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CLINICAL RESEARCH
Prevention/epidemiology

Stroke mortality and trends from 1990 to 2006 in 39 countries from Europe and Central Asia: implications for control of high blood pressure

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Aims The aim of the present study was to extend our understanding of international trends in stroke and major sequelae in Europe and countries peripheral to Europe by assessing: (1) current mortality rates, (2) the most recent 15-year prevalence trends, and (3) the relationship between systolic blood pressure in community surveys and national stroke mortality.

Methods and results Data were obtained from the World Health Organization (WHO www.who.int/whosis/database/mort/table.cfm), and represent national vital statistics as reported by 39 countries (European and Central Asian countries) using a standard format and population-based cardiovascular surveys. Total numbers of deaths by stroke (International Classification of Diseases 430–438, 444) and the age, sex-adjusted incidence rates were obtained and grouped according to three standard demographic categories: A, B, and C (WHO). A Bayesian linear mixed effect model was fitted to the annual mortality rates. Higher rates of stroke mortality were observed for B and C group countries as compared with those countries belonging to Group A (e.g. Bulgaria 273.9 and 281.1; Israel 37.7 and 45.4 per 100 000 men and women, respectively). Even though the mortality rates within the country groupings were relatively similar, countries with marked deviation from the average were observed, mainly in Groups B and C. Stroke mortality decreased sharply in Group A during the period of study; conversely it had increased substantially in Group B and to a lesser extent in Group C. For both sexes markedly higher rates were noted moving from west to east, with some exceptions.

Conclusion We have entered a period of rapidly increasing international inequality in stroke risk, where countries with low adult mortality in the latter 20th century extended their downward trend and countries with moderate as well as high mortality have on average seen unprecedented increases in death rates from stroke.

Keywords Stroke mortality • Hypertension control • Europe mortality

Introduction

Stroke has long been recognized as a major problem for public health. One, stroke ranks third (after MI and cancer) as a cause of death around the world.[1] Two, stroke is responsible for 3% of adult disability[2] and analyses based on vital record and data imputation have established that the 15 million incident strokes occurring each year around the world result in 5 million deaths and an additional 5 million patients living with permanent sequelae and dependency.[1] Three, because of the progressive ageing of the

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population, and the increased prevalence of major risk factors for stroke (hypertension, diabetes, obesity, etc.), stroke is expected to increase in the coming decades, leading to the prediction being that the rate of stroke may double by the year 2020.[2]

The above situation justifies current emphasis on the need to control risk factors that are responsible for the majority of strokes, above all hypertension.[3–7] It also justifies the growing attention being given to the prevalence of stroke and its temporal trends in different regions of the world, in order to incorporate new knowledge and have a better global insight into factors, (genetic, environmental, and health care system), that play a major role in determining stroke occurrence and outcomes. This has led to interesting although unexplained observations. For example, North American countries appear to have a markedly lower stroke mortality than Europe,[8–10] which is in turn characterized by a highly heterogeneous mortality rate between different countries and regions.[8,9] Also, although the burden of stroke has declined monotonically in many countries since 1900,[11] an increase has been reported in the second part of the 1st century for countries such as Portugal and from 1990 the stroke burden has shown an unexpected and startling new rise in the former Soviet Union and Eastern European countries.[12,13]

The aim of the present study was to extend our understanding of these international trends in stroke by assessing its mortality rate as well as recent 15-year trends using detailed data from Europe and countries peripheral to Europe, as available from the World Health Organization (WHO). Another goal of the study was to examine the extent to which these data can be used as a marker of the burden of uncontrolled hypertension in populations, given that an elevated blood pressure accounts for about two-thirds of strokes worldwide.[14]

Materials and methods

Study population

This analysis is based on information provided in the electronic databases of the WHO (www.who.int/whosis/database/mort/table.cfm). All data represent the vital statistics as reported from individual country ministries using a standard format. Stroke mortality (International Classification of Diseases 430–438, 444) rates stratified by age and sex are presented for countries in the region with a population of 500 000 or more. Rates were not computed for countries with a very low level of vital registration, <60%. Coverage was calculated for each country by dividing the number of stroke deaths reported for any given year by the total number of deaths estimated by WHO for the population of that country during that year. The WHO national population death estimate was based on the UN Population Division, 2006 revision.

It should be noted that the WHO estimates may not be completely accurate. First, for a given country data may not be entirely comparable due to incomplete vital registration, coverage of only some parts of the national population, or differences between the vital registration population and the *de facto* population as estimated by UN. Second, some national vital registration systems may record not only deaths of permanent residents but all deaths occurring in the country. Third, in some other cases deaths of citizens living abroad are included. No data were available in subjects <45 years of age. However, the total number of deaths is this group is known to be negligible. The WHO estimates of death rates by age and sex were adjusted for incompleteness and used to obtain the total number of deaths per country.

Mortality data

We included data from 35 countries (see Table 1) in Europe and Central Asia. A subset of countries from both geographical areas were excluded (Iceland, Luxemburg, Malta, San Marino and Turkey) due to absence of the required information. The data were obtained by permission of the WHO Office.

The total numbers of deaths produced by stroke and the age- and sex-adjusted incidence of fatal stroke were obtained for each country and grouped according to three demographic categories as designated by the WHO[15,16]: Category *A*, countries with very low child and adult mortality; Category *B*, countries with low child and adult mortality; category *C*, countries with low child and high adult (see Table 1).

Statistical analysis

A Bayesian linear mixed effect model[17] was fitted to the annual mortality rates with the year as an explanatory variable in the 39 countries analysed. Fixed effects were used to model the average linear trend for the three groups of countries. Random effects, for both the intercept and slope of the trend, have been included in the analysis to model the deviation of a country within its grouping. Independent standard deviations have been considered for the random effects in each of the three groups. Non-informative uniform prior distributions have been used for the coefficients of the fixed effect terms and for the standard deviations of the random effects. Results are presented as the mean and the 95% confidence interval. Inference on the Bayesian mixed effect regression model was made with the software WinBUGS 1.4.3. Data management and graphical representation of the results (including maps) were made with the R Statistical package (version 2.8.1).

Results

Stroke mortality, 2002

Across all countries, a total of 1 226 144 stroke deaths were recorded. There was a large excess mortality for stroke in women as compared with men (739 000 vs. 487 000, respectively), a consequence primarily of the female life expectancy advantage. Because stroke is pre-eminently a disease of the elderly, 60% of deaths occurred in persons >75 years old and only 4% in subjects <55. A strong age–sex interaction was thus apparent. Below 65 years of age the stroke mortality rates were significantly higher among men (male/female ratio = 1.72), whereas this relationship was reversed over 75 years of age (male/female ratio = 0.42). In absolute terms the mortality burden was maximal in the countries from Group C ($n = 673{,}601$), followed by Group A ($n = 397{,}473$) and B ($n = 155{,}070$). Although stroke mortality in all countries was concentrated in the oldest age groups, substantial numbers of deaths were observed among the younger individuals.

Age- and sex-adjusted stroke mortality rates per 100 000 inhabitants are presented in Table 1. Higher mortality rates for women as compared with men persisted in the majority of the countries, although this is in part a result of incomplete adjustment for age among the very elderly when 10 year age strata are used. Higher rates of stroke mortality were observed in countries in Groups

Table 1 Age-specific and age-adjusted stroke mortality by country, by sex, 2002 (per 100 000 inhabitants)

Country per WHO group[a]	Men					Women				
	Total	45–54	55–64	65–74	75+	Total	45–54	55–64	65–74	75+
Group A										
Austria	75.8	13	46.1	189.2	1109.2	124.4	13.4	27.4	118	1099.7
Croatia	169.1	58	191.4	644.3	2159.4	206.2	27.1	90.4	414.2	1907.9
Czech Rep	130.5	32.9	107.9	466.8	1988.6	192.1	14	54.2	312.7	2043.7
Finland	70.3	24.6	63.2	211.7	910.4	114.7	17.1	33.2	144.1	1035.6
France	53.1	15.1	34.9	132.7	634.2	69.4	8.7	16.3	67.4	625.3
Germany	70.3	15.3	48.2	184.3	934.9	116.6	10.5	24.9	108.4	991.9
Greece	143.9	23.3	76.3	306.3	1763.2	194.6	14.6	37.4	211.1	2177
Ireland	51	14.5	35	170.9	935.6	71.1	12.1	20.1	109.6	991.9
Israel	37.7	9.4	40.5	180.2	677.8	45.4	6.3	22.6	108.3	693.3
Italy	95.9	14.1	41.1	168.5	1129.2	133.5	9.8	24.3	101.4	1113.7
Netherlands	60.5	14.2	43.8	188.6	892.7	90.6	18.2	31.4	114.9	945.6
Norway	76.5	10	39.1	187.2	994.1	112.5	10.3	22	115.1	1031
Portugal	168.4	39.2	105.6	412.9	2048.1	207.6	18.7	52.8	249.6	2052.1
Slovenia	86.3	30	89.9	354.5	1265.3	114.4	20.4	43.1	162.4	1148
Spain	73.7	16.2	44.8	169.3	880.4	99.9	8.7	21	98.1	934.3
Sweden	91.4	13.3	43.1	186.3	992.1	132.4	11.9	28.2	124	1076.8
Switzerland	48	6.7	19.7	99	658.7	70.2	6.2	13.4	59.7	666.7
United Kingdom	88.3	18.5	49.2	202	1101.4	138	15.7	35.6	146.1	1274.4
Group B										
Albania	94.8	31.9	108	533.9	2547.8	97.1	14.5	65.3	420.7	2162.1
Azerbaijan	57	51	220.4	575.1	1293.9	69.9	37.3	168.4	500.8	1397.8
Bulgaria	273.9	98.1	308.1	890.8	2587.1	281.1	44.2	147.4	618.7	2398.3
Kyrgyzstan	118.6	174.4	618.3	1367.5	2348.5	138.4	126.3	411.6	968.9	2729.7
Poland	94	51.4	153.3	427.6	1291.9	119.9	28.6	72	282.5	1285.1
Romania	238.8	107	355.7	981.8	2785.9	267.2	60.5	203	722.5	2704.5
Serbia Montenegro	197.1	69	232.9	738.4	1936.9	237.8	49.2	167.5	644.9	1962.6
Slovakia	84.4	37	125.5	402.4	1344.7	92.5	8.5	40.7	248.8	1120.1
Group C										
Belarus	183.2	138	447.1	974.2	1848.4	219.7	67.2	242.5	655.8	1675.1
Estonia	160.5	73.3	249.4	716.1	1940.7	247.1	34.8	105.6	456.6	2145.1
Hungary	172.8	88.4	214.4	651.9	1920	190.8	34.4	94.3	366.4	1662.5
Kazakhstan	121.1	144.4	450.5	1087.8	2192.9	150.4	74.5	281.4	716.1	2387.7
Latvia	225.9	89.8	361	1000.7	2886.6	337	47.9	181.7	638.1	2794.3
Lithuania	120.9	56.1	173.7	499.9	1703.3	179.3	33.6	102.4	351.7	1680.9
Rep Moldova	164.8	124.4	441.1	1094.2	2485.2	197.6	85.2	339	821.9	2324.2
Russian Fed	275.4	159.3	605.4	1619.3	3553.4	396.6	76.9	304	1022.1	3687.4
Ukraine	190.3	117.9	369.6	873.4	2081.8	253.2	59.8	205.9	598.4	2046.6

Data not available for Belgium, Bosnia, Denmark and Georgi.
[a]Group according to ref. 15 (see text).

B and C compared with those in Group A. Even though the mortality rates within the groupings were relatively homogeneous, some outliers were observed. For example, in Group A, Greece and Portugal had rates twice the average. Large deviations from average values were also observed in Group B (highest rate in Bulgaria and Romania) and in Group C (highest rates in Latvia and the Russian Federation).

The higher rates of stroke mortality observed in Group B and C countries as compared with those in Group A were higher in the youngest groups. The stroke mortality rate in Group B was four times more than in Group A in subjects <65 years while it was only 1.7 times more in >75 years for men and women. Likewise, in Group C it was 5 times more than in Group A in the youngest and 1.8 times in the oldest.

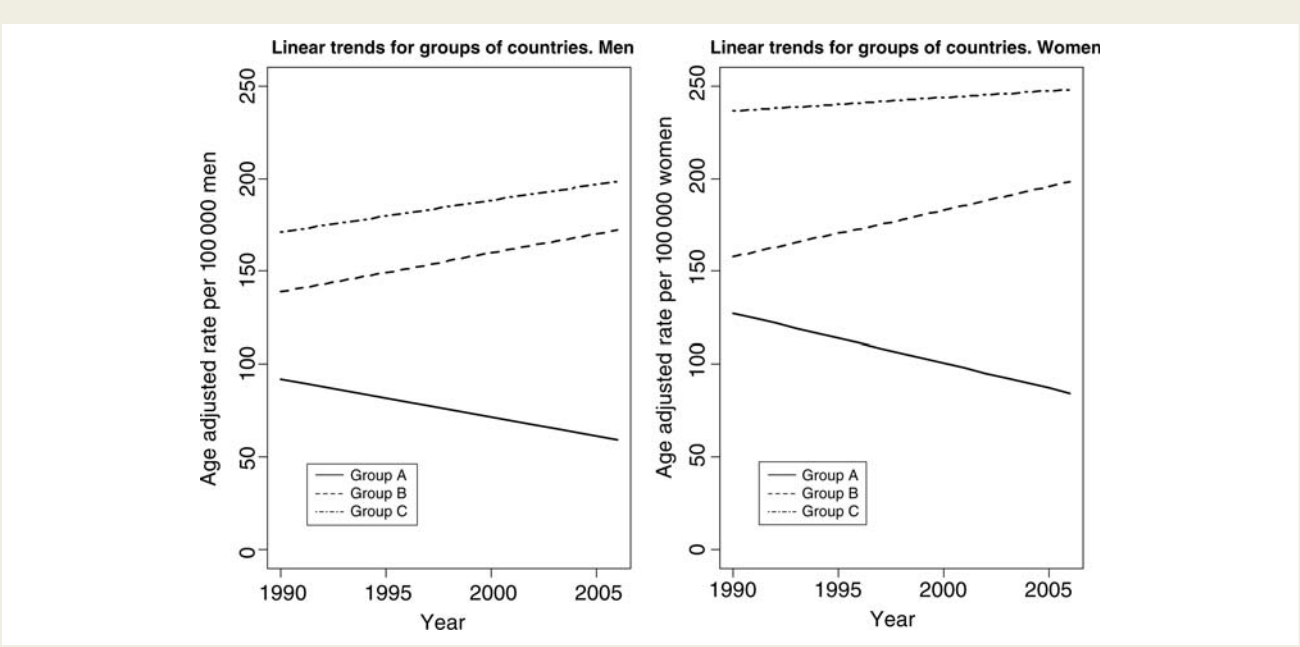

Figure 1 Mean trend for mortality rates for each of the country Groups A, B and C (see text).

Table 2 Means and 95% confident intervals in the mixed effect models for group of countries

Group of countries	Males	Females
Average rate for every group (per 100 000 people), year 1998		
Group A	93.94 [75.44, 112.30]	129.95 [107.50, 153.40]
Group B	136.87 [86.84, 186.49]	155.35 [108.00, 201.89]
Group C	169.55 [138.20, 199.69]	235.78 [185.61, 283.46]
Annual variation of the mortality rate for the whole period		
Group A	−2.03 [−2.62, −1.51]	−2.67 [−3.40, −1.86]
Group B	2.08 [−0.02, 4.25]	2.51 [−0.12, 4.96]
Group C	1.71 [−1.08, 4.23]	0.72 [−2.76, 4.11]
Standard deviation of the mortality rate (year 1998) for countries in every group		
Group A	41.53 [30.17, 59.56]	50.85 [36.46, 73.55]
Group B	76.00 [50.72, 98.13]	77.22 [53.82, 98.35]
Group C	46.11 [27.30, 81.78]	72.99 [49.33, 153.40]
Variability (SD) of annual variation of the rate for countries in every group		
Group A	1.26 [0.85, 1.82]	1.65 [1.14, 2.38]
Group B	3.06 [1.66, 5.65]	3.87 [2.20, 6.91]
Group C	3.84 [2.19, 6.90]	4.67 [2.59, 8.51]

Trends in stroke mortality, 1990–2006

Linear trends in stroke mortality were fitted for each group of countries, separately for males and females, using the mixed effect model. The corresponding average regression lines for every group of countries are shown in Figure 1. In Group A stroke mortality decreased sharply from 1990 to 2006 whereas in Group B and to a lesser extent in Group C an increase was observed. For each of the three country groupings the rate of mortality in the year 1998 (the mid-year of the study period), the annual variation during the whole period, and the standard deviations of the random effects around the mean of its group, is presented in Table 2. Data refer to individual countries. In both sexes the highest mortality rates were seen for Group C followed by sequentially by Groups B and A. The annual increment was higher for Group B than for Group C, although the difference was not statistically significant. The standard deviation of the annual variation among countries was lower in Group A than in Group B or C, indicating greater homogeneity.

Disaggregated country-specific data are summarized in Figure 2 in which the geographical distribution of the mortality rate for stroke is shown for the mid-year of the study period, i.e. 1998. For both sexes the stroke mortality rate shows marked between-country variations with a clear tendency to increase sharply moving from west to east. There were nevertheless also clear exceptions. For example, Portugal is at the upper range of mortality risk while Kyrgyzstan appears to be relatively low. For men, the country with the highest rate of stroke mortality is Bulgaria (267.6) whereas, the lowest mortality rate was observed in Israel (45.1). For women, the country with the highest rate is the Russian Federation (351.0), while the lowest rate was again Israel (51.6).

Figure 3 presents the geographic distribution of the annual rate of change in stroke mortality during the period 1990–2006 in each country, again based on mixed effects model. In general Western Europe has experienced a consistent decrease in stroke mortality.

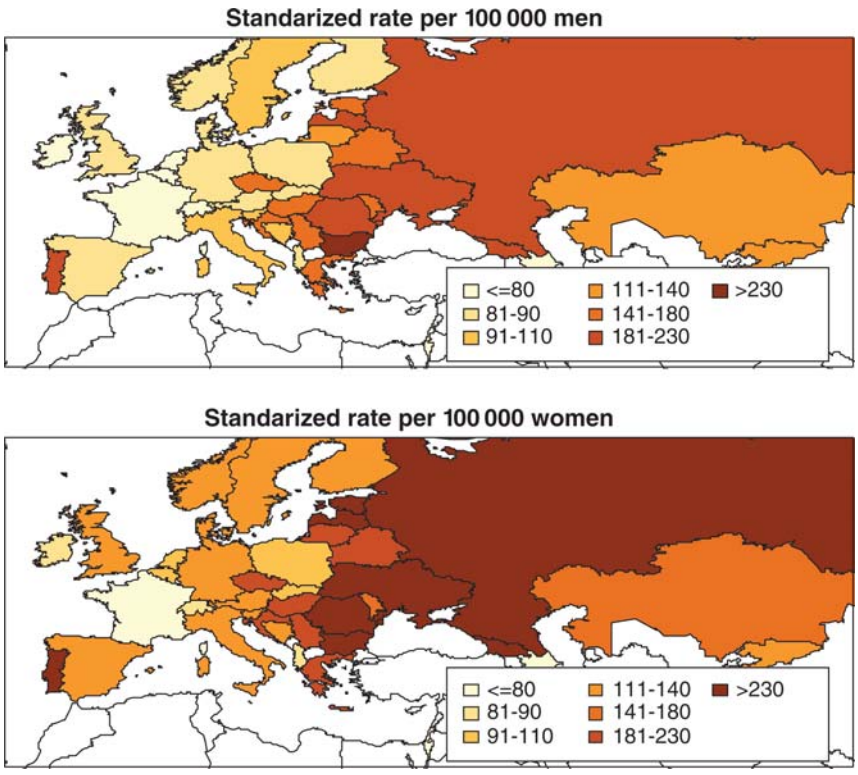

Figure 2 Geographical distribution of the mortality rate for stroke for the mid-year of the study period (1990–2006) in men (upper panel) and women (lower panel).

However, in Eastern Europe a single homogeneous pattern is not apparent, and countries with virtually no temporal changes can be seen vis-à-vis countries in which a considerable increase in mortality is recorded. For men the country with the highest annual increase in mortality rate is Serbia and Montenegro (annual increase of 6.9 deaths per 100 000 men), while the lowest one is Portugal (−4.9). For women, the country with the highest annual increase is again Serbia and Montenegro (9.1) while the greatest decrease is seen in Austria (−5.4).

Discussion

A downward trajectory in stroke mortality has been the historical norm and in some countries this pattern has been documented from as early as 1900.[11] In this report, we extend the description of stroke mortality trends in Europe, Russia, Central Asia and a group of smaller countries in the European sphere to the last 15 years. The striking conclusion that emerges is that stroke mortality has entered a period of rapidly increasing inequality between countries. Countries which had attained low mortality rates reached in the latter part of the 20th century experienced further declines, while countries with moderate as well as high stroke mortality (Groups B and C in this report) at the start of the period being examined had a further unprecedented increase in this cause of death.[13,18]

The data reported in the present study from the WHO permit a detailed analysis of the impact of stroke mortality in Europe and the differences among countries since 1990. As noted, stroke continues to exact a disproportionate toll among women. This sex imbalance reflects an age-crossover effect, whereby rates are higher among men at a younger age, but the longevity advantage of women allows more of them to reach the age of greatest stroke risk. This pattern is also consistent with the age-related cross-over in blood pressure (BP) levels among men vs. women and the selective survival of healthier men to old age. Secondly, age-adjusted stroke mortality varies four-fold among European countries, and most strikingly the current trends are also highly divergent. While a constant decrease was observed in most countries, some other countries show persistently high rates and another subset experienced a steep upward trajectory which continued into the last year analysed. Third, in general, countries with the highest economic standard of living showed the lowest incidence and the greatest decline in stroke mortality. However, some exceptions should be noted. For example, Portugal and Greece showed high rates of stroke mortality in the baseline year, but despite this a continuous decline was observed. In contrast, and with some exceptions, lower income countries were found to not only have higher stroke mortality in 1990 but a persistent increase over time. Also to be noticed is that in countries such as Portugal and Greece the high rate of stroke mortality coexists with a prevalence of coronary heart disease, which is known to be among the lowest in Europe.[19] This can be explained for differences in the prevalence and control of some risk factors, mainly hypertension.

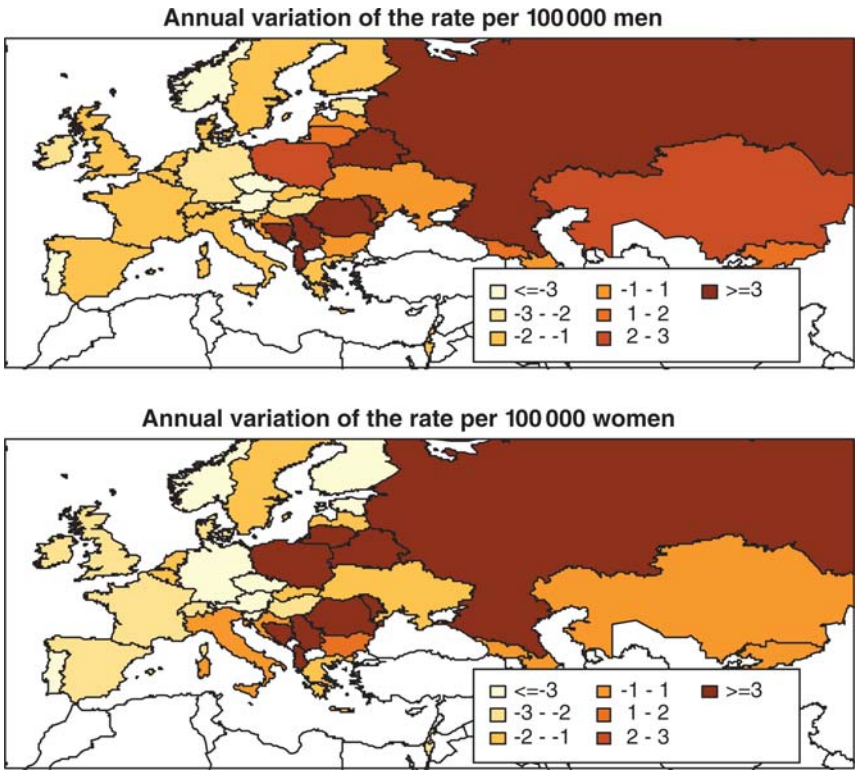

Figure 3 Geographical distribution of the annual rate of change in stroke mortality during the study period (1990–2006) in men (upper panel) and women (lower panel).

The present data raise a series of important questions. Why are there such large differences among the European countries? How can this variation be reduced so that more populations share the benefits of cardiovascular prevention? The reason for the large differences is an intriguing question that deserves careful reflection due to the huge impact on health care.[20,21] Considering the close relationship of stroke and BP independent of age and sex, simple variation in BP itself would appear to be a plausible explanation. A significant relationship in univariate and in a multivariate analyses between systolic BP and the stroke mortality among countries was reported for Johnston *et al.*,[14] although the importance of systolic BP values was surpassed by the variable income. Low income is an important marker of risk since it reflects not only a combination of socioeconomic variables, such as income itself and unemployment, but also derived psychosocial and dietary factors, prevalence of classic cardiovascular risk factors and access to medical care. Furthermore, estimates of country income are more reliable than country-level systolic BP values, thus also favouring a more robust relationship for income than for systolic BP.[22]

Prior ecological analyses—both among countries and among regions within countries—have shown a reasonably strong correlation between BP or hypertension prevalence and stroke mortality,[8,9,23] and the consistency of these relationships has suggested that stroke rates could serve as an outcome measure reflecting the success of high BP control efforts. It has also been recognized in the last few years that in populations with similar standards of living, such as North America and Western Europe, mean BPs among normotensive persons can vary substantially, presumably reflects the level of exposure to causal risk factors.[24] Taken together, this evidence suggests that at least part of the long-term decline in stroke has resulted from falling average BPs.

Wolf-Maier *et al.* estimated the prevalence of hypertension in Europe compared with the USA and Canada[8] and treatment strategies on Germany, Sweden, England, Spain, Italy, Canada, and the USA using national surveys conducted in the 1990s.[9] The prevalence of hypertension was 60% higher in Europe compared with the USA and Canada. Likewise, Redon *et al.*[25] in a cross-sectional study of population >60 years old in Spanish primary care centres, stroke mortality rates were significantly related to indexes of worse blood pressure handling, low control rates and high left-ventricular hypertrophy, independent of age, sex, obesity, diabetes, and urban setting. Moreover, Boshuizen *et al.*,[26] analysing 35-year follow-up data on mortality of stroke among subjects aged 65 years or more from nine cohorts of the Seven Countries Study, observed that past and recent SBP was related to stroke mortality. Asplund *et al.*[27] in the MOnica Risk, Genetics, Archiving and Monograph (MORGAM) Project concluded that the impact of the individual risk factors differed somewhat between countries/regions with high blood pressure being particularly important in central Europe (Poland and Lithuania). Recently, Campbell *et al.*[28]

reported a progressive reduction in hospitalization and mortality for stroke from 1999. This reduction started with the introduction of the Canadian Hypertension Educational Programme and was in parallel with an increment in antihypertensive prescriptions. The gap between improving hypertension control and reducing stroke mortality, however, remains a matter deserving close study.

Hypertension remains the leading cause of mortality and the third largest cause of disability worldwide[29]. Although estimates vary,[30] the consistent message is that in Europe the proportion of patients with acceptable BP control is low even among those who are diagnosed and treated in the first place[31]. Likewise BP control differs among countries in Europe, although there are limited data based on studies conducted with the same methodology. Recognizing the difficulties in obtaining timely and comparable population surveys, alternative methods to assess the BP status across populations could be an important quality indicator for health systems. Assessing the incidence and trends of hypertension-induced clinical conditions could prove useful in this regard. Among the options for a surveillance measure, stroke incidence presents an attractive option.[32]

If we assume that stroke mortality can serve as a proxy for average BP in a population, the data presented here clearly demonstrate the necessity to adopt actions to increase the diagnosis, treatment and hypertension control in the countries where the burden of hypertension sequelae is still growing. Policies to increase the rate of BP control offer the best approach, while primary prevention strategies must also be implemented.

The study has to be interpreted within the context of its limitations and strengths. With an ecological approach, we explored possible relationships between health statistics and population characteristics, stroke mortality rates, and prevalence of cardiovascular risk factors. Although inferences from associations observed in an ecological study may not necessarily pertain to the individuals within the group, especially when outcomes from long-term exposures were studied, they help to develop hypotheses for further evaluation with analytical studies and they have a distinct advantage because of their statistical power to detect small risks. Estimates may be subject to ecological bias[33] but neither theoretical nor empirical analysis has offered consistent guidelines for the interpretation of ecological analysis. In addition, changes in the codification of diseases over time can be contributed to some of the sharp jumps in mortality rates observed but the general trends would not result from the code changes.

Summary

Stroke mortality accounts for a large proportion of mortality in Europe and the trend is to increase in absolute numbers, due to an ageing population and for the increment observed in many countries. This underlying challenge which needs to be confronted is shifting the distribution curve of the blood pressure to the left in the population while increasing the rate of diagnosis, treatment and control of hypertension. Future studies should search for more detailed information concerning the role of stroke mortality as a proxy of the hypertension status in populations.

Conflict of interest: none declared.

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