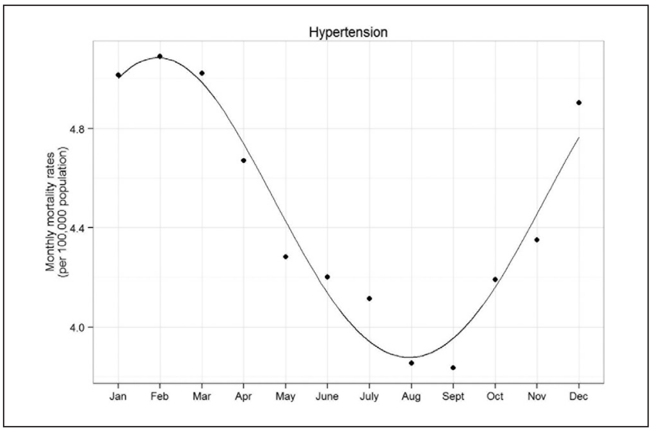

Fig. 2d *Hypertension.*

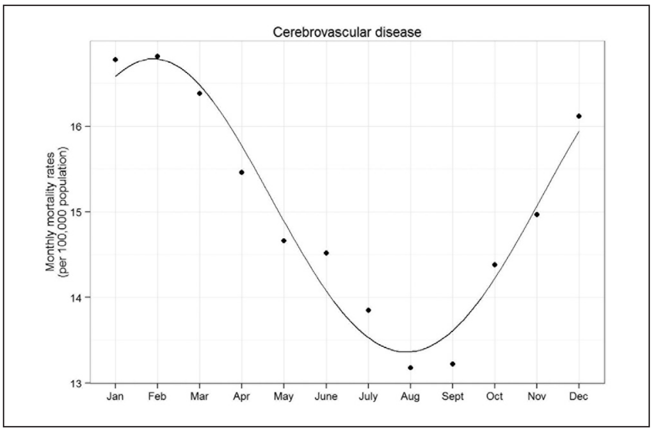

Fig. 2e *Cerebrovascular diseases.*

Fig. 2. *Seasonal variations in monthly mortality rates for all cardiovascular diseases, all heart diseases, coronary heart disease, hypertension and cerebrovascular diseases in Hungary between 1984 and 2013.*

Strengths and Weaknesses of the Study

Our population data were obtained from published tables. However, a long study period of 30 years was used in the analyses, allowing us to investigate trends in mortality rates. Our data were obtained from civil registers. In spite of the fact that the mortality data was coded according to the World Health Organization recommendations, these data could have been influenced by a simplified method of the categorization and by differences in two ICD revisions that were implemented in Hungary during the study period. Additionally, minor changes occurred in the structure of reported data during the thirty-year interval of the study. To accommodate these circumstances, we examined broad disease categories with negative binomial regression analyses. Overdispersion did not influence our results as the negative binomial regression method was used in both risk estimation and investigation of the annual mortality trend.

In the monthly cyclic trend analyses, we used the Walter-Elwood method with a long study period.

Data on mortality for hypertension were available as cause of death. Thus, hypertension was examined as the underlying cause of death, but high blood pressure can contribute to other cardiovascular diseases (comorbidity). However, we were not able to separate these effects based on the available data.

Comparison with Other Studies

Townsend et al. (1) reported that the age-standardized mortality rate from cardiovascular disease has decreased in most European countries during the past few decades. Rahimi et al. (9) concluded that myocardial infarction, ischaemic heart disease and heart failure mortality rates have been declining in England. Ma et al. (10) also found decreasing trends in age-standardized death rates from stroke and heart disease in the United States. Backholer et al. (11) reported declining age-standardized circulatory disease mortality rates in Australia. Like those studies, we found that cardiovascular death rates decreased significantly in Hungary during the thirty-year study period. However, Hungarian mortality rates were higher than the Western European rates (1). Hungarian mortality rates for all cardiovascular diseases are similar to those in Slovakia (12), but in contrast with those findings, the standardized mortality rate for ischaemic heart disease has decreased for men in Hungary. In agreement with our results, Vujcic et al. (13) observed significantly decreasing trends in coronary heart disease mortality rates among men, but not among women. Although no data was available on morbidity for cardiovascular diseases in Hungary, Bandosz et al. (14) reported that the fall in mortality from coronary heart disease in Poland can be attributed to reductions in major risk factors and that about one-third of this drop results from evidence-based medical treatments. The decreasing Hungarian mortality rates for cardiovascular disease were similarly explained in a review study by Bálint (15).

In spite of the decreasing trend in age-adjusted cardiovascular disease mortality in Western European countries, an increase in the number of cardiovascular patients is expected because of population ageing (1). Although age-standardized rates for stroke mortality have decreased worldwide in the past two decades, according to the Global Burden of Disease Study 2013, the absolute numbers of people who suffer a stroke every year are increasing (16).

In a study by Aylin et al. (17), a strong inverse association with temperature was reported in Great Britain and a trend of higher excess winter mortality with age was observed across all disease categories. Thus, the effects of cold weather are usually most apparent in mortality due to cardiovascular and respiratory diseases as well as in the elderly. Similarly, chronic heart failure deaths in France occurred with a striking annual periodicity and peaked in winter (December through January) (18). In a population-based study in Scotland between 1990 and 1996, Stewart et al. reported a significant seasonal variation in mortality among patients whose hospitalization was tied to heart failure (19). The peak was observed in December. Furthermore, a winter peak seasonality in cardiovascular disease deaths was reported in Australian State and Territory capitals between 1997 and 2004 (20). Major influences of seasonal change were also seen in heart and cerebrovascular diseases in a thirty-year study in Japan, with the highest rates in winter (21). A review of thirty-nine studies indicated that influenza can act as a trigger for acute myocardial infarction and cardiovascular death (22). Similarly, our findings suggest that the significant peaks in cardiovascular, heart and cerebrovascular mortality could be related to respiratory infections at the end of winter. Besides seasonal viral infections, excess winter mortality can be attributed to environmental factors such as temperature, air pollution, lifestyle factors (23), and seasonal changes in cardiovascular risk factor levels (24).

Cold-related mortality has been comprehensively examined in Western Europe, but there have been few studies conducted in Central European populations. Our study used a relatively long, thirty-year period to investigate both annual and seasonal trends in mortality from cardiovascular (heart and cerebrovascular) diseases.

CONCLUSION

In this study, a number of risk factors and trends were investigated in relation to cardiovascular mortality using well-established statistical methods. In spite of the decreasing trends in the annual mortality rates for cardiovascular diseases, the Hungarian mortality rate is still high. Moreover, this study has demonstrated a significant winter peak in mortality from cardiovascular diseases. The identification of groups at higher risk may be important for disease prevention.

Funding

Katalin Virág received funding from the European Union and the State of Hungary, co-financed by the European Social Fund within the framework of TÁMOP-4.2.4.A/ 2-11/1-2012-0001 'National Excellence Program'. Tibor Nyári received funding from the European Union and the State of Hungary, co-financed by the European Social Fund within the framework of EFOP-3.6.1-16-2016-00008.

Conflict of Interests

None declared

REFERENCES

1. Townsend N, Nichols M, Scarborough P, Rayner M. Cardiovascular disease in Europe - epidemiological update 2015. Eur Heart J. 2015;36(40):2696-705.
2. Hungarian Central Statistical Office. Demographic Yearbook 1984-2013 [Internet]. Budapest: Hungarian Central Statistical Office [cited 2018 May 14]. Available from: https://www.ksh.hu/?lang=en.
3. Day NE. A New measure of age standardized incidence, the cumulative rate. In: Waterhouse J, Muir C, Correa P, Powell J, editors. Cancer incidence in five continents. Vol. III. IARC scientific publications, no. 15. Lyon: IARC; 1976. p. 443-52.
4. Fay MP, Feuer EJ. Confidence intervals for directly standardized rates: a method based on the gamma distribution. Stat Med. 1997;16(7):791-801.
5. Standardized rates and age-period-cohort analysis. In: Newmwn SC. Biostatistical methods in epidemiology. New York: John Wiley & Sons; 2001. p. 249-61.
6. Walter SD, Elwood JM. A test for seasonality of events with a variable population at risk. Br J Prev Soc Med. 1975;29(1):18-21.
7. Stolwijk AM, Straatman H, Zielhuis GA. Studying seasonality by using sine and cosine functions in regression analysis. J Epidemiol Community Health. 1999;53(4):235-8.
8. StataCorp. Stata statistical software. Release 13. College Station: StataCorp LP; 2013.
9. Rahimi K, Duncan M, Pitcher A, Emdin CA, Goldacre MJ. Mortality from heart failure, acute myocardial infarction and other ischaemic heart disease in England and Oxford: a trend study of multiple-cause-coded death certification. J Epidemiol Community Health. 2015;69(10):1000-5.
10. Ma J, Ward EM, Siegel RL, Jemal A. Temporal trends in mortality in the United States, 1969-2013. JAMA. 2015;314(16):1731-9.

11. Backholer K, Steven C, Nusselder WJ, Boyko EJ, Moon L, Tonkin A. Age-specific trends in cardiovascular mortality rates in Australia between 1980 and 2005. Australas Epidemiol. 2011;18(1):33-7.
12. Svihrova V, Barakova A, Szaboova V, Kamensky G, Hudeckova H. Trends in standardized mortality rates for select groups of cardiovascular diseases in Slovakia between 1980 and 2010. Public Health. 2016;130:43-50.
13. Vujcic IS, Sipetic SB, Dubljanin ES, Vlajinac HD. Trends in mortality rates from coronary heart disease in Belgrade (Serbia) during the period 1990-2010: a joinpoint regression analysis. BMC Cardiovasc Disord. 2013 Dec 9;13:112. doi: 10.1186/1471-2261-13-112.
14. Bandosz P, O'Flaherty M, Drygas W, Rutkowski M, Koziarek J, Wyrzykowski B, et al. Decline in mortality from coronary heart disease in Poland after socioeconomic transformation: modelling study. BMJ. 2012 Jan 25;344:d8136. doi: 10.1136/bmj.d8136.
15. Bálint L. To what extent does Hungarian mortality fit the theory of epidemiological transition? Demográfia. 2016;59(1):5-57. (In Hungarian.)
16. Feigin VL, Krishnamurthi RV, Parmar P, Norrving B, Mensah GA, Bennett DA, et al. Update on the global burden of ischemic and hemorrhagic stroke in 1990-2013: The GBD 2013 Study. Neuroepidemiology. 2015;45(3):161-76.
17. Aylin P, Morris S, Wakefield J, Grossinho A, Jarup L, Elliott P. Temperature, housing, deprivation and their relationship to excess winter mortality in Great Britain, 1986-1996. Int J Epidemiol. 2001;30(5):1100-8.
18. Boulay F, Berthier F, Sisteron O, Gendreike Y, Gibelin P. Seasonal variation in chronic heart failure hospitalizations and mortality in France. Circulation. 1999;100(3):280-6.
19. Stewart S, McIntyre K, Capewell S, McMurray JJ. Heart failure in a cold climate. Seasonal variation in heart failure-related morbidity and mortality. J Am Coll Cardiol. 2002;39(5):760-6.
20. Barnett AG, de Looper M, Fraser JF. The seasonality in heart failure deaths and total cardiovascular deaths. Aust N Z J Public Health. 2008;32(5):408-13.
21. Nakaji S, Parodi S, Fontana V, Umeda T, Suzuki K, Sakamoto J, et al. Seasonal changes in mortality rates from main causes of death in Japan (1970-1999). Eur J Epidemiol. 2004;19(10):905-13.
22. Warren-Gash C, Smeeth L, Hayward AC. Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: a systematic review. Lancet Infect Dis. 2009;9(10):601-10.
23. The Eurowinter Group. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. Lancet. 1997;349(9062):1341-6.
24. Marti-Soler H, Gubelmann C, Aeschbacher S, Alves L, Bobak M, Bongard V, et al. Seasonality of cardiovascular risk factors: an analysis including over 230 000 participants in 15 countries. Heart. 2014;100(19):1517-23.

Received September 15, 2016
Accepted in revised form May 14, 2018