

Incidence of Stroke in Europe at the Beginning of the 21st Century

The European Registers of Stroke (EROS) Investigators*

Background and Purpose—Comparable data on stroke incidence across European countries are lacking because previous studies have used different methods of case ascertainment, different periods of observation, and different age restrictions.

Methods—Population-based stroke registers were established in 6 European countries: France (Dijon); Italy (Sesto Fiorentino); Lithuania (Kaunas); the United Kingdom (London); Spain (Menorca); and Poland (Warsaw). Standardized criteria were used among these registers including overlapping sources of notification. Overall, a source population of 1 087 048 inhabitants was observed, ranging from 47 236 in Sesto Fiorentino to 365 191 in Kaunas. All patients with first-ever stroke of all age groups from the source populations were included. Data collection took part between 2004 and 2006; 4 centers collected data for a 24-month and 2 for a 12-month time period. Crude annual incidence rates were age-adjusted to the European population.

Results—A total of 2129 patients with first stroke were registered. Median age was 73 years and 51% were female. Annual stroke incidence adjusted to the European population was found in men to be higher in Kaunas and lower in Sesto Fiorentino and Menorca and in women to be higher in Kaunas and Warsaw and lower in Sesto Fiorentino and Menorca compared with mean incidence rates. Total stroke incidence ranged in men from 101.2 per 100 000 (95% CI, 82.5 to 123.0) in Sesto Fiorentino to 239.3 per 100 000 (95% CI, 209.9 to 271.6) in Kaunas and in women from 63.0 per 100 000 (95% CI, 48.5 to 80.7) in Sesto Fiorentino to 158.7 per 100 000 (95% CI, 135.0 to 185.4) in Kaunas. Differences in prior-to-stroke risk factors were found among the populations with prevalence of hypertension highest in Warsaw and Kaunas (76% and 67%, respectively) and lowest in Menorca and Sesto Fiorentino (54% and 62%, respectively).

Conclusions—The risk of stroke among European populations in our study varied more than 2-fold in men and women. On average, higher rates of stroke were observed in eastern and lower rates in southern European countries. (*Stroke*. 2009;40:1557-1563.)

Key Words: Europe ■ incidence ■ stroke

Geographic comparisons of stroke incidence within countries and between countries are valuable for identifying high-risk populations and for generating new hypotheses for defining preventive interventions.^{1,2} Population-based stroke registers are perceived as the gold standard for measuring stroke incidence in the population.^{3,4} However, comparability of data on stroke incidence based on previous population-based registers in Europe is limited for several reasons. Population-based registers need to demonstrate adherence to standardized criteria for producing comparable results.^{5,6} Thus, comparability of results with previous studies might be hampered by several methodological differences in data collection.¹ In addition, the incidence of stroke shows substantial variations over time with decline in stroke incidence until the early 1980s, a stabilization or an increase in stroke incidence in the late 1980s and early 1990s,⁴ and few studies on trends in incidence since the beginning of the 21st century

with conflicting results.⁷⁻¹¹ Thus, comparing studies with different periods of observation might limit the comparability of their findings. Finally, some previously published population-based stroke registers also defined upper age restrictions for their source population such as an age limit of 65 years in the World Health Organization (WHO) Multinational MONItoring of trends and determinants in Cardiovascular disease (MONICA) Project.¹² Thus, it might be difficult to estimate the true impact of stroke for the whole population.

Therefore, we have set up population-based stroke registers, without age restriction, using uniform standardized criteria and over a similar period of observation to compare stroke incidence across different European populations.

Methods

Population-based stroke registers were established in 6 European countries representing populations in central (France), southern

Continuing medical education (CME) credit is available for this article. Go to <http://cme.ahajournals.org> to take the quiz.

Received August 19, 2008; final revision received November 4, 2008; accepted November 7, 2008.

*See the Appendix for a list of the investigators.

This study was presented in part as an oral presentation at the European Stroke Conference 2007 in Glasgow.

Correspondence to Professor Charles D. A. Wolfe, Division of Health and Social Care, King's College London, 7th Floor Capital House, 42 Weston Street, London SE1 3QD, UK. E-mail charles.wolfe@kcl.ac.uk

© 2009 American Heart Association, Inc.

Stroke is available at <http://stroke.ahajournals.org>

DOI: 10.1161/STROKEAHA.108.535088

Table 1. Extrapolation of the Source Population

Centre	Start of Study	End of Study	Available Population Figures	Extrapolation Method	Estimated Source Population 2005
Dijon	May 2004	April 2006	Census 1990 and 1999	Linear extrapolation for 2005	152 415
Sesto Fiorentino (northwest of Florence, Tuscany)	June 2004	May 2006	Official population register for 2005	None	47 236
Kaunas	June 2004	May 2005	Census 1989 and 2001	Linear extrapolation for 2005	365 191
London	May 2004	April 2006	Census 1991 and 2001	Linear extrapolation for 2005	326 885
Menorca	May 2004	April 2006	Census 1996 and 2001	Linear extrapolation for 2005	75 135
Warsaw	January 2005	December 2005	Census 2002	None	120 186
Total					1 087 048

(Italy, Spain), and eastern Europe (Lithuania, Poland) and the United Kingdom. Centers within different countries were selected based on previous experience in running population-based or hospital-based stroke registers. In Kaunas, Lithuania,¹³ Dijon, France,⁷ London, UK,¹¹ and Warsaw, Poland,¹⁴ well-established population-based stroke registers have been running since 1986, 1982, 1995, and 1991, respectively. In Menorca, Spain, and Sesto Fiorentino, Italy, hospital-based stroke registers were initiated for 2 previous European Union Biomedicine and Health Programme (BIOMED) II Projects starting from 1993^{15,16} and for this study, population-based registers were established in both centers. Patients with first-ever stroke of all age groups from the source populations of the respective centers were included.

Study Populations

The source populations in the respective centers were estimated based on available census figure for the 2 most recent censuses by assuming a linear trend. The size of the source populations was estimated for the midpoint of the study period (2005) where possible. In centers where no census data at 2 time points were available, the most recent official statistics were used (eg, single time census). In one center (Sesto Fiorentino), data from the constantly updated official population register were used based on the 2001 census. An overview of the methods used for estimating the source populations and about the size of the estimated source populations in the different centers is provided in Table 1. Overall, a source population of 1 087 048 inhabitants was observed, ranging from 47 236 in Sesto Fiorentino to 365 191 in Kaunas. Data collection took place at least over a 12-month time period. An extension of the data collection period for another 12 months was voluntary for all centers but compulsory for centers with an estimated source population of <100 000 inhabitants to ensure sufficient power for analyzing stroke incidence in different age groups.⁶ Data collection started in Dijon, London, and Menorca in May 2004; in Kaunas and Sesto Fiorentino in June 2004; and in Warsaw in January 2005 (Table 1). In Menorca, data on incidence of stroke subtypes were collected over a 24-month time period, but information on risk factors and health services use was only available for the first 12 months.

Case Ascertainment

Methods of case ascertainment were standardized across centers. Standardized criteria for ensuring completeness of cases ascertainment were applied, including multiple overlapping sources of information.⁶ Patients admitted to hospitals after the acute stroke event were identified by screening of all acute hospitals serving for the source population, including reviews of acute wards by the study team, checks of brain imaging referrals, and reviews of hospital discharge registers. Patients not admitted to a hospital were identified by a regular screening of all primary care facilities in the study area (eg, general practitioners and outpatient clinics). In addition,

nursing homes and community therapists in the study area were contacted and death certificates were checked regularly.

All patients with the diagnosis suspected of stroke documented in one of these sources of notification were investigated for eligibility of study inclusion. Standardized protocols for case ascertainment were provided and adapted according to the local center's need. External site visits by a multidisciplinary team from other centers were performed to ensure adherence of the centers to the defined protocols and standards.

Data Collection

A specially trained study nurse and/or specially trained fieldworkers collected data within the centers. The coordinating center in London provided regular training of fieldworkers in the participating centers to ensure reliable data collection. All participating centers met regularly at least once a year to discuss problems occurring during data collection. Continuous e-mail support by the coordinating center in London was offered to all participants. The questionnaires and the variable definitions used were developed within the European BIOMED program and updated for the current project.¹⁶ A common data collection tool was provided for all centers developed by the data center at the National Public Health Institute, Helsinki, Finland.

Stroke was defined according to the WHO definition.¹⁷ Stroke was classified into cerebral infarction (CI), primary intracerebral hemorrhage (PICH), and subarachnoid hemorrhage (SAH) based on results from at least one of the following diagnostic means: brain imaging performed within 30 days of stroke onset (CT or MRI), cerebrospinal fluid analysis (in all living cases of SAH in which brain imaging was not diagnostic), or necropsy examination. Cases without pathological confirmation of stroke subtype were classified as undefined. Data were collected on prior-to-stroke risk factors from the patient/family, general practitioner notes, and hospital records. Definitions and guidance for collecting information on history of specific risk factors or medical conditions was provided to all centers in a detailed manual. The information included hypertension (recorded history of hypertension prestroke [>140 mm Hg systolic or >90 mm Hg diastolic] or on antihypertensive medications); diabetes mellitus (recorded history of diabetes prestroke or on diabetic medication); atrial fibrillation (recorded history of atrial fibrillation); myocardial infarction (recorded history of myocardial infarction prestroke); smoking prestroke (nonsmokers and exsmokers versus current smokers); transient ischemic attack (recorded history of transient ischemic attack prestroke).

Statistical Analyses

The *t* test was used to test differences in continuous variables and the χ^2 test was used for differences in proportions. Crude incidence rates were calculated for age group, sex, and pathological stroke subtypes for each center; total and stroke subtype incidence rates were age-adjusted to the standard European population¹⁸ and presented for

Table 2. Differences in Sociodemographic Characteristics, Stroke Subtypes, and Vascular Risk Factors Among Centers*

	Total	Dijon	Sesto Fiorentino	Kaunas	London	Menorca	Warsaw	P†
n	2129	386	161	816	460	171	135	
Age, years								
Mean (SD)	70.7 (13.8)	73.2 (13.8)	75.9 (11.9)	69.9 (12.8)	68.2 (15.3)	72.2 (14.1)	69.0 (13.9)	
Median (IQR)	73 (62–81)	76.5 (66–82)	78 (69–84)	72 (62–79)	70 (60–79)	76 (63–83)	71 (58–81)	
Age group, years, n (%)								0.0047
<65	633 (29.8)	86 (22.3)	27 (16.8)	252 (30.9)	162 (35.2)	50 (29.2)	56 (41.5)	
65–74	507 (23.8)	77 (20.0)	35 (21.7)	228 (28.0)	119 (25.9)	27 (15.8)	21 (15.6)	
75–84	700 (32.9)	159 (41.2)	65 (40.4)	250 (30.7)	119 (25.9)	66 (38.6)	41 (30.4)	
85+	288 (13.5)	64 (16.6)	34 (21.1)	85 (10.4)	60 (13.0)	28 (16.4)	17 (12.6)	
Female sex, n (%)	1088 (51.1)	197 (51.0)	81 (50.3)	461 (56.5)	207 (45.0)	74 (43.3)	68 (50.4)	0.0002
Admission to hospital, n (%)	2013 (94.6)	365 (94.6)	149 (92.6)	789 (96.7)	429 (93.3)	150 (87.7)	131 (97.0)	0.0001
Prestroke risk factors, n (%)‡								
Hypertension	1329 (66.0)	249 (65.2)	100 (62.1)	542 (67.3)	297 (64.7)	41 (54.0)	100 (75.8)	0.0025
Diabetes mellitus	320 (15.9)	63 (16.5)	32 (19.9)	102 (12.7)	96 (21.2)	13 (17.1)	14 (10.7)	0.0017
Atrial fibrillation	427 (21.2)	81 (21.2)	30 (18.6)	204 (25.4)	69 (15.0)	10 (13.2)	33 (25.0)	<0.0001
Current smokers	396 (21.7)	78 (25.1)	20 (12.5)	108 (14.4)	139 (33.1)	13 (19.7)	38 (31.9)	<0.0001
Myocardial infarction	250 (12.4)	50 (13.1)	23 (14.3)	115 (14.3)	40 (8.7)	7 (9.3)	15 (11.4)	0.0492
Previous transient ischemic attack	220 (11.1)	53 (14.1)	22 (13.7)	75 (9.3)	56 (12.2)	4 (6.9)	10 (7.7)	0.14
Stroke subtype, n (%)								<0.0001
Ischemic stroke	1739 (81.7)	340 (88.1)	118 (73.3)	700 (85.8)	364 (79.1)	108 (63.2)	109 (80.7)	
Intracerebral hemorrhage	264 (12.4)	28 (7.3)	27 (16.8)	92 (11.3)	65 (14.1)	43 (25.2)	9 (6.7)	
SAH	62 (2.9)	2 (0.5)	3 (1.9)	20 (2.5)	22 (4.8)	7 (4.1)	8 (5.9)	
Unclassified/unknown	64 (3.0)	16 (4.2)	13 (8.1)	4 (0.5)	9 (2.0)	13 (7.6)	9 (6.7)	

*Patients with missing values in the respective variable were excluded.

†P value for differences among the centers adjusted for age and sex as appropriate by logistic regression.

‡In Menorca, data on risk factors were collected only for the first year.

IQR indicates interquartile range.

sex and center. Age-specific rates were calculated for 7 age groups in 10-year time intervals starting from 0 to 24 years up to ≥75 years. The latter age category was chosen as highest age group because data on older age groups were not available for all source populations. Mean European incidence rates were calculated as arithmetic mean of the center specific age-adjusted incidence rates as the source populations varies substantially between the centers. CIs for the incidence rate estimates were calculated using the Poisson distribution.¹⁹

Differences in sociodemographics, prior-to-stroke risk factors, and stroke subtypes among the centers were adjusted for variations in age and sex among the centers, as appropriate, by multivariable logistic regression and the probability value for the center effect was reported. Analyses were restricted to patients without missing values. For the incidence analyses, only one patient with unknown age from Kaunas was excluded; missing information for prior-to-stroke risk factors ranged from 5.3% for hypertension to 14.5% for smoking status. Statistical analyses were performed with SAS software, Version 9.1 (SAS Institute Inc, Cary, NC).

Ethics

Ethical approval for the study was obtained by the participating registers from their respective local ethic committee subject to local guidelines.

Results

A total of 2129 patients with first-ever stroke was included in the study. Overall, median age was 73 years (interquartile range, 62 to 81) and 1088 (51.1%) were female; 2013

(94.6%) of the patients were admitted to a hospital. The distribution of pathological subtypes was as follows: CI, 1739 (81.7%); PICH, 264 (12.4%); SAH, 62 (2.9%); and undefined, 64 (3.0%). Differences in sociodemographics, pre-stroke risk factors, and stroke subtypes among the centers are presented in Table 2. Significant variations across the centers were found for age, sex, proportions of patients admitted to a hospital, prevalence of prior-to-stroke risk factors, except history of previous transient ischemic attack, and distribution of pathological stroke subtypes (Table 2).

Differences in Stroke Incidence Among European Countries

Annual stroke incidence rates per 100 000 adjusted to the European population were for all centers 141.3 (95% CI, 118.9 to 166.6) in men and 94.6 (95% CI, 76.5 to 115.7) in women; for ischemic stroke, 114.7 (95% CI, 94.7 to 137.7) in men and 74.9 (95% CI, 58.9 to 93.9) in women; for PICH, 16.9 (95% CI, 9.8 to 27.1) in men and 12.4 (95% CI, 6.5 to 21.4) in women; for SAH, 4.8 (95% CI, 1.5 to 11.4) in men and 3.3 (95% CI, 0.7 to 9.2) in women; and for undefined, 4.9 (95% CI, 1.5 to 11.5) in men and 4.0 (95% CI, 1.1 to 10.2) in women.

Total and stroke subtype age-adjusted incidence rates in the different centers are presented in Table 3. Total stroke

Table 3. Annual Stroke Incidence Rate and 95% CI per 100 000 Population Adjusted to the European Population

	Total		CI		PICH		SAH		Undefined	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Dijon	122.5 (101.7–146.2)	75.9 (59.8–95.0)	112.6 (92.7–135.4)	64.0 (49.3–81.7)	4.0 (1.1–10.3)	7.0 (2.8–14.4)	0.8 (0.0–5.3)	0.2 (0.0–4.2)	5.1 (1.7–11.8)	4.7 (1.5–11.2)
Sesto	101.2 (82.5–123.0)	63.0 (48.5–80.7)	77.6 (61.3–96.9)	41.8 (30.1–56.6)	19.1 (11.5–29.8)	11.7 (6.0–20.6)	0.9 (0.0–5.4)	3.7 (1.0–9.8)	3.6 (0.9–9.7)	5.8 (2.1–12.7)
Kaunas	239.3 (209.9–271.6)	158.7 (135.0–185.4)	207.1 (179.8–237.3)	133.9 (112.2–158.6)	23.1 (14.7–34.7)	20.3 (12.5–31.3)	7.5 (3.1–15.0)	4.2 (1.2–10.5)	1.6 (0.1–6.6)	0.3 (0.0–4.4)
London	121.1 (100.5–144.7)	78.1 (61.8–97.5)	98.5 (80.0–119.9)	61.2 (46.9–78.6)	16.8 (9.7–26.9)	10.8 (5.4–19.4)	3.8 (1.0–9.9)	4.7 (1.5–11.2)	2.1 (0.3–7.4)	1.3 (0.1–6.2)
Menorca	116.3 (96.1–139.5)	65.8 (50.9–83.8)	73.1 (57.4–92.0)	40.8 (29.2–55.4)	27.1 (17.9–39.4)	19.7 (12.0–30.5)	7.9 (3.4–15.6)	1.5 (0.1–6.3)	8.1 (3.5–15.9)	3.9 (1.0–10.1)
Warsaw	147.2 (124.4–173.0)	125.9 (104.9–149.9)	119.3 (98.9–142.8)	107.8 (88.4–130.2)	11.2 (5.6–19.9)	4.8 (1.5–11.4)	8.1 (3.5–15.9)	5.3 (1.8–12.1)	8.6 (3.9–16.6)	8.0 (3.5–15.8)

incidence ranged in men from 101.2 (95% CI, 82.5 to 123.0) in Sesto Fiorentino to 239.3 (95% CI, 209.9 to 271.6) in Kaunas and in women from 63.0 (95% CI, 48.5 to 80.7) in Sesto Fiorentino to 158.7 (95% CI, 135.0 to 185.4) in Kaunas. Age-adjusted incidence rates were higher for men than women for total stroke and stroke subtypes except for PICH in Dijon and for SAH in Sesto Fiorentino. Total incidence rates increased with age in all centers for men and women. Compared with the mean adjusted annual incidence rate for all centers, total stroke incidence in men was higher in Kaunas and lower in Sesto Fiorentino and Menorca; in women, total stroke incidence was higher in Kaunas and Warsaw and lower in Sesto Fiorentino and Menorca (Figure). These patterns were similar for men and women for cerebral infarction in Sesto Fiorentino, Kaunas, and Warsaw; a decrease in incidence of CI for men and women in the population was slightly more pronounced in Menorca compared with total stroke incidence (Table 3). Compared with the mean adjusted incidence rates for all centers, incidence of PICH was lower in Dijon for men and in Warsaw for women; in Menorca, a higher incidence of PICH was found for men and in Kaunas for women. No other substantial differences in stroke incidence for PICH and SAH were observed among the populations.

Discussion

This is the first multipopulation study without age restriction using identical study criteria and periods of observation for presenting comparable information on stroke incidence from 6 European countries. Considerable differences in total stroke incidence were found across Europe. On average, lower rates of total stroke incidence were found in southern and higher rates in eastern European countries, especially in women. The observed variations in stroke incidence among the centers were mainly caused by differences in the incidence of CI. Incidence of PICH was found to be lower in men in Dijon, France, and in women in Warsaw, Poland; in Menorca, Spain, the incidence of PICH was higher in men and in Kaunas, Lithuania, in women. No other substantial differences in

incidence of hemorrhagic stroke were observed among European centers.

The observation of highest rates of total stroke incidence in eastern and lowest rates in southern European countries is comparable to previous studies. The WHO MONICA Project was the first, and until today the only, multinational study reported on geographical variations in stroke incidence using uniform criteria. Data collection in the WHO MONICA Project began between 1982 and 1985¹² and in 14 populations from 9 countries, data are available up to the early/mid-1990s.²⁰ In the last 3 years of the WHO MONICA Project, total stroke event rates were highest in Novosibirsk, Russia, followed by Kaunas, Lithuania, and lowest in Friuli, Italy.²⁰ At the end of the study, event rates varied between Novosibirsk, Russia, and Friuli, Italy, 3.7- and 6.6-fold in men and women, respectively, and between Kaunas, Lithuania, and Friuli, Italy, 2.9- and 3.1-fold, respectively.²⁰ Similar to these findings, we found highest rates of total stroke incidence rates in Kaunas, Lithuania, and lowest rates in Sesto Fiorentino, Italy. However, variation was slightly lower in our study with a 2.2-fold difference in total stroke incidence in men and a 2.3-fold difference in women between Kaunas and Sesto Fiorentino. This difference might be caused by the fact that in the WHO MONICA Project, event rates (first and recurrent strokes) rather than incidence rates (first stroke only) were reported because in some centers, separation of first and recurrent events was not always possible.²¹ In addition, in the WHO MONICA Project, only patients between 25 and 64 years of age were included¹² and the comparisons of the last 3 years of registration based on the age group 35 to 64 years.²⁰ In our data, the median age of the patients was 73 years and 46% of all first ever-stroke occurred in patients ≥ 75 years. Thus, the introduction of an upper age limit might limit the generalizability of the data in terms of estimating the true impact of stroke for societies.²² A recent overview of results from population-based stroke registers in the 1990s found smaller geographical variations in total stroke incidence compared with the WHO MONICA Project, except higher incidence rates of stroke in eastern European countries (Russia, Ukraine), similar to our findings.⁴

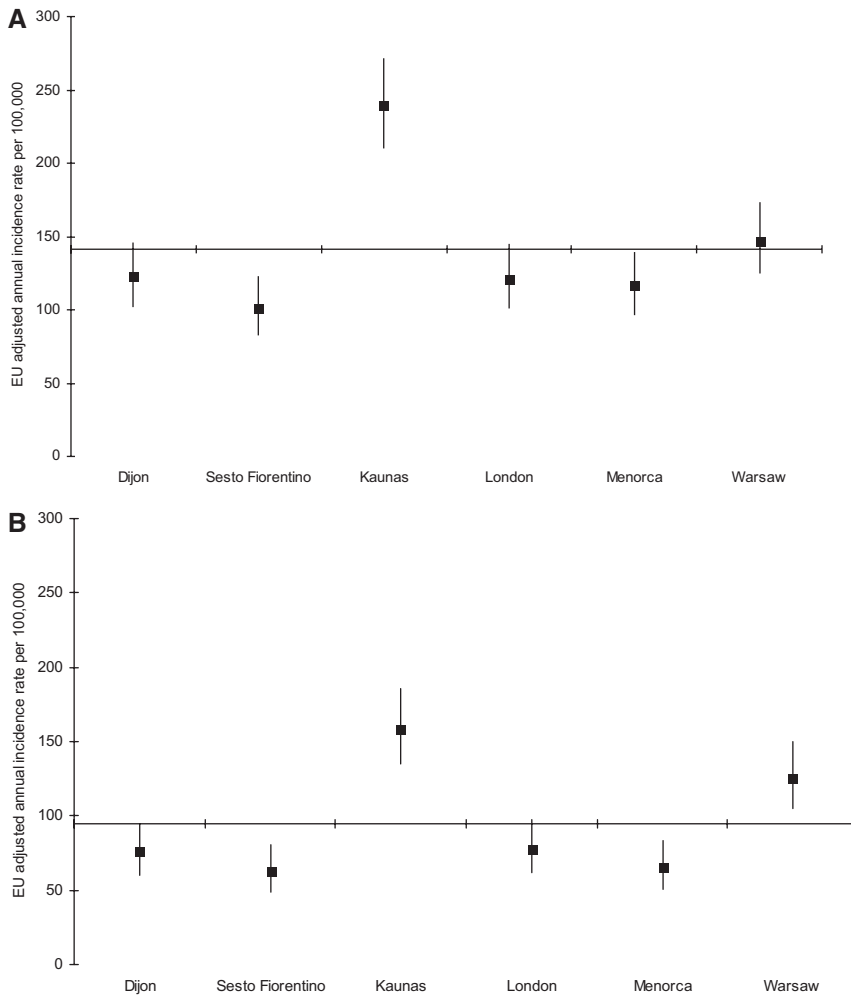


Figure. A, Annual stroke incidence rate and 95% CI per 100 000 population adjusted to the European population for males; the line represents the mean annual incidence rate adjusted to the European population for all centers. B, Annual stroke incidence rate and 95% CI per 100 000 population adjusted to the European population for females; the line represents the mean annual incidence rate adjusted to the European population for all centers.

The main variations in stroke incidence among the centers in our study were found for CI, with higher rates of CI in Kaunas, Lithuania, for men and women and in Warsaw, Poland, for women. In agreement with these findings, highest prevalence of prior-to-stroke hypertension and atrial fibrillation, risk factors associated with a great attributable risk for stroke,^{23,24} was found in Kaunas and Warsaw, the centers with the highest incidence of CI. On the other hand, risk of CI was lowest for men and women in Sesto Fiorentino, Italy, and Menorca, Spain, corresponding to a lower prevalence of prior-to-stroke hypertension and atrial fibrillation in these centers. The observed differences in risk of CI between the centers might also be caused by differences in lifestyle factors such as dietary habits. Adherence to a Mediterranean diet is associated with lower risk of death from coronary heart disease.²⁵ Although data on the direct association of stroke and Mediterranean diet are lacking, coronary heart disease and stroke share similar risk factors and, thus, similar effects of dietary habits and morbidity risk can be assumed.²⁶ In addition, healthcare systems in the participating countries might differ in terms of primary prevention strategies for the populations. No substantial variations in risk of CI were observed in the participating centers between men and women, except a higher risk of CI for women but not for men in Warsaw, Poland. Different developments in trends in

vascular risk factors between men and women in the general population in Poland might contribute to the gender differences in stroke risk. For example, the proportion of daily cigarette smokers aged 35 to 64 years in Poland in the CHD WHO MONICA Project showed a significant decrease in men but no changes in women over a 10-year study period.²⁷

Variations in incidence of PICH among the participating European countries were only seen in Dijon, Warsaw, Menorca, and Kaunas. The reasons for the lower rate of PICH in men in Dijon and in women in Warsaw remain unclear. No substantial variations in the proportion of main risk factors for PICH, hypertension and smoking, were observed between Dijon and the other centers and the prevalence of hypertension and smoking was even higher in Warsaw compared with the other centers. Thus, the lower incidence of PICH in Dijon and Warsaw might be attributed to variations in other, not recorded, risk factors such as dietary habits or to differences in genetic risk among populations. We observed higher incidence rates of PICH in Menorca, Spain, but were not able to link the observed increase in risk of PICH with a higher prevalence of main prior-to-stroke risk factors among patients in Menorca, including for hypertension as the most important risk factor for PICH. However, differences in the management of hypertension in the general population compared with other countries might contribute to the higher incidence

of PICH in Menorca because poor blood pressure control in the general population is associated with a higher stroke mortality.²⁸

A higher risk of SAH is partly associated with vascular risk factors such as smoking.^{29,30} However, SAH is most frequently caused by vascular malformations, and the risk of vascular malformations is influenced by genetic factors.³¹ Thus, the lack of a difference in risk of SAH among the centers might be caused by the greater impact of genetic factors on risk of SAH compared with other pathological subtypes. Therefore, the overall risk of SAH observed in our study might be similar to an average risk for SAH in the European populations.

Overall, in only 3% of all strokes, pathological stroke subtype could not be defined based on diagnostic tests, ranging from 1% to 8% in the centers. This proportion is remarkably low compared with previous population-based studies from the 1990s with a range of unclassified strokes from 2% up to 15%.⁴ The lower proportion of undefined strokes in our study might reflect a higher recognition of stroke as a medical emergency since the 1990s requiring immediate diagnostic verification among hospitalized as well as nonhospitalized patients with stroke. The proportion of patients with stroke admitted to a hospital in previous population-based studies from the 1990s was on average 81%, ranging from 41% to 95%.⁴ In our study, overall 95% of all patients with stroke were admitted to a hospital, ranging from 88% up to 97% among the centers. The diagnostic uptake is higher in hospitalized compared with nonhospitalized patients.³² Thus, the validity of diagnosis of pathological stroke subtypes in our study might be higher compared with previous studies.

Our study has strengths and limitations. Population-based stroke registers without age restriction have been implemented using uniform standardized criteria and observing similar observation periods for providing comparable data on variations in stroke incidence in participating centers. The centers were selected based on their previous experience in running stroke registers for increasing validity of case detection and case ascertainment. However, we cannot exclude that the results for each center may not be representative for the respective country. We introduced standardized criteria for case ascertainment among the centers, including multiple sources of information,^{5,6} to ensure completeness of case ascertainment and external site visits were performed to control adherence of centers to the defined standards. However, we were not able to provide any assessment of completeness of case ascertainment for all centers, eg, using capture–recapture methods.³³ Some of the variation in stroke incidence might be attributed to the observed differences in prevalence of prior-to-stroke risk factors. However, we had no information on control of these factors in individual patients and no data were available on differences in prevalence of lifestyle risk factors other than smoking, eg, dietary habits. In addition, the documentation of prior-to-stroke risk factors might vary across different centers or healthcare systems.

Conclusions

The risk of stroke among European populations in our study varied more than 2-fold in men and women. On average, higher rates of stroke were observed in eastern and lower rates in southern European countries. Differences in total stroke incidence among the participating European centers were mainly attributed to variations in risk of ischemic stroke; less variation was observed for hemorrhagic stroke. The prevalence of major risk factors for stroke differed among the centers, mainly in terms of hypertension and atrial fibrillation, and these differences might partly contribute to the observed variations in stroke risk between the populations. The impact of stroke on the European society is still substantial and sustained public health interventions and awareness campaigns for risk factor reduction are crucial, especially in eastern Europe.

Appendix

The following persons participated in the EROS project: Writing Group: Peter U. Heuschmann, Division of Health and Social Care Research, King's College London, UK, NIHR Biomedical Research Centre Guy's & St Thomas' NHS Foundation Trust and King's College London, London, UK, and Centre for Stroke Research Berlin, Charite-Universitaetsmedizin Berlin, Germany. Antonio Di Carlo, Institute of Neurosciences, Italian National Research Council, Florence, Italy, and the Department of Neurological and Psychiatric Sciences, University of Florence, Florence, Italy; Yannick Bejot, Stroke Registry of Dijon (Inserm, Invs), EA 4184, University of Burgundy, University Hospital of Dijon, Dijon, France; Daiva Rastenyte, Kaunas University of Medicine and Institute of Cardiology, c/o Kaunas University of Medicine, Kaunas, Lithuania; Danuta Ryglewicz, 1st Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland; Cinzia Sarti, National Public Health Institute, Helsinki, Finland; Mattias Torrent, Area de Salud de Menorca, *ib-salut*, Menorca, Spain; and Charles D. A. Wolfe, Division of Health and Social Care Research, King's College London, UK, and NIHR Biomedical Research Centre Guy's & St Thomas' NHS Foundation Trust and King's College London, London, UK.

Coinvestigators—Dijon: M. Giroud, Stroke Registry of Dijon, University of Burgundy, University Hospital of Dijon, Dijon, France; Sesto Fiorentino: D. Inzitari, M. Lamassa, P. Nencini, A. Poggesi, F. Pescini, and A. Cramaro, Department of Neurological and Psychiatric Sciences, University of Florence, Florence, Italy; M. Baldereschi, Institute of Neurosciences, Italian National Research Council, Florence, Italy; Kaunas: D. Sopagiene and D. Kranciukaite, Institute of Cardiology c/o Kaunas University of Medicine, Kaunas, Lithuania; London: I. Sayed and C. Coshall, Division of Health and Social Care Research, King's College London, London, UK; Menorca: J. Rodriguez-Mera, Area de Salud de Menorca, *ib-salut*, Menorca, Spain; Warsaw: H. Sienkiewicz-Jarosz, 1st Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland; M. Gluszkiewicz and A. Czlonkowska, 2nd Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland; and J. Pniewski, Neurology Department, Medical Research Centre, Polish Academy of Sciences/CSK MSWiA, Warsaw, Poland.

Data Center: V. Moltchanov, National Public Health Institute, Helsinki, Finland.

Acknowledgments

We thank all the patients and their families and the healthcare professionals involved in the different centers.

Source of Funding

This study was funded by the European Union with the Fifth Framework.

Disclosures

None.

References

1. Truelsen T, Piechowski-Jozwiak B, Bonita R, Mathers C, Bogousslavsky J, Boysen G. Stroke incidence and prevalence in Europe: a review of available data. *Eur J Neurol*. 2006;13:581–598.
2. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. *Lancet Neurol*. 2007;6:182–187.
3. Truelsen T, Heuschmann P, Bonita R, Arjundas G, Dalal P, Damasceno A, Nagaraja D, Ogunniyi A, Oveisgharan S, Radhakrishnan K, Skvortsova VI, Stakhovskaya V. Standard method for developing stroke registers in low-income and middle-income countries: experiences from a feasibility study of a stepwise approach to stroke surveillance (STEPS Stroke). *Lancet Neurol*. 2007;6:134–139.
4. Feigin VL, Lawes CMM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol*. 2003;2:43–53.
5. Feigin VL, Carter K. Editorial comment—stroke incidence studies one step closer to the elusive gold standard? *Stroke*. 2004;35:2045–2047.
6. Sudlow CL, Warlow CP. Comparing stroke incidence worldwide: what makes studies comparable? *Stroke*. 1996;27:550–558.
7. Benatru I, Rouaud O, Durier J, Contegal F, Couvreur G, Bejot Y, Osseby GV, Ben Salem D, Ricolfi F, Moreau T, Giroud M. Stable stroke incidence rates but improved case-fatality in Dijon, France, from 1985 to 2004. *Stroke*. 2006;37:1674–1679.
8. Carter K, Anderson C, Hackett M, Feigin V, Barber PA, Broad JB, Bonita R; Auckland Regional Community Stroke (ARCOS) Study Group. Trends in ethnic disparities in stroke incidence in Auckland, New Zealand, during 1981 to 2003. *Stroke*. 2006;37:56–62.
9. Kleindorfer D, Broderick J, Khoury J, Flaherty M, Woo D, Alwell K, Moomaw CJ, Schneider A, Miller R, Shukla R, Kissela B. The unchanging incidence and case-fatality of stroke in the 1990s: a population-based study. *Stroke*. 2006;37:2473–2478.
10. Rothwell PM, Coull AJ, Giles MF, Howard SC, Silver LE, Bull LM, Gutnikov SA, Edwards P, Mant D, Sackley CM, Farmer A, Sandercock PA, Dennis MS, Warlow CP, Bamford JM, Anslow P; Oxford Vascular Study. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet*. 2004;363:1925–1933.
11. Heuschmann PU, Grieve AP, Toschke AM, Rudd AG, Wolfe CD. Ethnic group disparities in 10-year trends in stroke incidence and vascular risk factors: the South London Stroke Register (SLSR). *Stroke*. 2008;39:2204–2210.
12. Thorvaldsen P, Kuulasmaa K, Rajakangas AM, Rastenyte D, Sarti C, Wilhelmsen L. Stroke trends in the WHO MONICA project. *Stroke*. 1997;28:500–506.
13. Rastenyte D, Sopagiene D, Virviciute D, Juriene K. Diverging trends in the incidence and mortality of stroke during the period of 1986–2002. A study from the stroke register in Kaunas, Lithuania. *Scand J Public Health*. 2006;34:488–495.
14. Czlonkowska A, Ryglewicz D, Weissbein T, Baranska-Gieruszczak M, Hier DB. A prospective community-based study of stroke in Warsaw, Poland. *Stroke*. 1994;25:547–551.
15. Wolfe CD, Tilling K, Beech R, Rudd AG. Variations in case fatality and dependency from stroke in western and central Europe. The European BIOMED Study of Stroke Care Group. *Stroke*. 1999;30:350–356.
16. Heidrich J, Heuschmann PU, Kolominsky-Rabas P, Rudd AG, Wolfe CD. Variations in the use of diagnostic procedures after acute stroke in Europe: results from the BIOMED II study of stroke care. *Eur J Neurol*. 2007;14:255–261.
17. Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bull World Health Organ*. 1976;54:541–552.
18. Doll R, Cook P. Summarizing indices for comparison of cancer incidence data. *Int J Cancer*. 1967;2:269–279.
19. Daly L. Simple SAS macros for the calculation of exact binomial and Poisson confidence limits. *Comput Biol Med*. 1992;22:351–361.
20. Sarti C, Stegmayr B, Tolonen H, Mahonen M, Tuomilehto J, Asplund K. Are changes in mortality from stroke caused by changes in stroke event rates or case fatality? Results from the WHO MONICA Project. *Stroke*. 2003;34:1833–1840.
21. Truelsen T, Mahonen M, Tolonen H, Asplund K, Bonita R, Vanuzzo D. Trends in stroke and coronary heart disease in the WHO MONICA Project. *Stroke*. 2003;34:1346–1352.
22. Feigin V, Hoorn SV. How to study stroke incidence. *Lancet*. 2004;363:1920.
23. Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke—a risk profile from the Framingham Study. *Stroke*. 1991;22:312–318.
24. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991;22:983–988.
25. Trichopoulos A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003;348:2599–2608.
26. Willett WC. The Mediterranean diet: science and practice. *Public Health Nutr*. 2006;9:105–110.
27. Evans A, Tolonen H, Hense HW, Ferrario M, Sans S, Kuulasmaa K. Trends in coronary risk factors in the WHO MONICA project. *Int J Epidemiol*. 2001;30:S35–S40.
28. Redón J, Cea-Calvo L, Lozano JV, Martí-Canales JC, Listerri JL, Aznar J, González-Esteban J; PREV-ICTUS Study. Differences in blood pressure control and stroke mortality across Spain: the Prevencion de Riesgo de Ictus (PREV-ICTUS) study. *Hypertension*. 2007;49:799–805.
29. Kurth T, Kase CS, Berger K, Schaeffner ES, Buring JE, Gaziano JM. Smoking and the risk of hemorrhagic stroke in men. *Stroke*. 2003;34:1151–1155.
30. Kurth T, Kase CS, Berger K, Gaziano JM, Cook NR, Buring JE. Smoking and risk of hemorrhagic stroke in women. *Stroke*. 2003;34:2792–2795.
31. Markus HS, Alberts MJ. Update on genetics of stroke and cerebrovascular disease 2005. *Stroke*. 2006;37:288–290.
32. Bhalla A, Dundas R, Rudd AG, Wolfe CD. Does admission to hospital improve the outcome for stroke patients? *Age Ageing*. 2001;30:197–203.
33. Tilling K, Sterne JA, Wolfe CD. Estimation of the incidence of stroke using a capture–recapture model including covariates. *Int J Epidemiol*. 2001;30:1351–1359.