Stroke Incidence and Case Fatality In Australasia

A Comparison of the Auckland and Perth Population-Based Stroke Registers

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Background and Purpose
Population-based studies are crucial for identifying explanations for the decline in mortality from stroke and for generating strategies for public health policy. However, they present particular methodological difficulties, and comparability between them is generally poor. In this article we compare the incidence and case fatality of stroke as assessed by two independent well-designed incidence studies.

Methods
Two registers of acute cerebrovascular events were compiled in the geographically defined metropolitan areas of Auckland, New Zealand (population 945,369), during 1991-1992 for 12 months and Perth, Australia (population 138,705), during 1989-1990 for 18 months. The protocols for each register included prospective ascertainment of cases using multiple overlapping sources and the application of standardized definitions and criteria for stroke and case fatality.

Results
In Auckland, 1803 events occurred in 1761 residents, 73% of which were first-ever strokes. The corresponding figures for Perth were 536 events in 492 residents, 69% of which were first-ever strokes. Both studies identified a substantial proportion of nonfatal strokes managed solely outside the hospital system: 28% in Auckland and 22% in Perth of all patients registered. The age-standardized annual incidence of stroke (all events) was 27% higher among men in Perth compared with Auckland (odds ratio, 1.27; P=.016); women tended to have higher rates in Auckland, although these differences were not statistically significant. In both centers approximately a quarter of all patients died within the first month after a stroke. There were significant differences in the prevalence of hypertension among first-ever strokes.

Conclusions
These two studies emphasize the importance of identifying all patients with stroke, both hospitalized and nonhospitalized, in order to measure the incidence of stroke accurately. The incidence and case fatality of stroke were remarkably similar in Auckland and Perth in the early 1990s. However, there are differences in the sex-specific rates that correspond to differences in the pattern of risk factors.

Key Words
Australia • cerebrovascular disorders • epidemiology • incidence • New Zealand

A fter a long period of neglect, there is now fresh interest in the epidemiology of stroke. In part this reflects a desire to explain the sustained decrease in mortality from stroke seen in many developed countries over recent decades as well as the increases in several Eastern European countries. It also reflects concern that rapid increases in both relative and absolute numbers of the elderly will overwhelm economic, medical, and social resources providing care for the disabled aged, many of whom have experienced a stroke. Despite advances in noninvasive neuroimaging techniques, the recognition of various risk factors for stroke, and improved epidemiologic methods, it is unclear whether there has been a change in the incidence of stroke or a change in natural history, with the average stroke becoming less severe. However, in the absence of definitive breakthroughs in the treatment of acute stroke, it seems likely that much of the fall in mortality from stroke can be attributed to changes in risk factors rather than to improvements in the medical management of stroke.

Largely because of methodological difficulties in measuring the incidence of stroke, there is a scarcity of well-designed epidemiologic studies of its trends and determinants. Although hospital-based studies are a popular source of data on stroke, they are complicated by selection bias and therefore are of limited use either for monitoring the effects of primary prevention or for planning of health services. Population-based studies, on the other hand, can provide the necessary data, but only if they adhere to several "ideal" criteria for definitions, design, and presentation of data. However, these studies are costly and demanding, particularly in regard to identifying nonfatal events managed entirely in the community. Clearly, incomplete case-finding would lead to an underestimation of the true incidence of stroke. In this article we present data from two stroke registers that met all the criteria for well-designed...
incidence studies, with the important objective of comparing the incidence and case fatality of stroke between two defined Australasian populations.

**Subjects and Methods**

**Study Populations**

The study populations were all residents of Auckland, New Zealand, and of a geographically defined segment of metropolitan Perth, Western Australia. The population of Auckland was 945,369 according to the 1991 Census. The study population in Perth was estimated at 138,708 (at June 30, 1989) by linear extrapolation of the relative change in the population of the study area for the intercensal period 1981 through 1986. The proportion of people 65 years and older was greater in Perth (12.3%) than Auckland (9.4%), but the structure and availability of hospital and other health services for stroke patients were similar. Both cities have experienced considerable postwar immigration flows and now have distinctive multicultural populations.

**Ascertainment of Stroke Events**

The Auckland register operated for 12 months from March 1, 1991; the study period for the Perth register was 18 months beginning February 20, 1989. Details of the case-finding procedures adopted by each stroke register are described elsewhere. In brief, each study included a wide range of overlapping sources, including daily checks of attendances at and admissions to all acute hospitals, routine searches for in-hospital events, radiology requests for axial computed tomographic (CT) scans, and perusal of death certificates and autopsy reports. In the studies, the incidence of stroke was estimated from carotid duplex ultrasound. Hospital morbidity data were also scrutinized for any mention of cerebrovascular disease (the International Classification of Diseases [9th revision, ICD-9] codes 430-438) as an additional check for completeness of ascertainment.

Both studies paid particular attention to identifying nonfatal events occurring outside the hospital setting. To enlist the active support of the two communities, considerable emphasis was given to widespread publicity. Before the Perth study began, all medical practitioners serving the study population were telephoned and sent a letter. The objectives of these contacts were to clarify the aims of the study and invite each doctor to refer all cases of suspected stroke or transient ischemic attack, irrespective of medical condition, to a central registration office. Access to this office was facilitated by the use of a 24-hour answering machine. Regular follow-up by telephone and progress reports ensured continuing cooperation from medical practitioners. Similarly, the Auckland study included regular phone calls to 170 general practitioners who represented a 25% random sample of all primary care physicians in the city. In Auckland, domiciliary visits by physiotherapists and speech therapists and by stroke field officers to stroke patients being cared for in the community were reviewed on a monthly basis as an additional check to the referrals by the participating doctors.

**Study Definitions**

Stroke was defined according to the World Health Organization definition as "rapidly developing signs of focal (or global) disturbance of cerebral function lasting 24 hours or longer, or leading to death, with no apparent cause other than vascular." This definition includes spontaneous subarachnoid hemorrhage but excludes subdural and extradural hematomas and transient ischemic attacks. First-ever strokes refer to patients who had no previous history of stroke; that is, they suffered their "first-ever-in-a-lifetime" stroke during the study period. Patients who gave a history of stroke before the study period were classified as having suffered a recurrent event only after careful review of all the available medical information. A recurrent event during the study period was considered to have occurred if more than 28 days had elapsed from the initial episode that brought the patient into the study. Total stroke events therefore refer to all events, rather than patients, and include patients both with and without a history of stroke. A case "managed in hospital" is one in which admission occurred within 28 days of stroke onset. Twenty-eight-day case fatality is defined as the proportion of all events that resulted in death within 28 days of onset.

**Study Variables**

Once it was established that the patient met the clinical criteria for inclusion, a semistructured personal interview covering the onset of the stroke and other medical and social factors was completed as soon as possible after the event. In the Perth study, a neurology registrar (C.S.A.) interviewed all patients, whereas in Auckland, trained nurses in liaison with a neurologist (N.E.A.) interviewed the patients. If the patient was dead or unable to communicate, an appointment was made with a close relative or friend to whom the same questions were directed. Both studies were also characterized by follow-up interviews at selected intervals in the year after the index event: 1, 6, and 12 months in the Auckland study and 4 and 12 months in the Perth study.

With regard to risk factors, diabetes mellitus was accepted on the basis of either a history of that condition or when a random blood glucose level was found to exceed 11.1 mmol/L poststroke. Smoking status was classified as "current smoker."
or "ex-smoker" (defined as a person who had given up smoking for at least 12 months). "Ever smoker" comprises all current smokers and ex-smokers. All patients were asked about any history of hypertension, myocardial infarction, or stroke.

Calculation of Age-Standardized Rates

In the Auckland study, the numerator for the cases includes a weighting by a factor of four for the 25% of nonfatal episodes of stroke treated at home (or in an institution) in patients under the care of the randomly selected doctors. In the absence of counts (for each age/sex group) of people unaffected by a previous stroke, normal census data were used for the denominators. Age-standardized rates were calculated using the direct method and weights from Segi's "world" population, 15 years and over. Rates are reported with 95% confidence intervals (CI); in the Auckland study, this included the sampling variance. Case fatality is presented for first-ever, recurrent, and total events. The \( \chi^2 \) test, unadjusted for sampling variance, was used for comparisons of proportions.


<table>
<thead>
<tr>
<th></th>
<th>Auckland (n=1305)</th>
<th>Perth (n=370)</th>
<th>Rate Ratio†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>153.3 (136-170)</td>
<td>191.5 (158-225)</td>
<td>1.27 (1.05, 1.53)</td>
</tr>
<tr>
<td>Women</td>
<td>128.6 (115-142)</td>
<td>108.3 (86-131)</td>
<td>0.86 (0.72, 1.07)</td>
</tr>
<tr>
<td>Total</td>
<td>141.5 (131-152)</td>
<td>145.6 (126-165)</td>
<td>1.05 (0.92, 1.21)</td>
</tr>
</tbody>
</table>

Values in parentheses are 95% confidence intervals.

*Age standardized to the world population 15 years and over by the direct method.

†Mantel-Haenszel age-adjusted.

Results

During the 12-month study period, 1803 events occurred in 1735 Auckland residents: 835 (46%) men and 968 (54%) women. The proportion of first-ever strokes was 72%. Almost 70% (1089 cases) were first recruited to the study from prospective monitoring; admissions to the hospital accounted for 60% and death records for 9%. An additional 21% were first recruited from a general practice. The pathological basis of 26% of the cases of stroke was confirmed by CT or magnetic resonance imaging scan or by necropsy.

During the 18-month period of the Perth study, 536 events occurred in 492 patients, of which 69% were first-ever strokes. These events occurred in 281 (52%) men and 255 (48%) women. Eighty-five percent (452 cases) were first recruited to the study either from a medical practitioner (75) or from prospective monitoring of admissions and discharges from hospitals (377). The pathological basis of 86% of the cases of stroke was confirmed by CT or magnetic resonance imaging scan or by necropsy. The incidence of defined pathological subtypes of stroke in Perth appear in an earlier article.

Table 1 shows the distribution of selected baseline variables for the events registered in each of the two studies. The age distribution was somewhat younger in the Auckland study, in which 24% were aged under 65 years and only 47% over 75 years, compared with 20% and 53%, respectively, for Perth. However, if Maoris and Pacific Islanders are omitted, age distribution was remarkably similar, with approximately one fifth of all registered patients being less than 65 years of age and just over half (51% in Auckland and 53% in Perth) aged 75 years or more. At the time of stroke, more than four
fifths of all patients registered in both studies were living in a private residence, the remainder being in institutional care; the proportions of patients married, living alone, and managed in hospital were similar.

The age- and sex-specific annual incidence (first-ever) rates for the two populations are presented in the Figure. These increase rapidly with age and are consistently and significantly higher in men than women in both studies. Although not shown in the Figure, in each age group the 95% CI values overlap around the rates (shown elsewhere56), suggesting no statistically significant difference in age-specific rates between the two populations. There was no significant difference between Auckland and Perth in overall annual age-standardized incidence rates (141.5 and 145.6 per 100 000, respectively) (Table 2). However, age-standardized rates in men in Perth were higher (191.5 per 100 000) than in men in Auckland (153.3 per 100 000); this difference was statistically significant (odds ratio, 1.27; 95% CI, 1.05-1.53; P= .016). The age-standardized rates in women were similar (128.6 and 108.3 per 100 000 in Auckland and Perth, respectively).

Table 3 shows there was no significant difference between the two populations in the 28-day case fatality for stroke. In both studies, the overall case fatality was 24% and was higher in women and in older people (75 years and older).

Table 4 compares selected characteristics of first-ever strokes for patients from the two populations. Among the men who suffered a stroke, the proportion with either a history of hypertension (P=.014) or on antihypertensive treatment (P=.007) was significantly higher in Perth. For women who suffered a stroke, a similar difference was found in the proportion with a history of hypertension (P<.0001) or on antihypertensive drugs (P=.011). Slight differences in data collection methods used in the two studies are thought unlikely to account for this difference.

The women in the Auckland study were more likely to have smoked, whereas men in Auckland were more likely to have a history of diabetes mellitus, although these differences did not reach conventional levels of significance.

Table 3. Comparison of 28-Day Case Fatality of Stroke by Age, Sex, Management, and Sequence in Auckland (1991) and Perth (1989-1990), All Events

<table>
<thead>
<tr>
<th>Variable</th>
<th>Auckland (N=1803)</th>
<th>Perth (N=536)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Age &lt;75 years</td>
<td>181/945</td>
<td>19</td>
</tr>
<tr>
<td>≥75 years</td>
<td>254/858</td>
<td>30</td>
</tr>
<tr>
<td>Sex: Men</td>
<td>178/835</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>257/968</td>
<td>27</td>
</tr>
<tr>
<td>Management</td>
<td>Hospital</td>
<td>321/1305</td>
</tr>
<tr>
<td></td>
<td>Nonhospital</td>
<td>114/498</td>
</tr>
<tr>
<td>History</td>
<td>First-ever stroke</td>
<td>305/1305</td>
</tr>
<tr>
<td></td>
<td>Recurrent stroke</td>
<td>130/498</td>
</tr>
<tr>
<td>Total</td>
<td>435/1803</td>
<td>24</td>
</tr>
</tbody>
</table>

Table 4. Prevalence of Selected Characteristics Between Auckland and Perth, By Sex, First-Event

<table>
<thead>
<tr>
<th>Variable</th>
<th>Auckland (n=835), %</th>
<th>Perth (n=281), %</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of hypertension</td>
<td>48</td>
<td>58</td>
<td>.014</td>
</tr>
<tr>
<td>On treatment for hypertension</td>
<td>30</td>
<td>41</td>
<td>.007</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>52*</td>
<td>49</td>
<td>NS</td>
</tr>
<tr>
<td>Current smoker</td>
<td>24*</td>
<td>28</td>
<td>NS</td>
</tr>
<tr>
<td>Ever smoker</td>
<td>76*</td>
<td>78</td>
<td>NS</td>
</tr>
<tr>
<td>History of myocardial infarction</td>
<td>19</td>
<td>23</td>
<td>NS</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>15</td>
<td>11</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Fifty-nine men with missing data were excluded from analysis.
†Forty-five women with missing data were excluded from analysis.
Discussion

Strict criteria have been established to ensure that geographical and secular trends in the incidence of stroke are not affected by changes in diagnostic fashion, incomplete ascertainment of cases, or under-enumeration of the denominator of reference. This article presents data from two population-based studies that adhered to these criteria and show that the total event rates and case fatality of stroke display little geographical variation within Australasia. However, the data also suggest there are different sex-specific rates between Auckland and Perth, which may reflect differences in the prevalence and management of factors such as hypertension and smoking.

Selection bias due to misclassification or incomplete ascertainment of cases, the two major pitfalls of population-based studies, is unlikely to be a problem here. Both registers were compiled prospectively using comprehensive sources and internationally accepted definitions for stroke. Objective evidence for the pathological basis of the stroke was obtained in a high proportion of cases, particularly in Perth. Although the diagnosis of stroke is essentially and certainly initially a clinical diagnosis made on the characteristic profile of the event, problems can occur among patients who present with impairment and have no reliable witness of the event or have symptoms and signs that rapidly resolve. Ideally, therefore, studies should include diagnostic assessment of patients by neurologists. This creates obvious logistic and cost difficulties for registers covering entire populations such as that in Auckland. However, we have no reason to suspect diagnostic errors in the Auckland study, because trained nurse interviewers used standardized questionnaires, with all doubtful diagnoses reviewed by the principal investigator (R.B.) and neurologist (N.E.A.).

Few community-based studies report in detail systematic efforts at identifying patients with acute stroke who are not subsequently admitted to the hospital. The proportion in this category varies widely around the world and attests to the limitations of hospital-based studies in measuring the true incidence of stroke. Although close cooperation and ease of referral of patients from medical practitioners are essential in this regard, additional methods of case-finding in the community, often overlapping with other sources, must be used. Although we cannot rigorously exclude a degree of under-ascertainment of events in either study considered here, the high degree of concordance in the 28-day case fatality, one useful test for the completeness of ascertainment, is an important index of the validity of these data.

In these two studies we found that, had those patients who died before reaching a hospital or who were managed at home or in long-term care facilities been omitted, the true incidence of stroke would have been underestimated by between one fifth and one quarter. These sources of error are particularly important in studies that include elderly people because many are already in institutional care.

Overall incidence and case fatality of stroke were similar in these two populations, although the incidence for men was higher in Perth than in Auckland. Because the inequalities in rates are not likely to be explained by incomplete case ascertainment or misdiagnosis of stroke, one would expect different risk factor profiles between men in Auckland and Perth. In fact the data do show that men in the Perth study were more likely to have a history of hypertension than men in the Auckland study, although there were no other significant differences. For women, incidence rates appeared similar despite lower rates of hypertension in the Auckland women.

A difference in the risk of stroke among men is of particular interest because the trend is opposite that seen for coronary heart disease, in which mortality rates are known to be lower among men in Perth compared with Auckland. This supports data indicating that different patterns of atherosclerosis, and presumably also of risk factors, exist for cerebrovascular disease and coronary heart disease. However, it also raises the question of whether a difference between the two centers in the natural history of coronary heart disease or its management could have contributed to differences in the incidence of stroke. It has been suggested that the decline in mortality rates from coronary heart disease, together with the aging of the population, may be one explanation for the increase in the incidence of stroke in Rochester, Minnesota, over the last decade. If correct, this hypothesis has important implications for the future prevention and management of stroke.

Although the importance of hypertension as a risk factor for stroke (both ischemic and hemorrhagic) is well established, controversy exists regarding the contribution of the treatment of hypertension to the decline in mortality from stroke. Despite concern that it is difficult to extrapolate the results of clinical trials to the wider community, epidemiologic studies have consistently shown that most strokes occur in people in the average range of blood pressure who have not been exposed to large-scale detection and management programs. Cigarette smoking is recognized as an important modifiable risk factor for stroke, but other aspects of lifestyle, and particularly dietary factors, could be responsible for such changes in a whole population.

Moreover, the large number of factors implicated in the etiology of stroke suggests that a large proportion of strokes are preventable.

In summary, ongoing monitoring of disorders such as stroke provides a measure of the effectiveness of primary and secondary efforts aimed at reducing the burden of cerebrovascular disease. The methods for such monitoring have been refined, as evidenced by the ability to identify comparable groups of patients in two independent populations. Both studies were characterized by a sizable proportion of nonfatal events managed outside the hospital setting. The comparable overall and hospital 28-day case fatality also suggest similarities in the natural history of cerebrovascular disease in the two populations. Finally, the tendency toward a greater risk of stroke among men in Perth supports public health measures aimed at changes in lifestyle factors relating to hypertension. Were they to be successful, such changes might result in additional sizable reductions in the absolute number of fatal and disabling strokes.

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