Age–Period–Cohort Analysis of Stroke Mortality in China
Data From the Global Burden of Disease Study 2013

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Background and Purpose—Stroke has been the leading cause of death in China. The aim of this study is to assess the long-term trends of stroke mortality in China between 1994 and 2013.

Methods—The mortality data were obtained from the GBD 2013 (Global Burden of Disease Study 2013) and were analyzed with the age–period–cohort framework.

Results—We found that the net drift was −2.665% (95% confidence interval, −2.854% to −2.474%) per year for men and −4.064% (95% confidence interval, −4.279% to −3.849%) per year for women, and the local drift values were below 0 in all age groups (P<0.05 for all) in both sexes during the period of 1994 to 2013. In the same birth cohort, the risk of death from stroke rose exponentially with age for both sexes after controlling for period deviations. The estimated period and cohort relative risks were found in similar monotonic downward patterns (significantly with P<0.05 for all) for both sexes, with more quickly decreasing for women than for men during the whole period (significantly with P<0.05 for both).

Conclusions—The decreased mortality rates of stroke in China are likely to be related to improvements in medical care and techniques, spectacular economic growth and fast urbanization, and better early life nutrition conditions of Chinese people. Besides, better education and better awareness of stroke-related knowledge in successive generations could also probably play a role. (Stroke. 2017;48:271-275. DOI: 10.1161/STROKEAHA.116.015031.)

Key Words: cause of death ■ China ■ mortality rate ■ risk ■ stroke ■ trends

Stroke is a major public health problem worldwide. According to the World Health Organization, it is the second leading cause of death globally, accounting for 11.9% of total deaths. In 2013 alone, stroke caused ≈6446 900 deaths and 112 878 900 disability-adjusted life years worldwide. In China, the world’s most populous country, the situation is even worse, with stroke being the leading cause of death and causing about one fifth of all deaths annually (≈1.6 million deaths). Furthermore, it is estimated that there are ≈7.5 million survivors of stroke in China, with ≈2.5 million new stroke cases per year.

Existing studies provide evidence that stroke mortality has changed over time in China, increasing from 1988 to 2000, declining from 2000 to 2004 and then increasing again from 2005 to 2013. However, none of these figures were adjusted, and so the influence of changing demographic and socioeconomic factors, as well as the effects of preventive health care programs, cannot be identified. To address these limitations, we aimed to investigate the long-term trends of stroke mortality in China between 1994 and 2013, examining age-, period-, and cohort-specific effects by sex with the aid of the age–period–cohort (APC) framework, using data from the GBD 2013 (Global Burden of Disease Study 2013). Findings from our study could give clues on resource allocation targeting vulnerable groups for the prevention of stroke, as well as provide certain etiologic implications on stroke mortality in China.

Methods

Data used in this study were obtained from the GBD 2013, which has provided internally consistent estimates of age- and sex-specific all-cause and cause-specific mortality for 240 causes of death globally, regionally, and nationally from 1990 to 2013. There were 5 main data sources that GBD 2013 adopted to provide data on causes of death in China, and the data of mortality of stroke were mainly extracted from 3 of them, that is, Disease Surveillance Points, Maternal and Child Surveillance System, and Chinese Center for Disease Control and Prevention Cause of Death Reporting System. Stroke was identified based on the 9th and 10th revision of the International Classification of Disease. To characterize the temporal trends in China, stroke mortality rates for males and females were age-standardized by the GBD 2013 global age-standard population.

The aim of APC analysis is to assess the contributions of age, period, and cohort effects on the outcomes, such as demographic or disease rates. The age effects represent a differing risk of the outcome associated with different age brackets; the period effects represent variations in the outcome over time that influence all age groups simultaneously; the cohort effects are associated with changes of the outcome across groups of individuals with the same birth years. Holford has proposed that if age, period, and cohort trends are orthogonally decomposed into their linear and nonlinear parts, many useful functions can be estimated. In this study, we mainly focused on the following estimable functions. Net drift, the overall log-linear trend by calendar period and birth cohort, indicates the...
overall annual percentage change; local drifts, the log-linear trend by calendar period and birth cohort for each age group, indicate annual percentage changes for each age group; longitudinal age curve indicates the fitted longitudinal age-specific rates in reference cohort adjusted for period deviations; the period (or cohort) RR would be the period (or cohort) relative risk adjusted for age and nonlinear cohort (or period) effects in a period (or cohort) versus the reference one.

To conduct APC analysis, the mortality and population data were arranged into consecutive 5-year periods from 1994 to 2013 (data from 1990 to 1993 were not considered because they were not enough for a 5-year period) and successive 5-year age intervals from 15 to 19 years to 75 to 79 years. Because the occurrence of death from stroke in those aged <15 years is rare, and individuals aged >80 years were only recorded as one group in GBD database, they were not considered in this study. We obtained the estimable parameters by the APC Web Tool21 (Biostatistics Branch, National Cancer Institute, Bethesda, MD). The central age group, period, and birth cohort were defined as the reference, respectively, in all APC analyses; in case of an even number of categories, the reference value was set as the lower of the 2 central values.21 Wald chi-square tests were adopted for the significance of the estimable functions. To compare the significance of the slope of the period/cohort RRs, we used general linear model to check the interaction effect between sex and calendar year/birth cohort. All statistical tests were 2-sided.

Results

Trends of the crude mortality rates and the age-standardized mortality rates (ASMR) for stroke by sex for the period of 1994 to 2013 are shown in Figure 1. We can observe that although the crude mortality rates for stroke of Chinese males and females showed overall increasing trends, from 123.5 to 154.7 per 100000 for men and 110.2 to 121.4 per 100000 for women, the ASMRs in both sexes showed general declining trends, from 232.8 to 188.9 per 100000 for men and 169.7 to 127.5 per 100000 for women. We should note that since 2009, the ASMR for stroke in males began to rebound slightly. The reduction in the ASMR for stroke from 1994 to 2013 was 18.9% in men and 24.9% in women. The net drift, which represents the overall annual percentage change, and local drifts, which represent annual percentage changes for each age group, are displayed in Figure 2. We found that the net drift was −2.665% (95% confidence interval, −2.854% to −2.474%) per year for men and −4.064% (95% confidence interval, −4.279% to −3.849%) per year for women. We should note that the downward trend of males decelerated from 2009 to 2013. Cohort RRs were also found in similar monotonic downward patterns for both sexes, with more quickly decreasing for women than for men overall (significantly with $P<0.05$), but these downward tendencies were slowing down in the recent cohorts, especially for those born after the year 1969. In addition, using the specific results of Wald tests, we found statistically significant cohort and period effects for both sexes ($P<0.05$ for all) and so were the net drift and local drifts ($P<0.05$ for all).

Discussion and Summary

This is the first published study, to our knowledge, to investigate the long-term trends of stroke mortality in China and to examine age-, period-, and cohort-specific effects by sex using the APC framework. Our results indicated that although the crude mortality rates for stroke of Chinese males and females generally increased during the period of 1994 to 2013, the age-standardized stroke mortality rates of them showed overall

![Figure 1. Trends of the crude mortality rates (CMR) and the age-standardized mortality rates (ASMR) per 100,000 population for stroke by sex in China, 1994 to 2013. Using the GBD 2013 (Global Burden of Disease Study 2013) global age-standardized population.](image)

![Figure 2. Local drift with net drift values for stroke mortality in China. Age group-specific annual percent change (local drift) with the overall annual percent change (net drift) in stroke mortality rate and the corresponding 95% confidence intervals (some of them were too narrow to show in the figure).](image)
decreasing trends with a decrease in the stroke mortality rate for every age group.

Age is the most important risk factor for stroke among a series of demographic factors. The risk of death from stroke varies from different life stages because of physiological changes, amassing of exposure to risk factors, unhealthy living habits, or a blend of these. In previous studies on stroke patterns in China, authors mainly focused on the age distribution of the incidence; only a few of them depicted the age pattern of stroke mortality. Although they found that stroke incidence and mortality rates rose rapidly with age, their studies were not comprehensive and accurate enough to some extent for their relatively small number of age groups and small sample size. More importantly, none of them took the uncontrolled cohort and period effects into account in their studies.

Using the most recent data from GBD 2013, our results showed that, in the same birth cohort, the risk of death from stroke rose exponentially with age after adjusting for period deviations. Specifically, the relative risk of the stroke mortality was about one and a half times each 5-year life stage from age 20 to 24 to 75 to 79 years for both sexes in China, which is similar to the findings of the Western countries. It should be noted that the crude mortality rates for stroke in Chinese males and females showed overall increased trends, which is different from the results of ASMRs in both sexes. We believed that the problem of aging society plays an important role in this difference. It is generally known that China has the largest population in the world, and it has witnessed a decreasing number of births since the 1990s, which will make its problem of aging society more serious because of the large amount of the elderly and the more rapidly aging population. In Figure 3, we can see that >70% of mortality risk from stroke in China occurred in people aged ≥65 years; >80% of that occurred in people aged ≥60 years. So there is no doubt that the increasing proportion of the elderly in China would lead to a growth in the crude mortality rate. According to World Population Ageing 2013 published by United Nations, China would witness an increase in the proportion of people aged ≥60 years from 12.4% to 28.1% in the next 3 decades (2010–2040). So we speculated that the death toll and the crude mortality rates for stroke in Chinese males and females will continue to rise in the future, given the fact that other factors are under their current trends.

Although the period effect and cohort effect can be estimated separately as the period RR and cohort RR by certain restriction, in fact, it is not easy to interpret them separately in the real world. This is because the period effect often influences certain age group(s) more or less when it influences all age groups simultaneously, which leads to the cohort effect to some extent. The cohort effect essentially reflects different birth cohorts’ various risk, but in reality, different cohorts were born in different periods and, thus, inevitably have confounding impact on the period effect to some extent. So we here comprehensibly discussed the possible reasons for the decreasing trends of period and cohort effects.
When it comes to the trend of ASMR for stroke, the first thing we should consider is the revision of International Classification of Diseases code during the study period. But it has been proven that changes from International Classification of Diseases-Ninth Revision to International Classification of Diseases-Tenth Revision had no substantial influence on the analysis of temporal trends for stroke,\(^2,24\) so the reason behind the decreasing trend of ASMR for stroke is likely to be other factors. Because many developed countries also experienced a declined ASMR of stroke, it is generally regarded as the consequence of improved medical care and the effective control of risk factors. For China, the main reason seems to be the former. Significant improvements on techniques for diagnosis, treatment, and management, accompanied by more and better healthcare professionals, played a critical role in the declining case fatality\(^6,25\) and, thus, decreasing stroke mortality. Most patients could receive computed tomography or magnetic resonance image scanning to aid diagnosis for stroke when they are in a county-level hospital or a more advanced one,\(^10\) and it is believed that early detection could also contribute to better treatment and the reduced mortality.\(^28\) What is more, spectacular economic growth and fast urbanization (the proportion of residents living in urban areas was \(\approx 26\%\) in 1990 and 50% in 2010\(^27\)) have made those medical-care services more available, accessible, and affordable for hundreds of millions of Chinese people, especially given the fact that the emergency services were usually centered in urban areas.

Improvement of early-life nutrition conditions is also likely to be one of the main reasons for the decreasing ASMR for stroke in China. There were many studies\(^28–32\) that indicated maternal and early-child undernutrition have strong associations with the risk of stroke. Although the mechanisms are not clear at present, it has been reported that\(^12,33\) undernutrition in early life would cause a high blood pressure and even a permanent harmful impact on vascular function and structure. In addition, better education and better awareness of stroke-related knowledge in successive generations probably played a partial role. We should note that in both sexes, the decreasing trend of the cohort effect witnessed a small deceleration in the cohorts born after 1980. This similar deceleration phenomenon also happened in many European regions\(^34\) and in Hong Kong,\(^26\) in earlier cohorts who were born approximately between 1950 and 1970. It is generally believed that\(^26,34\) the rising prevalence of the hazard factors (eg, hypertension, obesity, diabetes mellitus, vascular diseases, cholesterol level, and smoking),\(^10\) the more westernized dietary pattern, and the increasingly sedentary lifestyle were the underlying reasons for the decelerating cohort effect. This is basically in accordance with the fact that the lifestyle of the post-80s generation in China is different from that of preceding generations.\(^35\)

It should be noted that many major risk factors for stroke were actually not well controlled in China during the study period.\(^39\) For example, the prevalence of hypertension (the most important risk factor for stroke) in China has increased rapidly in adult population since 1991, according to existing studies.\(^35–39\) However, we should also note that effective and increasingly generalized use of antihypertensive treatments\(^10\) could make contributions to the decreasing period effect to some extent. The phenomenon that there was a decelerated decreasing trend and then a reversed slight increase of ASMR in men (see Figure 1) is somehow intriguing. We suggest that the underlying reason might be associated with the smoking. This is because there was a rapid increase of tobacco consumption in China since the early 1980s because men represent the overwhelming majority of Chinese smokers, and the lag period between smoking and stroke mortality was estimated to be \(\approx 20\) to 30 years.\(^40\)

Some limitations of the present study should be noted. First, because age and period intervals should be fixed and equal in APC analysis,\(^12\) seniors aged \(\geq 80\) years could not be considered in this study because of the data availability (they were only recorded as one group in GBD database). However, substantial numbers of death from stroke happen in seniors aged \(\geq 80\) years, and variations in people \(>80\) years do not necessarily reflect those of the older people. But we still can confirm from the data that the stroke mortality rate of Chinese seniors aged \(\geq 80\) years is also decreasing, which was just more moderate than that of younger age groups. This phenomenon was consistent with that in Figure 2, whose potential trends showed that age group–specific annual percent change in old people was getting smaller with age. Second, it is evitable that problems of completeness and accuracy on stroke mortality data in this study may somehow lead to bias, although there were many steps, including\(^41\) incompleteness, under-reporting, and misclassification corrections, as well as the redistribution of the garbage codes\(^3\) in GBD 2013, to enhance the data quality and comparability. But it is fair to say that the bias in the present study has been reduced a lot to some extent, compared with that of research using raw data without those correction and adjustment steps. Third, like other APC analyses, there was the inevitability of being affected by ecological fallacy because interpretations from results at population levels do not necessarily hold for individuals. Therefore, related hypotheses raised in this study still need further confirmation in the future individual-based studies.

In summary, our study showed that although the crude mortality rates for stroke of Chinese males and females generally increased from 1994 to 2013, the age-standardized stroke mortality rates of them showed overall decreasing trends. By APC analysis, we affirmed that in the same birth cohort, the risk of death from stroke rose exponentially with age for both sexes after controlling for period deviations. The estimated period and cohort RR\(_s\) were found in similar monotonic downward patterns for both sexes, with more quickly decreasing for women than for men during the whole period. The patterns are likely to be related to improvements in medical care and techniques, spectacular economic growth and fast urbanization, and better early-life nutrition conditions of Chinese people. Besides, better education and better awareness of stroke-related knowledge in successive generations could also probably play a role.

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Disclosures

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