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Effects of age, period, and cohort on stroke mortality among the Lithuanian urban population during the 24-year follow-up period

Research Article

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Abstract: The main purpose of this paper was to assess the effects of age, period, and cohort on stroke mortality among the urban Lithuanian population. Routine stroke mortality data among the Lithuanian urban population aged 25-64 years (1041 men and 724 women) between 1980 and 2004 were obtained from the official Kaunas region mortality register and classified by codes 430-438 and I60-I69 in the 9th and 10th revisions of the International Classifications of Diseases (ICD), respectively. Mortality rates per 100,000 persons for men and women were age-adjusted using the age distribution of the European Standard Population. Goodness of fit of the Poisson regression models was evaluated using the Pearson and Freeman-Tukey residuals. During the study period, mortality rates decreased from 46.8 to 33.0 per 100,000 for men, and from 20.2 to 18.1 per 100,000 for women (average annual decrease of -1.3%, $p<0.1$ for men, and -1.6%, $p<0.03$ for women). An age effect was present in both sexes. The definite upward period effect was observed from 1990 to 1994 both among men and women, and was followed by a sharp fall during 2000-2004. Cohort and period effects have contained relevant information that partially explained trends in stroke mortality among 25-64 year-olds in the Lithuanian urban population. The Poisson regression models could be applied for the examination and explanation of the different causes of the population mortality.

Keywords: *Mortality rates • Age-period-cohort model • Standardized mortality ratio*

1. Introduction

Stroke is the third most common cause of disease-related death in developed countries, third only to coronary heart disease and cancer [1]. Variations in stroke mortality could be due to age, to the time of death, and to the risk factors present in the person's early life (the cohort effect) [2]. The review of population-based studies of incidence, prevalence and mortality shows that the burden of stroke is high and likely to increase in future decades as a result of sociological, demographical and epidemiological transitions in populations. Significant differences in mortality rates from cerebrovascular diseases have been observed around the world together with a wide variation in mortality trends [3]. The highest mortality rates from cerebrovascular diseases for the population aged 25-64 years were observed in Eastern Europe and the ex-Soviet Union countries [4]. In 1990-1994, mortality rates from cerebrovascular diseases in Lithuania were the highest in the last decade: from 78.1 to 75.2/100,000 population per year among men and from 38.9 to 42.4/100,000 population among women, while the respective mortality rates in Austria were from 25.4 to 24.6/100,000 population per year among men and from 14.5 to 13.6/100,000 population among women. The mortality rates from cerebrovascular diseases in the post-Soviet countries were 5.7-fold higher among men as compared to the mortality among men in Austria, and 1.9-fold higher compared to that in Lithuania; similarly, mortality from cerebrovascular

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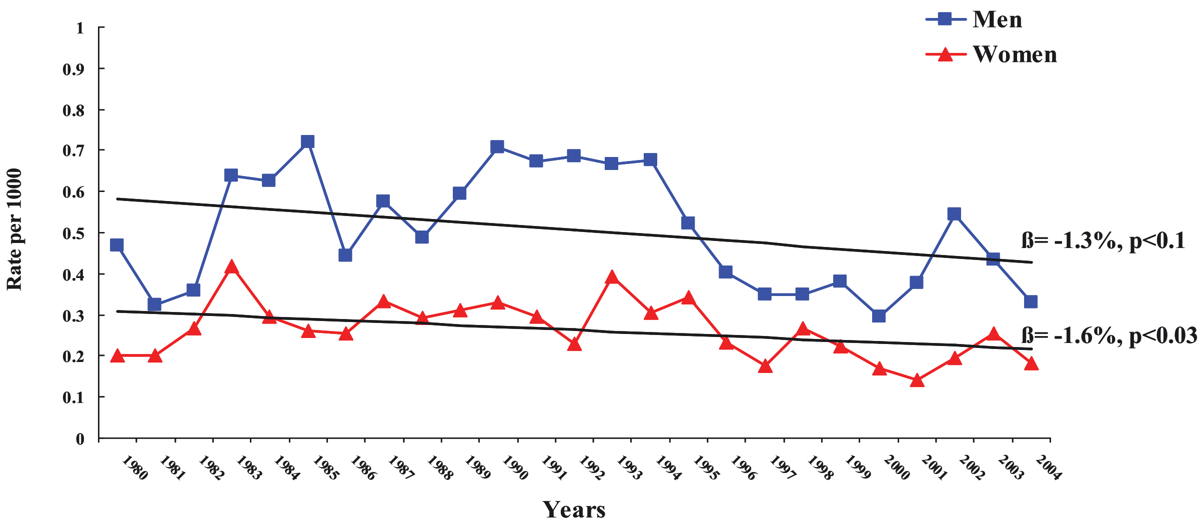
Figure 1. Time-trends in the mortality from stroke among men and women aged 25-64 years from 1980 to 2004 in Kaunas population.



diseases among women in post-Soviet countries was 5.6-fold higher than that in Austria and 2.0-fold higher than that in Lithuania. The changes in mortality may be due to either changes in the incidence of the diseases or the case-fatality rate. Incidence, in turn, is dependent on changes in cardiovascular risk profile in the community. Variations in case-fatality rate can be explained partly by changes in medical care. Changes in risk factor profile indirectly affect case-fatality by changing the severity of the disease.

The age-period-cohort model has been used to describe variations in mortality. The effect of birth cohort includes risk factors and environmental exposures that are present in early life. The effects of the period contain factors that act around the time of death. There is strong evidence that the changes in the mortality rates are associated with non-linear period and cohort effects. Age-period-cohort models are used to evaluate the changes in the mortality rates and provide the possibility to compare the later periods with the earlier periods. This paper investigates trends in mortality from stroke from 1980 to 2004 in eight age groups and five birth cohorts of the urban population in Kaunas, Lithuania, born between 1916 and 1980, and the effects of the variables - age, period and cohort - over this period.

2. Material and Methods

Age- and sex-specific stroke mortality data for men (N=1041) and for women (N=724) aged 25-64 years for the period of 1980-2004 were extracted from the official (Kaunas city, Lithuania) mortality register. For the analysis, deaths from stroke were classified according to the International Classification of Disease (ICD) 9th (430-438) and 10th (I60-I69) revisions. Mortality rates per 100,000 persons for men and women were age-adjusted using the European Standard Population. Time trends in the mortality from stroke were calculated by linear regression. Data for the Poisson regression models were compiled in such a way as to include eight age groups and five periods from 1980 through 2004, and birth cohorts from 1916 through 1980. Data analysis was made using Poisson regression statistical method. The goodness of fit of the Poisson regression models was examined by the Pearson and the Freeman-Tukey residuals. In most cases, residuals had a normal distribution. The predictor variables (age, cohort and period) were sequentially included in the model. Age was considered first because mortality increases significantly with age. The age-period and age-period-cohort models provided a significantly better fit than a model with the factors "age" and "cohort" (Table 1). Data analysis was performed, and the Poisson regression models were created using the SAS system (5).

The following regression model was used for the estimation of expected mortality from stroke rate $\hat{\pi}$:

$$\hat{\pi} = \exp(b_0 + b_1X_1 + b_2X_2 + ... + b_nX_n) \cdot \quad (1)$$

$$\ln(\hat{\pi}) = b_0 + b_1X_1 + b_2X_2 + ... + b_nX_n \, . \quad (2)$$

$b_1,...,b_n$: estimated parameters of regression model. $X_1,...,X_n$: variables of regression model, n: number of variables. The mortality rate π = N / Y. N: number of cases. Y: number of observed population.

The age-period-cohort analysis was carried out using Poisson regression to control for age, period and cohort simultaneously using a logarithmic link function. The following models were used:

Model	Equations
sex + age	$\hat{\pi}_k = \exp\left(\hat{\alpha} + \hat{\beta} \times sex_k + \sum_{i=1}^{7} \hat{\gamma}_i \times age_{ik}\right)$
sex + age + period	$\hat{\pi}_k = \exp\left(\hat{\alpha} + \hat{\beta} \times sex_k + \sum_{i=1}^{7} \hat{\gamma}_i \times age_{ik} + \sum_{j=1}^{4} \hat{\eta}_j \times period_{jk}\right)$
sex + age + cohort	$\hat{\pi}_k = \exp\left(\hat{\alpha} + \hat{\beta} \times sex_k + \sum_{i=1}^{7} \hat{\gamma}_i \times age_{ik} + \sum_{l=1}^{12} \hat{\lambda}_l \times cohort_{lk}\right)$
sex + age + period + cohort	$\hat{\pi}_k = \exp\left(\hat{\alpha} + \hat{\beta} \times sex_k + \sum_{i=1}^{7} \hat{\gamma}_i \times age_{ik} + \sum_{j=1}^{4} \hat{\eta}_j \times period_{jk} + \sum_{l=1}^{12} \hat{\lambda}_l \times cohort_{lk}\right)$

where $\hat{\pi}_k$: estimated mortality rate for people in the kth subset that are included in model; $\hat{\alpha}, \hat{\beta}, \hat{\gamma}_i, \hat{\eta}_j, \hat{\lambda}_l$: estimated parameters of model; and

$$sex_k = \begin{cases} 1, \textit{ if the } k^{th} \textit{ subset describes women}, \\ 0, \textit{ if the } k^{th} \textit{ subset describes men}; \end{cases}$$

$$age_{ik} = \begin{cases} 1, \textit{ if the } k^{th} \textit{ subset describes people from the } i^{th} \textit{ age stratum}, \\ 0, \textit{ otherwise}; \end{cases}$$

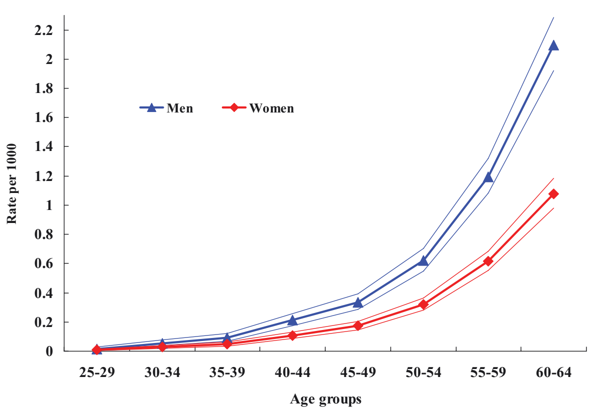
$$period_{jk} = \begin{cases} 1, \textit{ if the } k^{th} \textit{ subset describes people from the } j^{th} \textit{ period}, \\ 0, \textit{ otherwise}; \end{cases}$$

$$cohort_{lk} = \begin{cases} 1, \textit{ if the } k^{th} \textit{ subset describes people from the } l^{th} \textit{ cohort}, \\ 0, \textit{ otherwise}. \end{cases}$$

Table 1. Goodness of fit of Poisson regression models.

Model	Deviance/Degree of freedom
Sex + age	1.011
Sex + age + period	0.812
Sex + age + cohort	1.727
Sex + age + period + cohort	0.992

Figure 2. Stroke mortality rates by age and sex.



3. Results

During the studied period (1980-2004), a total of 1765 deaths (1041 deaths among men and 724 among women) occurred and were extracted from the routine death register. Figure 1 shows time-trends in the mortality from stroke among 25-64 year-old men and women from 1980 to 2004. Mortality rates for stroke decreased from 0.468 to 0.330 per 1,000 population for men and from 0.202 to 0.181 per 1,000 population for women (annual decrease of -1.3% per year, $p<0.1$ for men, and -1.6% per year, $p<0.03$ for women).

Stroke mortality increased significantly with age for both men and women, with rates being somewhat higher in men (Figure 2). Mortality rates in the young women and men age groups (25-29, 30-34, and 35-39 years of age) remained relatively stable, while increasing from the age group of 40-44 years, with the highest rates being in the age group of 60-64 years - both for men and women.

Figure 3 shows age-adjusted stroke mortality rates for males and females for the period of 1980-2004. A number of noticeable fluctuations for both men and women were evident throughout the period. For all age groups, the mortality rate increased from 1980-1984

Figure 3. Stroke mortality rates among men and women by age and periods.

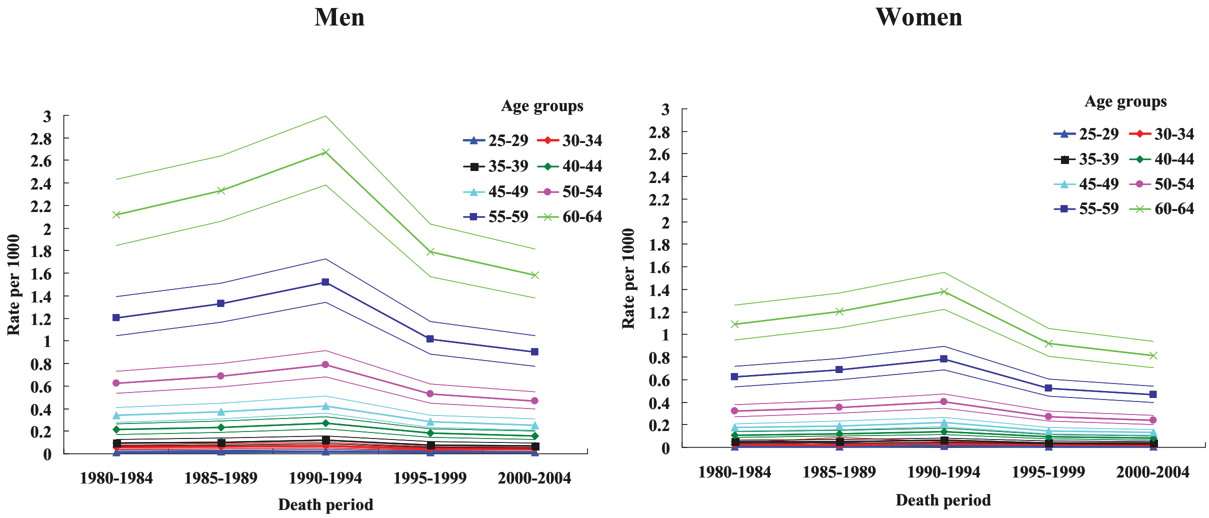
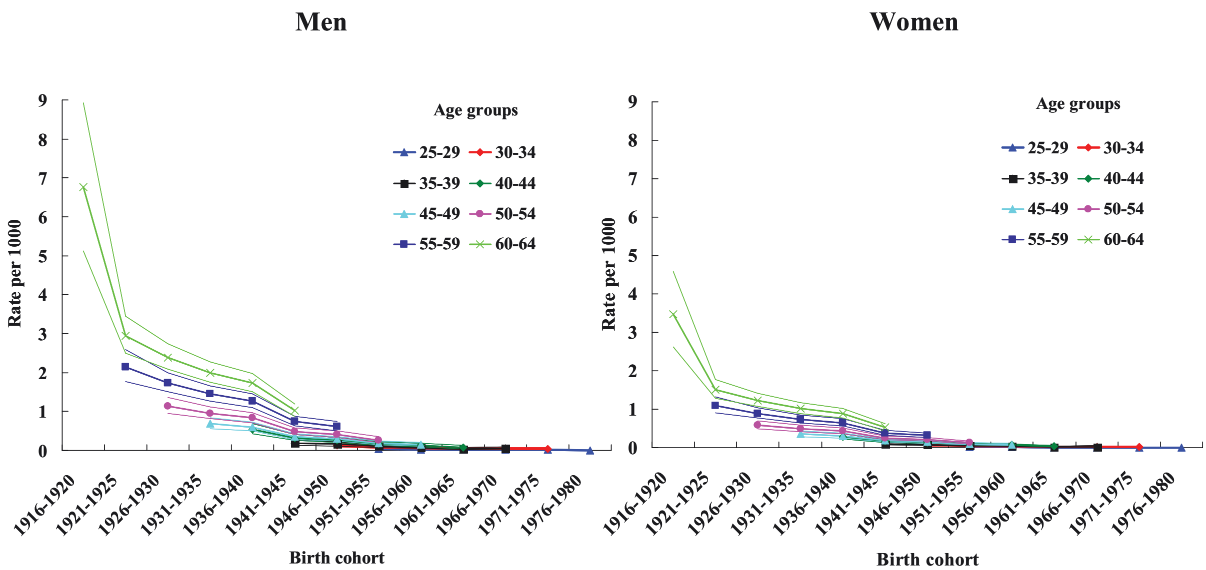


Figure 4. Stroke mortality rates among men and women by age and birth cohorts.



to 1990-1994 death period, with the peak in the 1990-1994 period. In both men and women aged 60-64 years the mortality rate (MR) peaked in 1990-1994, and men had higher MR than women (MR=2.67, 95% CI 2.38-2.99; and MR=1.38, 95% CI 1.22-1.55 for males and females respectively). The mortality rate from then on declined for both men and women, and in 2000-2004 the mortality rate was MR=1.58, 95% CI 1.38-1.82 for men and MR=0.82, 95% CI 0.71-0.94 for women.

Figure 4 shows the stroke mortality rates by sex and birth cohort. Mortality rate decreased with increasing birth cohort, i.e. mortality rates were lower in later birth cohorts. The decrease in mortality rate with increase in birth cohort was greater in the younger age groups. For the oldest group, the mortality rate decreased from 6.76 (95% CI 5.12-8.93) to 1.02 (95% CI 0.87-1.20) among men, and from 3.47 (95% CI 2.63-4.59) to 0.52 (95% CI 0.44-0.62) among women. In the age group of 45-49 years, the mortality rate decreased from 0.69 (95% CI 0.56-0.84) to 0.15 (95% CI 0.10-0.21) among men, and from 0.35 (95% CI 0.29-0.43) to 0.08 (95% CI 0.05-0.11) among women.

4. Discussion

In the most industrialized countries the declining trend of age-adjusted stroke mortality has been more rapidly decreasing since the 1960 [3]. The decrease in mortality rates has been more marked for women. Mortality from CVD increased among Lithuanian men and showed a tendency for decrease in women throughout the period of 1970-1995. The decline in mortality rates in 1985-1988 synchronized with the period of political changes in the Soviet Union and the restrictive alcohol policy. The greatest increase in CVD mortality in Lithuanian population appeared in 1991-1993, which was characterized by innovative changes in political and socioeconomic structures. In this study from 1980 to 2004, time-trends in the mortality from stroke among men did not change but significantly decreased among women. The factors underlying trends in mortality from CVD are variable and include changes in exposure to risk factors, such as decreased smoking, improvements in diet and physical exercise, and better control of hypertension. In the WHO MONICA study in Kaunas from 1983 to 2002 the prevalence of hypertension and obesity among women decreased, but among men there were no dynamics [6]. However, trends of these factors are insufficient for an explanation for the decreasing mortality rate from stroke among women and no dynamics among men. Nutritional habits have the tendency to be healthy in the Lithuanian population, as the proportion of persons in 1994-2003 using vegetable oil for cooking increased from 31% to 75%, and eating fresh vegetables from 25% to 53% [7]. On the other hand, changes in mortality from stroke could be explained by changes in incidence rate or by changes in case fatality rate. A multinational comparison of attack rates and case fatality rates of subarachnoid hemorrhage show large variations in attack rates across 11 populations in Europe and China [8]. Data from the World Health Organization MONICA study show that the incidence of stroke in Sweden has not been changing in women, whereas in men there has been a moderate shift toward higher ages during 1985-1991 [9]. Other studies from Sweden report a decreasing case fatality during the 1970-1980 years. A generally accepted view that women have a higher risk of subarachnoid hemorrhage than men does not apply to all populations. Marked differences in the outcome of this disease add to the wide gap in the burden of stroke between the East and West in Europe. The investigations of stroke in women across different ethnic groups demonstrated that there were ethnic differences emerging that were related to population changes. The stroke events were associated with high blood pressure and diabetes in Pacific women [10]. In Lithuania case fatality significantly decreased both among men and women and incidence of stroke significantly increased among women during 1986-2002 [11]. Declining case fatality can result from better medical management or a change in the severity of stroke. Strong support must be given for increasing public awareness of risk factors and warning signs of stroke, and utilizing community-based education programs and mass media [12].

The age-period-cohort models were used to analyze stroke mortality in the Kaunas urban population between 1980 and 2004. The cohorts of males and females born in 1916-1920 had higher mortality rates than younger birth cohorts. Declining mortality rates were observed both in men and women for cohorts 1926-1930 and 1946-1950. Predicted rates for stroke mortality were assessed to be 2.14 per 1000 persons and 1.1 per 1000 persons for men and women aged 55-59 respectively in 1921-1925, and 0.61 per 1000 persons and 0.31 per 1000 persons respectively in 1946-1950. Cohort effects may result from the lifetime experiences of the individuals born at a given point in time that influence the disease outcome. Currently observed patterns of association between age and mortality from stroke may result from cohort effects related to changes in diet (fat food meal and alcohol consumption) or smoking habits of adolescent and young adults over time. Thus, a young adult's dietary and/or smoking habits may influence early atherosclerosis development and subsequently risk of stroke. However, findings of our study must be interpreted carefully. The cohort values for the earliest periods especially from the 1916-1920 and 1926-1930 groups are based on a few deaths, since at that time there were no rigorous scientific methods of data information. Therefore to validate the risk from stroke mortality in different determined cohorts would seem complicated. Numerous studies estimated that genetic and environmental factors may interact to alter an individual's susceptibility to a variety of diseases including stroke. The living conditions in early childhood may influence population levels of stroke mortality [13]. A strong positive association was found between cohort specific infant mortality levels and stroke mortality rate. Stroke mortality rates for adults in England and Wales are higher among persons who had lower birth weights [14]. The odds of stroke were more than double for those with birth weights <2500 g as compared with those weighing >4000 g. Birth weight may be influenced by a variety of factors, including the mother's socioeconomic status [15]. The areas of England and Wales with current high stroke mortality rates were characterized by poor living standards when present-day 60-, 70-, 80-year olds were born. Authors hypothesize that relatively poorer maternal nutrition during pregnancy may underlie their children's relatively higher stroke-related mortality in later life. Additionally the epidemiologic data of "stroke belt" explained association between stroke mortality and region of the country [16]. South Carolina has one of the highest mortality rates in the southeastern "stroke belt" region of the US. Those born and residing in South Carolina have higher stroke mortality rates than those who were born outside and then moved to the state.

A number of reports have examined period effects to establish factors that act around the time of death. In our study time-trends in the mortality from stroke analyzed by period of death revealed a peak in the cohorts for 1990-1994 both in males and females and a subsequent fall in the 2000-2004 periods. The peaks in the cohorts coincided with the political and economical reforms in the beginning of 1989. After the collapse of the previous Soviet Union, the population of Lithuania has been exposed to the new political, economical and social changes. Inhabitants of Lithuania aged 50-64 years then seemed to be the most vulnerable group of society, who felt continuous stress and reacted negatively to the new changes in the country. In 1995-1999 there was a tendency for the stroke mortality rate to decline for every birth cohort both among men and women. In 1995-2000 healthcare services reform in Lithuania has been accompanied by major improvements in the healthcare system [17]. There has been an increase in the number of physicians per 100,000 inhabitants and the newly established primary health-care centers. Changes in mortality rate over the years could be explained by changes in case-fatality rate. The study outlined by the WHO MONICA Project during the 17-year period assessed that the 28-day case fatality and mortality rates of stroke among the Kaunas population aged 25-64 decreased significantly in both sexes [11]. Declining case-fatality can result from better medical management or a change in the severity of stroke. In Lithuanian hospitals since 1990 availability of qualified medical attention and better medical technologies were implemented and may explain a substantial improvement in case-fatality and subsequent declining period effect. These results were supported by another study [18] in which from the mid-1980s stroke incidence, particularly among more recent generations, has ceased to decrease and/or has been increasing in other western European countries and New Zealand [19,20]. Possible reasons for this rise lie in increasing survival from diabetes and heart disease, the drift toward healthier diets, and decreasing prevalence of hypertension and smoking [21].

Data on stroke mortality rates were analyzed using the mortality statistics of the 9th and 10th revisions of the ICD codes. The results of our study showed that the differences in the 9th and 10th revisions of the ICD codes are small and are in accordance with the data of Anderson and colleague [22].

In summary, the age-period-cohort model provides a method to assess significance of the three interrelated factors (age, calendar period of death, and birth cohort) on stroke mortality. Both cohort and calendar period factors contain information relevant to the explanation of variations in stroke mortality trends. Analysis of period effect disclosed a statistically significant mortality peak in the 1990-1994 years among men and women exposed to the political and socioeconomic changes in the new democratic countries. Whereas the age-period-cohort models must be applied for predictions of future stroke mortality rates, cohort effects seem to have less significance in predicting stroke mortality among the middle-aged Lithuanian population during the period of 1980 through 2004.

References

[1] Harwood R.H., The epidemiology of stroke, Brit. J. Cardiol., 2001, 8, 507-513

[2] Peltonen M., Asplund K., Age-period-cohort effects on stroke mortality in Sweden 1969-1993 and forecasts up to the year, Stroke, 2003, 27, 1981-1985

[3] WHO/Europe, European mortality database MDB, 2006

[4] Levi F., Lucchini F., Negri E., La Vecchia C., Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world, Heart, 2002, 88, 119-124

[5] The SAS System Online Doc. Cary, NC, USA, SAS Institute Inc., 2006

[6] Domarkienė S., Tamošiūnas A., Rėklaitienė R., D. Šidlauskienė D., Jurėnienė K., Margevičienė L., et al., Trends in main cardiovascular risk factors among middle-aged Kaunas population between 1983 and 2002, Medicina, 2003, 39, 1193-1199

[7] GrabauskasV., Klumbienė R., Petkevičienė J., E. Šakytė E., Kriaučionienė V., Paalanen L., et al., Health behaviour among Lithuanian adult population, 2006, Helsinki, Finland, 2007

[8] Asplund K., Mahonen M., Bonita R., A multinational comparison of subarachnoidal hemorrhage epidemiology in the WHO MONICA stroke study, Stroke, 2000, 31, 1054-1061

[9] Stegmayr B., Asplund K., Wester P.O., Trends in incidence, case fatality rate, and severity of stroke in northern Sweden, 1985-1991, Stroke, 1994, 25, 1738-1745

[10] Dyall L., Carter K., Bonita R., Anderson C., Feigin V., Kerse N., Incidence of stroke in women in Auckland, New Zealand, Ethnic trends over two decades 1981-2003, N. Z. Med. J., 2006, 19, U2309. D

[11] Rastenyte D., Sopagiene D., Virviciute D., Jureniene K., Diverging trends in the incidence and mortality of stroke during the period 1986-2002: A study from the stroke register in Kaunas, Lithuania, Scand. J. Public Health, 2006, 34, 488-495

[12] Evci E.D., Memis S., Ergin F., Beser E., A population-based study on awareness of stroke in Turkey, Eur. J. Neuro., 2007, 14, 517-522

[13] Amiri M., Kunst A.E., Jansen F., Mackenbach J.P., Cohort-specific trends in stroke mortality in seven European countries were related to infant mortality rates, J. Clin. Epidemiol., 2006, 59, 1295-1230

[14] Barker D.J.P., Lackland D.T., Prenatal influences on stroke mortality in England and Wales, Stroke, 34, 2003, 1598-1603

[15] Howard V.J., Anderson R., Johnson N.J., Sorlie P., Russell G., Evaluation of social status as a contributing factor to the stroke belt region of the United States, Stroke, 1997, 28, 936-940

[16] Lackland D.J., Egan B.M., The association birth weight and stroke in the US stroke belt, Stroke, 2003, 34, 289

[17] Lithuanian health program (in Lithuanian), Lithuanian Health Ministry, 1997

[18] Medrano J., Lopez-Abente G., Barrado G., Pollan M., Almazan J., Effects of age birth cohort, and period of death on cerebrovascular mortality in Spain, 1952 through 1991, Stroke, 1997, 28, 40-44

[19] Harmsen P., Tsipogani A., Wilhemsen L., Stroke incidence rates were unchanged, while fatality rates declined, during 1971-1987 in Geteborg, Sweden, Stroke, 1992, 23, 1410-1415

[20] Bonita R., Broad J.B., Beaglehole R., Changes in stroke incidence and case-fatality in Auckland, New Zealand, 1981-9, Lancet, 1993, 342, 1470-1473

[21] Tuomilehto J., Bonita R., Stewart A., Nissinen A., Salonen J.T., Hypertension, cigarette smoking, and the decline in stroke incidence in eastern Finland, Stroke, 1991, 22, 7-11

[22] Anderson R.N., Rosenberg H.M., Disease classification: Measuring the effect of the tenth Revision of the International Classification of Diseases on cause-of-death data in the United States, Stat. Med., 2003, 22, 1551-1570