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Incidence and Case-Fatality of Stroke on the East Border of the European Union

The Grodno Stroke Study

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Background and Purpose—The epidemiology of stroke in Belarus is unclear. Therefore, a population-based register of stroke was set up in western Belarus to determine incidence and case-fatality in a defined urban population.

Methods—The Grodno Stroke Study is a prospective community-based research among 311 134 residents of the city of Grodno, Belarus. Standard definitions and multiple overlapping sources of ascertainment were used to identify all cases of first-ever-in-a-lifetime strokes in all age groups occurring between January 1, 2001, and December 31, 2003.

Results—During 3 years, 2069 cases of first-ever-in-a-lifetime strokes were registered. Mean age at stroke onset was 65.8 ± 11.6 years; rate of hospitalization was 89.7%. The crude annual incidence rate of first-ever-in-a-lifetime strokes for the study period was 222 per 100 000 (95% CI, 212 to 233). Incidence adjusted to the European standard population and to the World Health Organization world standard population was 287 per 100 000 (95% CI, 274 to 301) and 220 per 100 000 (95% CI, 210 to 231), respectively. The 28-day case-fatality rate was 26.1%. The prevalence of hypertension among all first-ever-in-a-lifetime stroke patients was 87.5%; 529 (25.6%) were current smokers. A total 23.1% of patients had atrial fibrillation, 19.1% had past myocardial infarction, 14.7% had diabetes mellitus, and 22.1% had hypercholesterolemia.

Conclusions—High incidence and case-fatality rates determine the considerable burden of stroke in Belarus and might at least partly be related to the high prevalence of risk factors among the population. (*Stroke*. 2010;41:2726-2730.)

Key Words: case-fatality ■ epidemiology ■ incidence ■ population-based ■ stroke

Stroke is one of the leading causes of death and disability in Europe and absorbs a considerable proportion of healthcare budgets.¹⁻⁴ The most reliable data on stroke incidence and case-fatality come from population-based incidence studies.⁵ They increase social knowledge of stroke epidemiology and facilitate healthcare planning, prevention, and management of stroke. No population-based study on stroke epidemiology has been performed in Belarus up to date. Belarus is a landlocked east European non-European Union country with a population of 9.6 million inhabitants and has 1 of the lowest life expectancies in Europe, exactly being on rank 105 by expectancy within the United Nations human development index of 2007.⁶ According to the World Bank's country classification, it belongs to the upper middle income group. The Grodno Stroke Study (GROSS) is a community-based, prospective study of stroke incidence and outcome in a large defined urban population of Belarus.

Subjects and Methods

Study Area and Population

Grodno is an urban area in western Belarus. According to the data of the Grodno Regional Statistical Department, in the year 2002, average annual population was 311 134 inhabitants (estimates of 1999 census data); the proportion of people aged ≥ 65 years was 8.0%. The population is a mixture of Belarusian (62%), Polish (24%), Russian (10%), Ukrainian (2%), Jewish (0.4%), Lithuanian (0.3%), and Tatar (0.3%) ethnicity. There were no considerable migration and change in the ethnic structure of the population during the last 30 years.

There is the unified state health care in Belarus which is free of charge, and all inhabitants have the equal access to medical aid. Since Year 2000, a system of staged health care for patients with stroke has been in use in Belarus. According to it, all patients with stroke must be referred to specialized stroke neurological departments (in large cities) or stroke wards (in small towns). There is a stroke neurological department for 60 beds (including an intensive care unit for 6 beds) in Grodno City Clinical Hospital No. 1. All

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patients with suspected stroke revealed by emergency service, neurologists at outpatient clinics, and general practitioners are referred to this department where a neurologist is available 24 hours a day. A small proportion of patients with stroke is treated at home. They are usually patients with minor stroke who refuse to be admitted to the hospital or severely disabled patients with just another recurrent stroke. The small number of patients is treated at other city hospitals: patients with in-hospital minor strokes, patients with severe strokes and contraindications for transportation, and patients with primary intracerebral hemorrhage referred for surgical treatment. If a patient dies due to stroke (or any other disease) before receiving medical care, an autopsy is obligatory.

Case Ascertainment

All suspected strokes occurred among residents of Grodno between January 1, 2001, and December 31, 2003, were identified and assessed for all age groups. Patients who had a stroke at the time of temporarily being away from Grodno were included, but visitors to Grodno who had no permanent registration at the place of residence were excluded. Standard criteria for stroke were used.⁷ All cases were categorized as first-ever-in-a-lifetime strokes (FELS) or recurrent strokes on the basis of the clinical history rather than the findings on brain imaging. A fatal event was defined as death within 28 days of the onset of an acute stroke.

We used multiple overlapping sources of ascertainment as suggested by Sudlow and Warlow⁸: (1) daily review of admission and discharge records of the stroke neurological department; 3 doctors of this department were involved in the study; (2) weekly personal or telephone contact with chief general practitioners and neurologists of 12 areas covered by 4 city outpatient clinics; 1 neurologist in each outpatient clinic was responsible for the study; he or she also checked for cases of stroke medical records of the patients who were treated outside the city; (3) weekly telephone enquiries with neurologists of another 5 city hospitals about new cases of stroke; (4) weekly checks of emergency service calls; (5) weekly review of all autopsy protocols; and (6) weekly checks of all death certificates; for patients who died at home without autopsy, medical records were reviewed; cases were registered as a stroke only if a focal neurological deficit could be confirmed; fatal cases involving sudden loss of consciousness or sudden death without neurological deficit were excluded. The additional post hoc control for survivors was made with official registers of subsidized prescriptions for poststroke treatment at outpatient clinics.

Basic demographic data and main vascular risk factors (hypertension, current smoking, atrial fibrillation, past myocardial infarction, hypercholesterolemia, and diabetes mellitus) were recorded for all patients when available. Hypertension was defined as a history of hypertension or newly diagnosed hypertension according to World Health Organization-International Society of Hypertension 1999 criteria⁹ after admission to the hospital due to stroke. Smoking was defined as current daily smoking at least 1 cigarette. Diabetes was defined as history of diabetes mellitus or newly diagnosed diabetes mellitus by an endocrinologist according to World Health Organization 1999 criteria¹⁰ after admission to the hospital due to stroke. Atrial fibrillation and previous myocardial infarction were defined as concurrent with stroke permanent or transient atrial fibrillation revealed on electrocardiogram and history of myocardial infarction and electrocardiographic data, respectively. Hypercholesterolemia was defined as value of total cholesterol ≥ 5.17 mmol/L (measured during the acute phase of stroke).

Statistical Analysis

All patients' data were introduced into an electronic database; integrity of the database was controlled by the principal investigator (S.D.K.) personally. The incidence and mortality because of stroke is expressed in the number per 100 000 persons by age and sex with corresponding 95% CIs, which were calculated assuming a Poisson distribution for the number of events. To make results comparable with other population-based studies, data are presented in 10-year age bands and adjusted to the standard European population and to the World Health Organization world population.¹¹ Analyses were

processed using STATISTICA (data analysis software system), Version 6.0 (StatSoft, Inc, Tulsa, Okla).

Results

During 3 years, 2923 suspected stroke cases were identified. One hundred seventy-six cases were excluded because of a final diagnosis other than stroke: transient ischemic attack ($n=87$), brain tumor ($n=27$), vascular dementia ($n=14$), vestibular neuritis ($n=12$), craniocerebral trauma ($n=11$), encephalitis ($n=7$), hypertensive encephalopathy ($n=6$), benign paroxysmal vertigo ($n=5$), metabolic encephalopathy ($n=5$), and migraine ($n=2$). Exclusion was made on the basis of a combination of clinical findings and CT/MRI or autopsy in 77 patients (43.7%) and on the basis of clinical findings only in 99 patients (56.3%). Twenty-three more patients were excluded due to their residency outside of Grodno. Of the remaining 2724 cases, 652 (23.9%) were recurrent strokes; 3 cases of nontraumatic subdural hematoma were also excluded. Finally, 2069 patients (1015 men and 1054 women) with confirmed diagnosis of FELS were included in the assessment.

In 627 (30.3%) patients, brain CT scan ($n=519$) or MRI ($n=108$) was performed. Autopsies were performed in 346 patients, of whom 65 had premortem brain imaging. In total, 908 (43.9%) patients underwent either neuroimaging or autopsy, and it was not possible to analyze reliably stroke subtypes in this study.

Patients' age ranged from 16 to 106 years (mean \pm SD age, 65.8 ± 11.6 years). Men were approximately 6 years younger than women (62.7 ± 11.3 versus 68.8 ± 11.0 years, $P < 0.001$). Rate of hospitalization was 89.7% (1855 patients); 179 patients (8.6%) were treated at home, and 35 patients (1.7%) died before medical treatment.

The Table shows the age- and sex-specific incidence of FELS per 100 000 per year. The crude annual incidence rate of FELS for the period 2001 through 2003 was 222 per 100 000 (95% CI, 212 to 233); for men 234 (95% CI, 220 to 248) and for women 211 (95% CI, 198 to 224). Incidence adjusted to the European standard population and to the World Health Organization world standard population was 287 per 100 000 (95% CI, 274 to 301) and 220 per 100 000 (95% CI, 210 to 231), respectively.

The incidence rates increased significantly with each decade of life up to the age group 75 to 84 years inclusively (2161 per 100 000; 95% CI, 1969 to 2377; Figure) and were higher in men than in women. In the age group of ≥ 85 years, the significant decline of incidence to 1494 per 100 000 (95% CI, 1151 to 1943) was detected.

Five hundred forty-one patients (26.1%) died within 28 days of stroke onset. The 28-day case-fatality rate was 24.4% for men and 27.8% for women. The crude annual mortality rate of FELS was 58 per 100 000 (95% CI, 53 to 63); for men 57/100 000 (95% CI, 50 to 64) and for women 59 per 100 000 (95% CI, 53 to 66). Age-specific mortality data are shown in the Figure.

The prevalence of hypertension among all FELS patients was 87.5%; 529 (25.6%) were current smokers. A total of 23.1% of the patients had atrial fibrillation, 19.1% had past myocardial infarction, and 14.7% had diabetes mellitus. The

Table. Age- and Sex-Specific Annual Incidence of FELS per 100 000 Person-Years in Grodno, Belarus, 2001 to 2003

Age Group, Years	Men			Women			Total		
	No./No. at Risk	Rate	95% CI	No./No. at Risk	Rate	95% CI	No./No. at Risk	Rate	95% CI
<25	3/57 669	2	0.4–5	0/58 085	0	...	3/115 754	1	0.2–3
25–34	8/22 945	12	5–23	3/25 198	4	1–12	11/48 143	8	4–14
35–44	40/25 180	53	38–72	20/29 075	23	14–35	60/54 255	37	28–48
45–54	192/18 952	338	293–388	109/23 580	154	126–188	301/42 532	236	210–264
55–64	328/11 239	973	875–1080	188/14 185	442	381–512	516/25 424	677	619–737
65–74	286/6270	1520	1356–1703	382/10 484	1215	1100–1336	668/16 754	1329	1233–1435
75–84	146/2025	2403	2028–2836	305/4931	2062	1839–2309	451/6956	2161	1969–2377
≥85	12/299	1338	692–2341	47/1017	1540	1123–2064	59/1316	1494	1151–1943
All	1015/144 579	234	220–248	1054/166 555	211	198–224	2069/311 134	222	212–233
Total ASR*		356	334–377		236	222–250		287	274–301
Total ASR†		266	250–282		180	169–191		220	210–231

*Age-standardized rates (ASR) adjusted to the European population.

†Age-standardized rates adjusted to the World Health Organization world population.¹⁰

level of total cholesterol was measured in 556 of FELS patients, and hypercholesterolemia was detected in 123 of them (22.1%).

Discussion

GROSS is the first population-based register providing epidemiological data on stroke incidence and case-fatality in Belarus. The basic eligibility criteria for community-based registers were used: multiple overlapping sources of ascertainment, prospective study design, large well-defined stable population, and recent census data.^{5,8} Careful case ascertainment was the most important issue in this study, because published official incidence statistics of cerebrovascular diseases in Belarus over 1995 to 2000 demonstrated contradictory and differently directed trends in some regions of the country with up to a 10-fold difference in rates during 1 to 2 years.¹² Therefore, in GROSS, we made every effort to ensure near-complete case ascertainment of all FELS cases (6 overlapping sources). The fact that 199 cases of suspected stroke were excluded indicates the overinclusive approach taken in finding cases in the community.

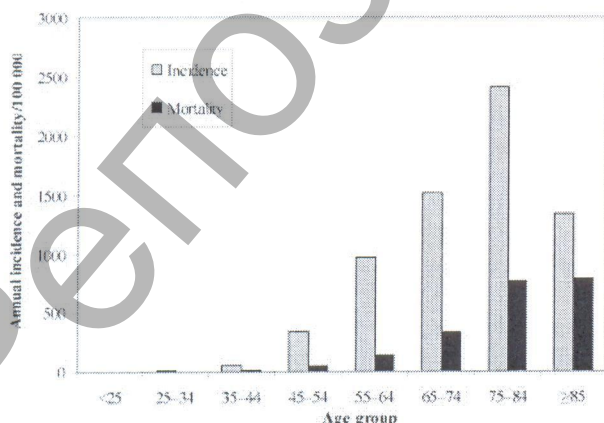


Figure. Annual incidence and mortality of FELS per 100 000 in Grodno, Belarus, 2001 to 2003.

To evaluate the data quality obtained in our study, we used 5 key indicators identified by Asplund et al in the World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) stroke study¹³: (1) the ratio of fatal cases in the GROSS to stroke deaths in routine mortality statistics is 0.86. This is higher than the limit of 0.75, which was set as an indicator of possible underreporting of stroke deaths in the register¹³; (2) the proportion of fatal cases that are not hospitalized should be >10%; in GROSS, this indicator is 24.8% (134 of 541); (3) with the 26.1% 28-day case-fatality, our study would rank tenth among the 21 MONICA populations; therefore, we suggest that not too many nonfatal events were missed in our register; (4) the proportion of nonfatal cases that are not hospitalized in GROSS is 3.9% (80 of 2069), and our study would rank also tenth among the 21 MONICA populations; therefore, we think case ascertainment in our register is not less than optimal; and (5) the proportion of fatal cases autopsied or examined by a physician before death ranged from 31% to 100% in the 21 MONICA populations and is 99.3% (537 of 541) in our study; therefore, we suggest that the accuracy of the assignment of diagnostic category in fatal cases was required. Thus, GROSS fulfilled all 5 criteria allowing multinational comparisons.¹³

Among the advantages of our study, we can point to the large defined study population, the big number of registered stroke cases, high rate of hospitalization, concentration of patients in hospital (86% of all FELS were treated in Grodno City Clinical Hospital No. 1), and high rate of autopsies in patients with stroke who died before medical treatment (89% [31 of 35]).

Our study has a number of limitations: low rate (43.9%) of imaging/autopsy, absence of computer databases for searching nonhospitalized cases, and lack of data concerning etiology for ischemic strokes. For these reasons, misdiagnosis of stroke in GROSS might have occurred, thereby leading to the inclusion of patients with stroke-like episodes but no strokes. On the other hand, it is possible that some cases of

stroke (especially minor ones) were missed, but the same limitation affects most population-based registers.

The age-standardized rate (to the World Health Organization world standard population) of stroke incidence in Grodno of 220 per 100 000 (95% CI, 210 to 231) is high as compared with other published studies. Among 69 population-based registers from the recent review of Feigin et al,⁵ arranged according to descending age-standardized incidence, the GROSS rate takes 14th. FELS incidence in Grodno is higher than in the most countries of the European Union, except of Finland (Turku),¹⁴ Sweden (Soderhamn),¹⁵ Portugal (Porto, rural population),¹⁶ and Estonia (Tartu, 1991 to 1993)¹⁷; is similar to those reported from the Ukraine (Uzhgorod, 238 per 100 000)¹⁸ and Russia (Krasnoyarsk, 233 per 100 000; Novosibirsk, 1982, 203 per 100 000)^{19,20}; but higher than those reported from other low- to middle-income countries from all parts of the world.⁵ Incidence in men is higher than in women as in most other series.

Mean age at stroke onset in Grodno (65.8 ± 11.6 years) is broadly similar to those of the studies from low- to middle-income countries. Thus, it is equal to the corresponding total index (65.8 years) of 4 2000 to 2008 registers from low- to middle-income countries (Georgia, Chile, Brazil, India)^{21–24} included in the mentioned review.⁵ At the same time, the mean age at stroke onset in GROSS is lower than those in population-based studies from high-income countries in 1990 to 2008. For example, it is significantly ($P < 0.00001$) lower than the corresponding total index (70.7 ± 13.8 years) in 6 countries of the European Registers of Stroke (EROS) project.²⁵

Such a younger age of the patients in GROSS may explain the peculiar shift of peak incidence rates toward the group of 75 to 84 years, whereas most studies describe a constant increase of rates with each decade with a maximum in the age group ≥ 85 years. Theoretically, the lower stroke incidence, which we found in the latter group compared with the younger one, might be due to the inadequate identification of stroke cases in the very old population. However, in conditions of the current Belarusian healthcare system for stroke and sources of ascertainment used in GROSS, there was no difference in registration of patients aged 75 to ≥ 84 years. Moreover, the similar shift was also observed in Novosibirsk (1984, 1987, 1992 years of registration)²⁰ and in Uzhgorod.¹⁸ In Tbilisi, Georgia, rates in both mentioned groups were almost equal (1029 per 100 000 to 1030 per 100 000, accordingly),²¹ and in Iquique, Chile, only a slight increase in the older group was detected (1037 per 100 000 to 1089 per 100 000, accordingly).²² In our opinion, the shift of peak incidence rates toward the group of 75 to 84 years detected in our study is real and it is connected with the lower mean age at stroke onset. We agree with the standpoint of Bejot and Giroud that this index is an instructive tool, which gives meaning to the findings provided by epidemiological studies.²⁶

The 28-day case-fatality rate in Grodno (26.1%) is high. Among 58 population-based registers from the review of Feigin et al⁵ (11 studies did not report such rate), arranged in decreasing sequence, the GROSS rate takes 20th. Although early case-fatality in Grodno is lower than in 3 of 4 2000 to 2008 registers from low- to middle-income countries,^{21–24} it is

considerably higher than the goal for 2015 (15%), which was set in the Helsingborg Declaration 2006.¹ The high case-fatality rate may partly be caused by underascertainment of mild strokes and excess of hemorrhagic strokes characterized by higher mortality.

In comparison with other 2000 to 2008 registers,^{22,24,25,27–30} the prevalence of main vascular risk factors in GROSS is high. The rate of hypertension (87.5%) is the highest as reported, although definition of this factor was different in Dijon²⁷ and Oxford²⁸ as well as in Tartu²⁹ and Perth,³⁰ in which hypertension was not especially defined. The prevalence of atrial fibrillation is similar to Dijon²⁷ and total prevalence in the EROS project,²⁵ higher than in Oxford²⁸ and Iquique,²² but lower than in Tartu.²⁹ The rate of previous myocardial infarction (19.1%) is also similar to Dijon (17.9%, $P > 0.05$),²⁷ but significantly higher ($P < 0.05$) as compared with findings of Tartu,²⁹ Oxford,²⁸ the EROS registers,²⁵ and Iquique.²² The prevalence of diabetes mellitus in the incident-stroke Grodno population (14.7%) is between the highest in Iquique (21%)²² and the lowest in Oxford (9.5%),²⁸ whereas the prevalence of current smoking is significantly higher ($P < 0.01$) as compared with other reported data. The rating of hypercholesterolemia is complicated by a low proportion of measurements in GROSS (556 of 2069) and different definitions of this factor in other studies.

In summary, the age-standardized stroke rate in an urban population of Belarus is higher than in the most developed and developing countries. The mean age at stroke onset is comparable to that reported in low- to middle-income countries and lower than in high-income countries. High incidence and case-fatality rates determine the considerable burden of stroke in Belarus and might at least partly be related to the high prevalence of risk factors among the population. The high case-fatality rate may partly be caused by underascertainment of mild strokes and excess of hemorrhagic strokes characterized by higher mortality.

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Disclosures

None.

References

1. Kjellstrom T, Norrving B, Shatchkute A. Helsingborg Declaration 2006 on European stroke strategies. *Cerebrovasc Dis*. 2007;23:231–241.
2. Kolominsky-Rabas PL, Sarti C, Heuschmann PU, Graf C, Siemonsen S, Neundoerfer B, Katalinic A, Lang E, Gassmann KG, von Stockert TR. A prospective community-based study of stroke in Germany—the Erlangen Stroke Project (ESPro). *Stroke*. 1998;29:2501–2506.
3. Kolominsky-Rabas PL, Heuschmann PU, Marschall D, Emmert M, Baltzer N, Neundörfer B, Schöffski O, Krobot KJ; for the CompetenceNet Stroke. Lifetime cost of ischemic stroke in Germany: Results and national projections from a population-based stroke registry: the Erlangen Stroke Project. *Stroke*. 2006;37:1179–1183.
4. 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.
5. Feigin VL, Lawes CMM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56

- population-based studies: a systematic review. *Lancet Neurol.* 2009;8:355-369.
6. Human Development Report 2009, United Nations Development Programme. Available at: http://hdrstats.undp.org/en/countries/country_fact_sheets/cty_fs_BLR.html. Accessed May 28, 2010.
 7. Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. *Bull World Health Organ.* 1980;58:113-130.
 8. Sudlow CLM, Warlow CP. Comparing stroke incidence worldwide: what makes studies comparable? *Stroke.* 1996;27:550-558.
 9. 1999 World Health Organization/International Society of Hypertension. Guidelines for the management of hypertension. *J Hypertens.* 1999;17:151-183.
 10. WHO Consultation Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Geneva: World Health Organization, 1999. Report no. 99.2. Available at: http://whqlibdoc.who.int/hq/1999/WHO_NCD_NCS_99.2.pdf. Accessed May 28, 2010.
 11. Ahmad OB, Boschi-Pinto C, Murray CJL, Lozano R, Inoue M. Age standardization of rates: a new WHO world standard. Available at: www.who.int/entity/healthinfo/paper31.pdf. Accessed May 28, 2010.
 12. Astapenko AV. An analysis of incidence statistics of cerebrovascular diseases in Belarus and its regions over 1995-2000 years. In: Smeyanovich AF, Antonov IP, eds. *Actual Problems of Neurology and Neurosurgery*. Belorusskaya nauka: Minsk, Belarus; 2003:7-13.
 13. Asplund K, Bonita R, Kuulasmaa K, Rajakangas AM, Feigin V, Schaedlich H, Suzuki K, Thorvaldsen P, Tuomilehto J. Multinational comparisons of stroke epidemiology: evaluation of case ascertainment in the WHO MONICA stroke study. *Stroke.* 1995;26:355-360.
 14. Numminen H, Kotila M, Waltimo O, Aho K, Kaste M. Declining incidence and mortality rates of stroke in Finland from 1972 to 1991: results of three population-based stroke registers. *Stroke.* 1996;27:1487-1491.
 15. Terent A. Trends in stroke incidence and 10-year survival in Soderhamn, Sweden, 1975-2001. *Stroke.* 2003;34:1353-1358.
 16. Correia M, Silva MR, Matos I, Magalhaes R, Lopes JC, Ferro JM, Silva MC. Prospective community-based study of stroke in northern Portugal: incidence and case fatality in rural and urban populations. *Stroke.* 2004;35:2048-2053.
 17. Kõrv J, Roose M, Kaasik A-E. Stroke registry of Tartu, Estonia, from 1991 through 1993. *Cerebrovasc Dis.* 1997;7:154-162.
 18. Mihalka L, Smolanka V, Bulecza B, Mulesa S, Bereczki D. A population study of stroke in west Ukraine: incidence, stroke services, and 30-day case fatality. *Stroke.* 2001;32:2227-2231.
 19. Feigin VL, Wiebers DO, Nikitin YP, Whisnant JP, Novokhatskaya MV, Belenko AI, Khatsenko VN, O'Fallon WM. Epidemiology of stroke in different regions of Siberia, Russia, 1987-1988: population-based study in Novosibirsk, Krasnoyarsk, Tynda and Anadyr. *Eur J Neurol.* 1996;3:16-22.
 20. Feigin VL, Wiebers DO, Whisnant JP, O'Fallon WM. Stroke incidence and 30-day case-fatality rates in Novosibirsk, Russia, 1982 through 1992. *Stroke.* 1995;26:924-929.
 21. Tsiskaridze A, Djibuti M, van Melle G, Lomidze G, Apridonidze S, Gaurashvili I, Piechowski-Jozwiak B, Shakarishvili R, Bogouslavsky J. Stroke incidence and 30-day case-fatality in a suburb of Tbilisi: results of the first prospective population-based study in Georgia. *Stroke.* 2004;35:2523-2538.
 22. Lavados PM, Sacks C, Prina L, Escobar A, Tossi C, Araya F, Feuerhake W, Galvez M, Salinas R, Alvarez G. Incidence, 30-day case-fatality rate, and prognosis of stroke in Iquique, Chile: a 2-year community-based prospective study (PISCIS project). *Lancet.* 2005;365:2206-2215.
 23. Minelli C, Fen LF, Minelli DPC. Stroke incidence, prognosis, 30-day, and 1-year case fatality rates in Mato, Brazil: a population-based prospective study. *Stroke.* 2007;38:2906-2911.
 24. Dalal PM, Malik S, Bhattacharjee M, Trivedi ND, Vairale J, Bhat P, Deshmukh S, Khandelwal K, Mathur VD. Population-based stroke survey in Mumbai, India: incidence and 28-day case fatality. *Neuroepidemiology.* 2008;31:254-261.
 25. The European Registers of Stroke (EROS) Investigators. Incidence of stroke in Europe at the beginning of the 21st century. *Stroke.* 2009;40:1557-1563.
 26. Bejot Y, Giroud M. Mean age at stroke onset: an instructive tool from epidemiological studies. *Eur J Neurol.* 2009;16:e3.
 27. 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.
 28. Rothwell PM, Coull AJ, Giles MF, Howard SC, Silver LE, Bull LM, Gutnikov SA, Edwards P, Mant D, Sackley CM, Farmer A, Sandercock PAG, Dennis MS, Warlow CP, Bamford JM, Anslow P. 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.
 29. Vibo R, Kõrv J, Haldre S, Roose M. First-year results of the third stroke registry in Tartu, Estonia. *Cerebrovasc Dis.* 2004;18:227-231.
 30. Islam MS, Anderson CS, Hankey GJ, Hardie K, Carter K, Broadhurst R, Jamrozik K. Trends in incidence and outcome of stroke in Perth, Western Australia during 1989 to 2001: the Perth community stroke study. *Stroke.* 2008;39:776-782.