Incidence, Event Rates, and Early Outcome of Stroke in Dublin, Ireland
The North Dublin Population Stroke Study

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Background and Purpose—The World Health Organization has emphasized the importance of international population-based data for unbiased surveillance of stroke incidence and outcome. To date, few such studies have been conducted using recommended gold-standard ascertainment methods. We conducted a large, population-based stroke study in Dublin, Ireland.

Methods—Using gold-standard ascertainment methods, individuals with stroke and transient ischemic attack occurring over a 12-month period (December 1, 2005–November 30, 2006) in North Dublin were identified. Disability was assessed using the modified Rankin score and stroke severity (<72 hours) by the National Institutes of Health Stroke Scale. Stroke-related deaths were confirmed by review of medical files, death certificates, pathology, and coroner’s records. Crude and standardized (to European and World Health Organization standard populations) rates of incidence, risk factors, severity, and early outcome (mortality, case-fatality, disability) were calculated, assuming a Poisson distribution for the number of events.

Results—Seven hundred one patients with new stroke or transient ischemic attack were ascertained (485 first-ever stroke patients, 83 recurrent stroke patients, 133 first-ever transient ischemic attack patients). Crude frequency rates (all rates per 1000 person-years) were: 1.65 (95% CI, 1.5–1.79; first-ever stroke), 0.28 (95% CI, 0.22–0.35; recurrent stroke), and 0.45 (95% CI, 0.37–0.53; first-ever transient ischemic attack). Age-adjusted stroke rates were higher than those in 9 other recent population-based samples from high-income countries. High rates of subtype-specific risk factors were observed (atrial fibrillation, 31.3% and smoking, 29.1% in ischemic stroke; warfarin use, 21.2% in primary intracerebral hemorrhage; smoking, 53.9% in subarachnoid hemorrhage; 46%; 95% CI, 28.8%–64.5%) were greater in Dublin.

Conclusions—Using gold-standard methods for case ascertainment, we found high incidence rates of stroke in Dublin compared with those in similar high-income countries; this is likely explained in part by high rates of subtype-specific risk factors. (Stroke. 2012;43:2042-2047.)

Key Words: acute stroke ■ cerebrovascular disease ■ epidemiology ■ health policy ■ outcomes

Cardiovascular diseases are the leading cause of death globally, with almost 6 million deaths attributable to stroke in 2005.1 Stroke incidence rates are increasing rapidly in low- and middle-income countries, whereas substantial increases in the absolute numbers of individuals affected by stroke are projected in high-income countries, because of lifestyle changes and increasing population life-expectancy.2–4

To develop policy, health-service, and public health measures to address the challenge of increasing global stroke frequency, the World Health Organization has emphasized the importance of developing robust national surveillance systems to monitor stroke frequency and outcome.4–6

Large studies from population-based samples are generally acknowledged to be most reliable and to avoid bias that may
occur in comparisons of mortality statistics, hospital registers, or clinical trial data. However, even among population studies, methodological differences are common, which limit direct comparisons. In particular, underascertainment of stroke data (eg, in the very old population) may result in underestimation of stroke incidence and overestimation of case-fatality.

Standard methodological criteria, including core ascertainment methods, have been adopted by many studies, but independent assessment has demonstrated that these may underestimate true stroke incidence. For near-complete case identification, supplementary methods combined with direct assessment of ascertainment from independent sources have been validated and recommended as gold-standard methods. As yet, few studies have systematically applied these gold-standard methods to measure stroke incidence and outcome.

In Ireland, stroke was not included in the early development or implementation of cardiovascular health policy, with subsequent underdevelopment of stroke services compared with those of other chronic diseases. We performed a population-based study of stroke and transient ischemic attack (TIA) in a large sample (almost 7%) of the Irish population. We aimed to provide data for international comparison and to inform the development of a national stroke policy for Ireland.

Methods

Procedures

We used identical ascertainment methods and definitions to those used in the OXVASC study, which have been previously described. In brief, hot and cold pursuit was performed to identify incident and recurrent stroke events, using multiple overlapping hospital and community sources according to recommended core methods for stroke epidemiological studies. In addition, the following supplementary ascertainment sources were used: regular checking of all referrals for brain and neurovascular imaging, assessment of all cases with definite or possible TIA diagnosis, and follow-up of all confirmed TIA cases for stroke occurrence. Independent validation has indicated that supplementary methods increased ascertainment by 7% compared with core methods alone, and together provide near-complete ascertainment.

Following a 10-week pilot study to refine procedures, individuals with stroke and TIA occurring over a 1-year period (December 1, 2005–November 30, 2006) were identified. Ascertainment was continued for an additional 3 months to identify eligible participants who delayed seeking medical attention. Definitions of stroke, TIA, and stroke pathological subtypes are detailed in the Web Appendix.

To replicate OXVASC core ascertainment methods, we used recommended multiple overlapping sources, combining hot and cold pursuit. For community ascertainment, 180/190 of North Dublin general practitioners (94%) and 17 of 18 nursing homes (95%) participated. A 5-day TIA clinic was established to facilitate early referral of community-treated patients. All general practitioners and nursing homes were contacted every 2 weeks, with physician verification of community-treated patients in the clinic or at their homes.

Five adult general and 7 specialist nonacute hospitals exist in the North Dublin region. For hospital ascertainment, a hot pursuit strategy was employed in adult acute hospitals with daily checking of all emergency room and elective admissions, consultation requests, and visits to specialist wards and intensive care units (see Web Appendix). Patients with suspected stroke who died were ascertained by review of death certificates and pathology or coroner’s records.

We replicated the OXVASC supplementary ascertainment methods by reviewing computerized results for brain and neurovascular imaging in all radiology units serving the region (6 magnetic resonance imaging, 6 computed tomography, 2 angiography, 5 carotid ultrasound) twice weekly, with physician assessment of patients with suspected stroke/TIA. We assessed and followed all suspected TIA patients to detect minor stroke and new stroke after TIA. Patients with TIA, those in whom the diagnosis of stroke was unclear, and those with possible recurrent stroke were reviewed in-person by a study physician and eligibility for study inclusion was agreed upon by consensus.

We replicated the OXVASC direct ascertainment assessment method by following high-risk patients presenting during the first 2 months of the study for occurrence of later TIA or stroke. Patients were those with acute coronary and peripheral vascular diseases and hospital referrals for vascular investigation, treatment, or endovascular/surgical intervention. As no single computerized general practitioner database exists in North Dublin, this method of ascertainment validation used by OXVASC could not be replicated.

Disability was assessed using the modified Rankin Scale within 72 hours and at 28 days conducted by a trained research staff member using a standard algorithm. Acute stroke severity (<72 hours) was assessed by certified raters using the National Institutes of Health Stroke Scale. Ischemic stroke subtype was assigned by TOAST criteria by a single trained rater.

The source population was quantified from 2006 census data for North Dublin, conducted close to the midpoint of the study. The total population was 294,529 individuals, comprising 7% of the Irish population and is relatively stable, with low in- and out-migration.

Statistical Analysis

Crude incidence, event, and mortality rates were calculated with 95% CIs, assuming a Poisson distribution for the number of events. For comparison with published incidence rates from other countries, rates of first-ever stroke were age-adjusted to the World Health Organization standard population, and to the Standard European Population (stratified by sex). Parametric and nonparametric subtype-specific comparisons were performed using the t test, t test, analysis of variance, or equality-of-medians test, as appropriate. Bonferroni correction was applied for multiple comparisons where indicated. All significance tests were 2-sided. Statistical analysis was performed using Stata version 10 (StataCorp).

Ethics committee approval was obtained from participating hospitals and the Irish College of General Practitioners, and informed consent was obtained.

Results

Overall, 701 patients with new stroke or TIA during the study period were ascertained. Of 568 patients with new stroke, the qualifying event (first stroke after study onset) was first-ever stroke (FES) in 485 patients (85.4%) and recurrent stroke in 83 patients (14.6%). The crude incidence rate of FES was 1.65/1000 person-years (95% CI, 1.5–1.79; Supplemental Table I). The crude event rate of all strokes was 1.93/1000 person-years (95% CI, 1.77–2.09), and that of recurrent stroke was 0.28/1000 person-years (95% CI, 0.22–0.35). First-ever TIA occurred in 133 individuals. The crude incidence rate of TIA was 0.45/1000 person-years (95% CI, 0.37–0.53).

Of patients with FES, 439 patients were admitted to the hospital (90.5%) and 46 patients were treated in the community (9.5%). Pathological subtype was confirmed in 466 FES patients (96.1%), by brain computed tomography or magnetic resonance imaging in 455 patients (median onset-imaging interval, 1 day; interquartile range, 1–3), and at autopsy in an additional 11 patients. Of these, 79.2% of strokes were ischemic (384/485), 11.6% of strokes were primary intrac-
rebral hemorrhage (PICH; 56/485), 5.4% of strokes were subarachnoid hemorrhage (SAH; 26/485), and 3.9% of strokes were of unknown pathological type (19/485).

Demographic and clinical characteristics are described in Table 1. Atrial fibrillation (AF) was observed in almost one third of ischemic stroke (31%), and in 21% of PICH compared with in 4% of SAH (P < 0.002). Warfarin anticoagulation was substantially more common in patients with PICH compared with ischemic stroke (21.2% versus 8.3%; P < 0.004). No difference was observed between ischemic stroke and PICH in the frequency of diagnosis or treatment of hypertension, or of mean systolic or diastolic blood pressure before stroke onset. However, acute systolic blood pressure was greater immediately after stroke in PICH compared with in ischemic stroke (P = 0.01), as was diastolic blood pressure (P = 0.02). Patients with SAH were younger and more likely to smoke at stroke onset (P < 0.001).

No difference was observed for treatment rates with lipid-lowering agents (mainly statins) and poststroke lipid levels. Rates of ischemic stroke TOAST categories have been previously described.17

Among patients with FES, acute (within 72 hours) National Institutes of Health Stroke Scale score was measured on 83.5% of patients (405/485; Table 1). Acute National Institutes of Health Stroke Scale score was greater for PICH and SAH, compared with ischemic stroke (P < 0.0001). Similarly, stroke severity measured by acute modified Rankin Scale (72 hours) was greater for PICH and SAH (P < 0.0001). Information regarding the model of stroke care was available for 93.8% hospitalized FES patients (402/439). Of these, 283 patients were treated by a specialist stroke team (68.4%), 74 patients were treated in a stroke unit (17.8%), and only 1 patient received thrombolysis (0.2%).

Follow-up at 28 days was complete in 97.3% FES patients (472/485). Proportional frequencies of good (independence,
modified Rankin Scale score 0–2) and fatal stroke outcomes are described in Table 2. Overall, 41.5% of patients had good functional outcome by 28 days. Good outcome was more common in ischemic stroke (44.4%) compared with in PICH (26.8%) or SAH (30.8%; \( P = 0.02 \)). Stroke severity at onset measured by National Institutes of Health Stroke Scale was highly correlated with 28-day modified Rankin Scale (\( r = 0.73; P < 0.0001 \)). Overall 28-day case-fatality was 21% (95% CI, 17.6%–24.9%) and crude mortality rate was 0.34/1000 person-years (95% CI, 0.27–0.41). Early death was substantially more frequent among patients with PICH and SAH compared with those with ischemic stroke (\( P < 0.001 \)).

To validate independently the completeness of ascertainment, in the first 2 months of the Dublin study, 590 high-risk patients referred for investigation or acute treatment of carotid, coronary, or peripheral vascular disease were identified and followed for subsequent cerebrovascular events. Of these, 14 new strokes or TIAs occurred (2.4%), all who had been ascertainment by the core and supplementary methods.

**Discussion**

In the first Irish population-based study using gold-standard methods, we found high incidence rates of stroke in Dublin compared with those reported from other high-income countries over a similar time period. When compared with other high-income countries (age-adjusted to the World Health Organization standard population), stroke incidence rates in Dublin (1.18/1000 person-years; 95% CI, 1.07–1.29) were higher than those recently (2000–2009) reported from England, France, Italy, and Australia, but similar to those reported from Sweden. Similarly, when sex-specific rates were compared with 6 recent European population-based samples (age-adjusted to the standard European population), incident stroke rates in Dublin were higher than those reported in all European sites, with the exception of in Kaunas, Lithuania (Figure; Supplemental Table II). Although higher stroke rates were particularly marked for ischemic stroke in men and for SAH in women, sex-specific rates were generally high for all pathological subtypes in Dublin compared with in other European samples (Supplemental Table II).

Higher incidence rates observed in our study may be partially explained by our use of supplementary ascertainment methods, which improved case-finding by 7% in the OXVASC Study compared with recommended core methods alone. However, improved ascertainment in our study is unlikely to explain fully the higher stroke incidence in Dublin, as the excess in observed incidence greatly exceeds that expected from methodological differences alone. Our view is additionally supported by the greater stroke incidence in Dublin compared with OXVASC, as near-identical core and supplementary ascertainment methods were used in both studies.

The higher stroke rates observed may reflect differences in prevalence or treatment of established vascular risk factors in the Dublin population, which have been associated with higher stroke incidence and prevalence in some studies. Lower socioeconomic status has been associated with higher prevalence of vascular risk factors, and the North Dublin population includes several communities where social disadvantage is common. AF was present in almost one third of Dublin patients with stroke, substantially higher than in earlier population studies. This may partially be explained by our definition of AF, which included all sustained and paroxysmal AF before or within 1 month of stroke onset, unlike earlier studies that reported only prestroke AF. It is also possible that higher prevalence of AF risk factors (eg, heart failure, hypertension) or improved detection of paroxysmal AF in our population may contribute to the high rates observed. Despite a workplace smoking ban in Ireland since 2004, one third of Dublin patients were smokers at stroke onset, ranking joint-highest (with London) by comparison with 7 recent European population-based samples.

Over one fifth of patients with PICH in our study were treated with warfarin anticoagulation at stroke onset. Warfarin was associated with higher risk of PICH compared with other pathological subtypes, consistent with emerging data suggesting that the risk of incident PICH attributable to antithrombotic therapy is increasing. Confirming previous reports, we found that smoking was associated with higher risk of SAH compared with ischemic stroke or PICH subtypes. We cannot exclude the possibility that differences in genetic (eg, ApoE) or other environmental risk factors (eg, alcohol intake) may have contributed to the higher rates observed in our study, although no clear relation with self-reported alcohol intake and either AF or hemorrhagic stroke was observed.
Compared with other recent studies, Dublin patients were similar for age and prevalence of hypertension, coronary disease, and diabetes mellitus, and had similar or higher rates of treatment with antihypertensive, antiplatelet, and statin medications before stroke onset. However, it is possible that residual confounding because of undetected differences in the duration or control of hypertension or other risk factors may also have contributed to the differences in stroke risk between populations.  

Overall early case-fatality in Dublin was 21%, which is within the range of 17% to 30% recently reported from high-income countries. Whereas case-fatality for ischemic stroke was similar, early fatality in Dublin following PICH (41%) and SAH (46%) were greater than in recent studies (25%–35%). Although the reasons for this variation are unclear from available data, it is possible that it may relate to differences in severity or early treatment of hemorrhagic stroke between studies. At the time of our study, only 1 Dublin hospital had a dedicated stroke unit. We acknowledge the possibility that the low availability of stroke unit provision may have been associated with less intensive control of factors (eg, temperature, blood pressure) known to be associated with poor outcome after hemorrhagic stroke. However, since 2006, stroke units have been established in all Dublin hospitals.

Strengths of our study include more comprehensive case ascertainment than in earlier studies, a large sample size, in-person physician assessment to verify eligibility for inclusion, measurement of stroke severity, and high rates of follow-up. We used core and supplementary ascertainment strategies, combined with an independent direct assessment, to achieve recommended gold-standard ascertainment methods. Inclusion of incident cases and all events (first-ever and recurrent) within the study period provided a more accurate reflection of the population disease burden than did incident stroke alone, which would have underestimated the stroke event rate by 15%. We followed stroke survivors to determine residual disability, which is rarely described in population studies. We acknowledge limitations, including the unavailability of more detailed information on the severity and duration of prestroke risk factors, socioeconomic status, lifestyle factors (eg, diet), and acute treatment. As our study ascertained events over a 12-month period, we acknowledge the possibility of a contribution of seasonal variation in stroke rates to our findings and were unable to analyze trends in stroke rates over time. For comparability with OXVASC and other epidemiological studies, and to avoid potential bias associated with a requirement for absence of diffusion abnormality on acute magnetic resonance imaging to define TIA, we used the traditional time-based TIA definition rather than the tissue-based definition.

Conclusion

Our findings illustrate that substantial disparities exist in the population frequencies of stroke within high-income European countries, associated with high rates of fatality for important patient subgroups. Although age is a major determinant of stroke frequency, accumulating evidence indicates that shifts in population risk factor profiles may be associated with secular declines in the incidence of vascular disease, providing opportunities to reduce the societal burden of stroke.  

Our data also illustrate the potential of high-quality population studies to influence national health policy to improve stroke care. The Dublin population study was a component of a multifaceted approach (including an advocacy campaign, national stroke audit, and cost analysis) to persuade the Irish government to develop and fund a comprehensive national stroke policy, which was achieved in 2010. Implementation of measures is now well-advanced in Ireland to develop stroke networks with stroke unit and thrombolysis services, national telestroke and stroke register systems, and structured programs for stroke prevention and rehabilitation. In response to the increasing international burden of stroke identified by the World Health Organization, the Irish example may contribute some useful insights as strategies are developed to meet this challenge.

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Disclosures

None.

References


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Supplemental Methods:

Adult (≥18 years) patients with a new (first-ever or recurrent) stroke or TIA were eligible for inclusion. Stroke was defined according to the WHO definition. As in OXVASC, the qualifying event was coded as first-ever stroke if no history of clinical stroke was present (regardless of sub-clinical vascular disease on brain imaging) and as recurrent stroke if a history of clinical stroke existed prior to study onset.

Ischaemic stroke was defined in the presence of an appropriate clinical syndrome, with evidence of cerebral infarction on brain magnetic resonance imaging (MRI) or computerised tomography (CT), or normal neuro-imaging with absence of brain haemorrhage, or pathological evidence of recent cerebral infarction at autopsy. Primary intracerebral haemorrhage (PICH) was verified by evidence of acute intraparenchymal haematoma on brain imaging or autopsy, and subarachnoid haemorrhage (SAH) as an appropriate clinical syndrome, with supportive brain imaging, cerebrospinal fluid, or pathological data. If neither brain imaging nor pathological examination were performed, the pathological subtype was coded as ‘Unknown’. As in OXVASC, we classified stroke of unknown type as ischaemic for comparison of pathological types.

First-ever TIA was defined according to the Oxfordshire Community Stroke Project (OSCP) clinical definition. To ensure comparability with previous studies, patients with symptom duration <24 hours in whom brain imaging showed recent minor ischaemic injury were categorised as TIA. Patients with non-focal symptoms (eg. vague weakness), isolated vertigo, diplopia, syncope, or transient global amnesia were excluded.

Medical notes of all patients assessed and discharged from emergency departments were reviewed and suspected stroke/TIA cases were assessed by a study physician. Staff at specialist (geriatric, neurology, vascular surgery, ophthalmology) outpatient clinics were
regularly contacted to encourage referral of eligible patients. Senior physicians in obstetric, psychiatric, and orthopaedic hospitals in the region were contacted regularly.

The source population was defined as North Dublin city, according to the District Electoral Division and County Borough (Ward) system. Residency was defined as usual address within a defined North Dublin Ward during the ascertainment period. Individuals with stroke/TIA whose usual address was outside North Dublin city, but who were treated in North Dublin hospitals were excluded. Detailed demographic data are available from the 2006 Census, which was conducted during the study ascertainment period. The total population was 294,529 individuals, comprising 149,761 women (50.85%) and 144,698 men (49.15%), with 5.7% (16,638 individuals) aged 75 years or greater. The population is relatively stable, with low in- and out-migration. For identification of events in North Dublin residents who were treated outside the North Dublin area, clinicians involved in stroke care in other Dublin hospitals were directly contacted and the study publicised at regional and national meetings of general practitioners and stroke clinicians to encourage notification of eligible patients.

Supplemental Results:

To provide a general estimate of cases treated outside North Dublin, we searched the Irish Hospital In-patients Enquiry (HIPE) database for all patients with a North Dublin city postal code who were discharged with a primary diagnosis of stroke or TIA (ICD-10 codes I60, I61, I63, I64, G45.0-G45.3, G45.9) from Irish hospitals outside North Dublin during the study period. During this time, 15 patients with a postal address in North Dublin city were discharged from hospitals outside North Dublin coded with a primary stroke or TIA diagnosis on the national Irish hospital database. Due to data privacy regulations, further verification of diagnosis, pathological type, or date of onset was not possible in these cases. With the most
conservative assumptions that all diagnoses were accurate, all events occurred within the study period, and that similar proportions were first-ever cases, a sensitivity analysis indicated that minimal increases in the crude incidence rates of first-ever stroke and TIA would occur if these were included (from 1.65 to 1.68/1,000 person-years for stroke and from 0.46 to 0.47/1,000 person-years for TIA).

**Supplemental Table Legends:**

Supplemental Table 1. Crude incidence rates of stroke in North Dublin (first-ever stroke), stratified by age and gender

Supplemental Table 2: Comparison of stroke incidence rates in Dublin and other European populations
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<th>Men</th>
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**Supplemental Table 2:** Comparison of stroke incidence rates in Dublin and other European populations

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<th>Location</th>
<th>Ischaemic stroke Rate (95% CI)</th>
<th>PICH Rate (95% CI)</th>
<th>SAH Rate (95% CI)</th>
<th>Year(s)</th>
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<td>23.1 (14.7-34.7)</td>
<td>20.3 (12.5-31.3)</td>
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<td>Dublin, Ireland</td>
<td>153.6 (132-175.3)</td>
<td>97.3 (82.4-112.2)</td>
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<td>17.9 (11.2-24.6)</td>
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<td>119.3 (98.9-142.8)</td>
<td>107.8 (88.4-130.2)</td>
<td>11.2 (5.6-19.9)</td>
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<td>64 (49.3-81.7)</td>
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Fiorentino,

Italy