Incidence of the Major Stroke Subtypes
Initial Findings From the North East Melbourne Stroke Incidence Study (NEMESIS)

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Background and Purpose—Population-based stroke incidence studies are the only accurate way to determine the number of strokes that occur in a given society. Because the major stroke subtypes have different patterns of incidence and outcome, information on the natural history of stroke subtypes is essential. The purpose of the present study was to determine the incidence and case-fatality rate of the major stroke subtypes in a geographically defined region of Melbourne, Australia.

Methods—All suspected strokes that occurred among 133 816 residents of suburbs north and east of Melbourne, Australia, during a 12-month period of 1996 and 1997 were identified and assessed. Multiple overlapping sources were used to ascertain cases, and standard criteria for stroke and case-fatality were used. Stroke subtypes were defined by CT, MRI, and autopsy.

Results—Three hundred eighty-one strokes occurred among 353 persons during the study period, with 276 (72%) being first-ever-in-a-lifetime strokes. Of these, 72.5% (95% CI 67.2% to 77.7%) were cerebral infarction, 14.5% (95% CI 10.3% to 18.6%) were intracerebral hemorrhage, 4.3% (95% CI 1.9% to 6.8%) were subarachnoid hemorrhage, and 8.7% (95% CI 5.4% to 12.0%) were stroke of undetermined type. The 28-day case-fatality rate was 12% (95% CI 7% to 16%) for cerebral infarction, 45% (95% CI 30% to 60%) for intracerebral hemorrhage, 50% (95% CI 22% to 78%) for subarachnoid hemorrhage, and 38% (95% CI 18% to 57%) for stroke of undetermined type.

Conclusions—The overall distribution of stroke subtypes and 28-day case-fatality rates are not significantly different from those of most European countries or the United States. There may, however, be some differences in the incidence of subtypes within Australia. (Stroke. 2001;32:1732-1738.)

Key Words: cerebral hemorrhage ■ cerebral infarction ■ cerebrovascular disorders ■ epidemiology ■ incidence ■ subarachnoid hemorrhage

A large component of the burden of stroke is described by overall stroke incidence and mortality rates. However, stroke is not a homogeneous condition but rather is a mix of clinically distinct subtypes that have differing risk profiles, incidence rates, management, and outcomes. Because of these differences, important information can be gained by accurately distinguishing stroke subtype in a majority of cases when determining stroke incidence. Accurate assessment of the incidence of stroke subtypes can be achieved only when several “ideal” criteria have been met; these include the use of imaging techniques to diagnose stroke subtypes accurately in a majority of cases. A recent Australian study, performed in Perth (on the west coast), that conformed to these ideal criteria, has provided evidence that overall incidence rates may be lower than those in Melbourne. It is not known whether this difference in incidence is due to lower incidence rates among all subtypes of stroke in the Perth study or whether the difference is due to a reduced incidence among only one subtype. It is also possible that this difference may be due to chance and differences in methodology, particularly case-finding.

The main aim of the North East Melbourne Stroke Incidence Study (NEMESIS) was to obtain an accurate measure of the incidence of the major stroke subtypes in an Australian community through the use of CT scanning and autopsy to accurately assess subtypes in a majority of cases.

Materials

The study methods have been described in detail previously. Briefly, NEMESIS was conducted in a defined area of inner...
northeast Melbourne between May 1, 1996, and April 30, 1997. According to a census conducted in this region during the study period, the total population was 133,816, of whom 20,976 (15.7%) were 65 years old or older.

Ascertainment of Cases
Multiple overlapping sources were used to ascertain stroke patients. The major sources of case finding were the daily admission lists and stroke unit lists of the 14 major public and 28 private hospitals both within the study region and in the surrounding areas. Patients with a wide range of admitting diagnoses, including TIA, were considered to be potential cases. Where available, the radiology and carotid duplex ultrasound lists of public hospitals within the area were also regularly scrutinized. Computerized hospital discharge lists that identified patients with International Classification of Diseases—Ninth Revision (ICD-9) codes 430 to 438, 342, and 781 were obtained on a regular basis from public and private hospitals.

Cases of stroke managed solely in the community comprise a significant proportion of strokes and are more difficult to find. To assist in the ascertainment of these cases, all medical practitioners potentially able to refer patients to the study (general practitioners, physicians, neurologists, geriatricians, and rehabilitation specialists) were contacted regularly by letter, facsimile, and newsletter. In addition, managers or nursing directors of all 24 nursing homes and 24 hostels located within the study region were telephoned every 2 weeks throughout the study period to inquire about potential cases. The NEMESIS project was also advertised on numerous occasions in Divisional General Practice newsletters, local newspapers, and ethnic newspapers and on a local Melbourne daily newspaper.

Cases in which stroke was noted as either a primary or secondary cause of death among persons whose "usual" residence was within the postal code region were identified through lists supplied by the Australian Bureau of Statistics. Further information was sought from hospital or nursing home medical records, the certifying medical practitioner, the State Coroner’s Office, and/or from the next of kin to determine eligibility according to the study definitions. All participants in the study were also followed up with use of the National Death Index to determine whether any patients lost to follow-up had died.

After informed consent was obtained, potential cases of stroke were interviewed and examined by a trained research nurse as soon as possible after the stroke event. When such persons had died or were discharged from the hospital before they could be examined by a nurse or were treated privately within the community, medical records were reviewed and/or the treating or certifying medical practitioner was contacted so that clinical details could be obtained. All potential stroke cases were formally reviewed by an expert panel before inclusion or exclusion. The panel consisted of 2 to 4 neurologists and an epidemiologist, each with a particular interest in stroke. Clinical details of all potential cases were presented, and consensus was required before a final radiological diagnosis was made.

Definitions
Stroke was defined according to the World Health Organization (WHO) definition as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death) with no apparent cause other than of vascular origin.” The definition excludes cases of primary cerebral tumor, cerebral metastasis, subdural hematoma, postsiezure palsy, brain trauma, and TIA.

Cerebral infarction was defined as a stroke for which a CT scan performed within 28 days of the onset of symptoms showed an area of low attenuation or a normal appearance in the vascular territory that corresponded to the recent symptoms and signs; or MRI showed a slight hypointensity with or without mass effect on T1-weighted images and a bright area of hyperintensity with or without mass effect on T2-weighted images. Alternatively, cerebral infarction was confirmed on autopsy.

Intracerebral hemorrhage (ICH) was defined as a stroke in which a CT scan demonstrated an area of hyperdensity within the brain parenchyma with or without extension into the ventricles or subarachnoid space or, for scans performed beyond 1 week, an area of attenuation with ring enhancement after injection of contrast; MRI showed an area of hypointensity or isointensity on T1-weighted images or an area of marked hypointensity on T2-weighted images. Alternatively, the autopsy demonstrated the origin of the hemorrhage as the cerebral parenchyma.

Subarachnoid hemorrhage (SAH) was defined as an abrupt onset of severe headache, loss of consciousness, or both, with or without focal neurological signs. Lumbar puncture may have demonstrated uniform blood staining (red blood cells >2×10^6/L), xanthocromia, or both; or CT scan showed focal or generalized high signal in the basal cisterns and convexity of the subarachnoid space with or without intraventricular high signal or hydrocephalus. Alternatively, hemorrhage in the subarachnoid space was demonstrated on autopsy. All SAHs were included regardless of whether there were focal neurological signs.

An "undetermined stroke" was a stroke in which a patient had not undergone CT scanning within 28 days of the onset of symptoms and an autopsy had not been performed.

A “possible stroke” was defined as any episode of neurological disturbance that was suggestive of stroke but there was insufficient information available to categorize the case definitively as “stroke” or “not stroke” according to the WHO definition or it was insufficiently clear whether the duration of focal neurological disturbance was >24 or <24 hours.

“First-ever strokes” were defined as strokes that occurred in patients without any prior stroke event. Incidence rates were based on “first-ever-in-a-lifetime” stroke subtypes. Past history of stroke was determined using all available information from hospital records and general practitioners, and patients with a verified past history were not included in the incidence rates. The presence of a clinically silent past cerebral infarction or hemorrhage found on CT scanning was not considered to constitute a stroke.

For inclusion, (1) stroke onset was required to be within the study time period, (2) the person in whom the stroke occurred was required to be resident within the defined geographic region of the study at the time of their stroke, and (3) the event must have been detected and diagnosed by a medical practitioner within 28 days of onset. Registration, however, could occur later.

Follow-Up
If the patient died during the 12-month period after the stroke, all available medical records were reviewed, and occasionally the treating doctor was contacted, to establish the timing and cause of death.

Data Collection and Calculation of Rates
Incidence (first-ever stroke only) rates are reported as crude rates, age-specific rates, and rates standardized to the “world” population of Segi and to the “European” population using 10-year age strata. The latter standardization of rates allows comparison of incidence rates between populations. The data are reported with 95% CIs. Comparison of incidence rates between centers was undertaken by determining whether the CIs for the incidence rates overlap. Comparison of incidence rates between men and women in the present study was undertaken using Mantel-Haenszel age-adjusted rate ratios and 95% CIs for each subtype. Case-fatality rates are reported for deaths that occurred within 28 days and 1 year of the stroke.

Ethics Committee Approval
The study was approved by ethics committees at each of the participating institutions. Informed consent was obtained from each participant before any interview or neurological examination was conducted. When the participant was cognitively impaired or dys-
phasic or had altered consciousness, consent was obtained from the next-of-kin.

Results

In total, 1371 “potential stroke” patients were referred to the study. After a careful review of the medical records, a review of the results of investigations, and, in some cases, a clinical assessment, 990 patients were excluded. The majority of exclusions were due to patients living outside the geographically defined study region (21.6%), occurrence of TIA (12.7%), and events occurring outside the study time frame (12.7%). Due to the prolonged interval from neurological symptoms to establishment of diagnosis, 10 patients were considered not to have had a stroke.12 Ten patients were excluded who had a stroke documented on CT scanning but did not for SAH. The corresponding incidence rates approximately doubled by doing so (95% CI 4 to 16 for SAH, and 8 (95% CI 3 to 14) and 14 (95% CI 7 to 21) for undetermined stroke, respectively. When age-adjusted incidence rates of stroke subtypes were compared between men and women with the Mantel-Haenszel rate ratio (M-H RR), we found similar incidence rates for ICH (M-H RR 1.74, 95% CI 0.93 to 3.28), SAH (M-H RR 0.39, 95% CI 0.10 to 5.76), and undetermined stroke (M-H RR 0.56, 95% CI 0.21 to 4.51); however, incidence rates for cerebral infarction were significantly greater in men than in women at conventional levels (M-H RR 1.34, 95% CI 1.01 to 5.04).

The 28-day and 1-year case-fatality rates for first-ever strokes by subtype are shown in Table 4. The overall 28-day and 1-year case-fatality rates for all first-ever strokes were 20% (95% CI 16% to 25%) and 37% (95% CI 32% to 43%), respectively.

Discussion

When assessing incidence rates of stroke subtypes, it is essential that an accurate method for classification of subtypes be used in a majority of cases. SAH can be accurately defined by the findings of brain CT or autopsy.21–23 Sudlow and Warlow17 suggested that an “ideal” stroke incidence study should have CT available for at least 70% of cases. The present study conforms to this ideal criterion, in that 91% of individuals underwent CT, MRI, or autopsy (mainly CT) to provide pathological confirmation of stroke. Comparison of our incidence rates with those of other population-based studies is complicated by the fact that between studies, different methods are used for case ascertainment, for definition and epidemiological purposes on the basis of clinical observation alone.19,20 Cerebral infarction and ICH can be accurately distinguished only according to the findings of CT scan, autopsy, or MRI. 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classification of stroke, and for presentation of incidence rates. For the present analysis, 2 comparison methods were used. First, so that a comparison could be made with another Australian stroke incidence study, the 1995 to 1996 Perth Community Stroke Study, incidence rates that were age and sex adjusted to the “world” population of Segi were compared.18 This comparison was necessary because these are the only adjusted rates published for this study. Second, so that the present incidence rates could be compared with other studies conducted worldwide, we used age- and sex-standardized incidence rates for the age group 45 to 84 years adjusted to the European population.18 These standardized rates were given by Sudlow and Warlow4 in their international comparison study.

### TABLE 2. Age-Specific Incidence Rates for Men (per 100 000 Population per Year) for First-Ever-in-a-Lifetime Stroke by Subtype in Melbourne, Australia (1996–1997)

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Population at Risk</th>
<th>Cerebral Infarction</th>
<th>ICH</th>
<th>SAH</th>
<th>Undetermined Stroke</th>
<th>All Stroke</th>
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</thead>
<tbody>
<tr>
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<td>0 0 0 ...</td>
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<td>15–24</td>
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<td>1 11 0–33</td>
<td>0 0 0 ...</td>
<td>0 0 0 ...</td>
<td>1 11 0–33</td>
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<td>25–34</td>
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<td>1 9 0–26</td>
<td>0 0 0 ...</td>
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<td>1 9 0–26</td>
<td>0 0 0 ...</td>
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<tr>
<td>35–44</td>
<td>9 911 4 40 1–80</td>
<td>1 10 0–30</td>
<td>1 10 0–30</td>
<td>0 0 0 ...</td>
<td>6 61 12–109</td>
<td></td>
</tr>
<tr>
<td>45–54</td>
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<td>1 13 0–40</td>
<td>2 27 0–64</td>
<td>0 0 0 ...</td>
<td>10 135 51–218</td>
<td></td>
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<tr>
<td>55–64</td>
<td>6 149 14 228 109–347</td>
<td>2 33 0–78</td>
<td>0 0 0 ...</td>
<td>0 0 0 ...</td>
<td>16 260 133–388</td>
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</tr>
<tr>
<td>65–74</td>
<td>5 478 21 383 220–547</td>
<td>7 128 33–222</td>
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<td>3 55 0–117</td>
<td>31 566 367–765</td>
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<tr>
<td>75–84</td>
<td>2 725 34 1248 831–1664</td>
<td>5 183 23–344</td>
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<td>1 37 0–109</td>
<td>40 1468 1016–1919</td>
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<td>≥85</td>
<td>6 28 15 2389 1194–3583</td>
<td>4 637 15–1259</td>
<td>0 0 0 ...</td>
<td>2 318 0–759</td>
<td>21 3344 1938–4750</td>
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<tr>
<td>All ages</td>
<td>64 684 95 147 117–176</td>
<td>22 34 20–48</td>
<td>3 5 0–10</td>
<td>6 9 2–17</td>
<td>126 195 161–229</td>
<td></td>
</tr>
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</table>

Standardized rate*  
1995–1996 Perth standardized rate*  

*Age adjusted to the world population of Segi by the direct method.18

### Australian Comparison of Incidence Rates Adjusted to the World Population

A comparison of incidence rates of stroke subtypes, adjusted to the world population of Segi,18 between the present study and the 1995 to 1996 Perth Community Stroke Study appears to yield some interesting differences. Although overall incidence rates of stroke subtypes are not statistically different, when men and women are considered separately, there is an apparent greater incidence rate of cerebral infarction among women in the present study, whereas the incidence of ICH among men also appears to be greater. However, because the raw data for the Perth study have not yet been published, we cannot test whether these incidence rates are statistically different. It is possible that they are not statistically different.

### TABLE 3. Age-Specific Incidence Rates for Women (per 100 000 Population per Year) for First-Ever-in-a-Lifetime Stroke by Subtype in Melbourne, Australia (1996–1997)

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Population at Risk</th>
<th>Cerebral Infarction</th>
<th>ICH</th>
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<td>1 8 0–24</td>
<td>0 0 0 ...</td>
<td>6 49 10–89</td>
<td></td>
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<td>25–34</td>
<td>12 142 3 25 0–53</td>
<td>2 16 0–39</td>
<td>1 8 0–24</td>
<td>0 0 0 ...</td>
<td>6 49 10–89</td>
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<td>55–64</td>
<td>6 548 7 107 28–186</td>
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<td>1 15 0–45</td>
<td>11 168 69–267</td>
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<td>65–74</td>
<td>6 307 25 396 241–551</td>
<td>3 48 0–101</td>
<td>2 32 0–76</td>
<td>2 32 0–76</td>
<td>32 507 332–683</td>
<td></td>
</tr>
<tr>
<td>75–84</td>
<td>4 328 36 832 561–1102</td>
<td>6 139 28–249</td>
<td>2 46 0–110</td>
<td>7 162 42–281</td>
<td>51 1178 857–1500</td>
<td></td>
</tr>
<tr>
<td>≥85</td>
<td>1 510 28 1854 1174–2535</td>
<td>4 265 6–524</td>
<td>1 66 0–196</td>
<td>8 530 164–896</td>
<td>41 2715 1895–3535</td>
<td></td>
</tr>
</tbody>
</table>

Standardized rate*  
1995–1996 Perth standardized rate*  

*Age adjusted to the world population of Segi by the direct method.18
because the 95% CIs overlap slightly. East-west differences in coronary heart disease in Australia have previously been reported, with the incidence of nonfatal myocardial infarction and coronary deaths being significantly higher in Newcastle (on the east coast) than in Perth. These results provide some support for the notion that differences in the incidence of stroke between Melbourne and Perth are plausible. It is interesting to speculate on the reasons for these differences. There may be disparity in certain lifestyle habits or in the ethnic mix that accounts for these differences. For example, Perth has a warmer climate than Melbourne, and it is possible that more people undertake outdoor activities or have other lifestyle differences, but this possibility is merely speculative. Unfortunately, this type of information for the Perth population has not been reported, and so an informed comparison cannot be made. Alternatively, the higher, although nonstatistically, case-fatality rate for cerebral infarction in the 1995 to 1996 Perth Community Stroke Study may actually reflect incomplete case ascertainment, particularly regarding the milder strokes, so the differences may not be real.

### Worldwide Comparison of Incidence Rates Adjusted to the European Population

In their international comparison study, Sudlow and Warlow provided age- and sex-standardized rates for the group aged 45 to 84 years adjusted to the European population for a number of incidence studies. The incidence rates of first-ever stroke overall and for men and women separately vary little between studies, except possibly for Dijon, where overall rates are somewhat lower, and for incidence rates in Novosibirsk, where rates are somewhat higher. The incidence rates of cerebral infarction for these studies, as well as those for the Arcadia and Erlangen studies and for the present study, are summarized in Figure 1. In the present Melbourne study, the incidence rate for cerebral infarction for the 45- to 84-year-old age group is similar to those for Perth (1989 to 1990), Umbria, Valle d’Aosta, Arcadia, and Erlangen. However, similar to overall incidence rates, the incidence rates of cerebral infarction appear to be lower for Dijon than for the present Melbourne study, and the 95% CIs do not overlap. It is possible that the lower rate in Dijon is in part due to the

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**Figure 1.** Age- and sex-standardized annual incidence per 100,000 population for cerebral infarction for the group aged 45 to 84 years, standardized to the European population. Studies are arranged in order of study year. The numbers shown are point estimates, and the error bars are 95% CIs.
higher incidence of unknown subtype, which may include some cases of cerebral infarction that have not been included in this category. For the remaining studies, the 95% CIs do not overlap with those of the present study and are somewhat higher. It is consequently possible that the present study has significantly lower incidence rates for cerebral infarction than those obtained in the remaining studies.

Differences in the incidence rate of stroke of undetermined type between registers make comparisons of incidence rates of hemorrhagic stroke difficult (Figure 2). This is because hemorrhagic strokes are likely to be overrepresented in the undetermined category; the evidence for this is the high case-fatality rate among both hemorrhagic stroke categories and among the stroke of undetermined type category. Consequently, any true differences in incidence rates for the 2 hemorrhagic stroke subtypes may be obscured. Similar rates of stroke of undetermined type are observed between Melbourne, Oxfordshire, and Erlangen. These registers also exhibit similar incidence rates of ICH, but the Melbourne study has significantly lower incidence rates for SAH. These less common subtypes have small numbers of events and wide 95% CIs, and the estimates of their incidence are thus likely to be less precise than those for cerebral infarction. Thus, low power may account for the observed differences. Alternatively, the observed differences may be real, although a firm statement regarding this cannot be made.

Despite the possibility that overall incidences of stroke may differ, the proportion of each major subtype is in large part similar between the present study and those presented by Sudlow and Warlow4 in their international comparison. This lack of difference might be attributed to the similarities (predominantly white race and Western lifestyles) of the populations being studied.

Comparison of Case-Fatality Rates

The case-fatality rate of cerebral infarction in the present study was not statistically different from that in the 1989 to 1990 Perth Community Stroke Study or the Erlangen Stroke Project at both 28 days and 1 year.9,36 Some differences have been observed, however, such as better 1-year survival from cerebral infarction in the Oxfordshire Community Stroke Project and lower 28-day case-fatality rates for ICH in the 1989 to 1990 Perth Community Stroke Study.9,36 The higher incidence and case-fatality rates of undetermined stroke in the Perth study might in part account for this latter difference. The group of undetermined strokes is likely to differ between the NEMESIS cohort and the other studies because there was no attempt to influence stroke management by the NEMESIS investigators (ie, any brain imaging or autopsy performed was only part of the treating physician’s usual management). Thus, in Melbourne, the group of undetermined events included a number of mild strokes. In contrast, the Perth study investigators tried to influence imaging practices, those not imaged in the Oxfordshire study were either very old or very frail, and in the Erlangen study, nonhospitalized patients (of whom 62.5% were not imaged) were older than the hospitalized patients. One must keep in mind that all of these figures for case fatality are based on relatively small numbers of observations, and firm statements about their relative position, compared with other populations, should not be made.

In summary, the overall distribution of major stroke subtypes is similar to that of other community-based studies in mainly white populations. There is some heterogeneity, however, and even within Australia the incidence of different subtypes of stroke appears to vary. In particular, the incidence rates of cerebral infarction among women and of ICH among men may be greater in the present study than in the 1995 to 1996 Perth Community Stroke Study. It is possible that these differences occurred by chance, are due to differences in case-ascertainment methodology, or are due to the distribution of subtypes within the undetermined category. There are, however, many reasons why these putative differences in incidence rates may occur, such as differences in lifestyle and ethnic mix, but further research would be required to establish this with more certainty.

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References


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