transplantation in the placebo group). When these values are used in this model the ratio for prevention through use of pravastatin drops to £11 893 per life year gained (discounted).

More importantly, these situations are not strictly comparable. The transition from health to cardiovascular disease (primary prevention) represents a much larger loss than that from one degree of illness to another (secondary prevention). A decision to focus only on the latter would force a healthy person to experience and survive a cardiovascular event in order to become eligible for treatment, and this experience entails more than just hospital costs and life years gained. When this fact is acknowledged, the benefits achieved with primary prevention are greater than those of secondary prevention.

Although widespread use of pravastatin for primary prevention may seem like an unjustified additional burden on already strained healthcare resources, the results of the West of Scotland coronary prevention study provide evidence that this intervention can be economically sound.

The members of the executive committee of the West of Scotland coronary prevention study are J Shepherd (chairman), S M Cobbe, A R Lorimer, J H McKillop, I Ford, C J Packard, P W Macfarlane, G C Isles.

We especially thank Dr Andrew Whitehouse for all his help in data collection. We acknowledge the help from the information and statistics division of the NHS in Scotland in supplying data from the Scottish record linkage system.

Funding: This work was supported in part by grants from Bristol-Myers Squibb.

Conflict of interest: JC is the scientific director of Caro Research, a consultancy that received a contract to carry out this analysis (it is explicitly stated in that contract that all authorship decisions will be made on the basis of scientific consideration with no editorial role for the sponsor); IF receives a research grant from Bristol-Myers Squibb for his work on the project; DP is an employee of Bristol-Myers Squibb, which manufactures pravastatin; and JS advises Bristol-Myers Squibb from time to time on patient treatment strategies and clinical use of pravastatin.

1 *On the State of the Public Health. The annual report of the chief medical officer of the Department of Health for the year 1994.* London: HMSO, 1995.
2 *Health in Scotland. Report of the chief medical officer on the state of Scotland's health for the year 1994.* Edinburgh: HMSO, 1995.
3 Secretary of State for Health. *The health of the nation: a strategy for health in England.* London: HMSO, 1992.
4 The West of Scotland Coronary Prevention Study Group. A coronary primary prevention study of Scottish men aged 45-64 years: trial design. *J Clin Epidemiol* 1992;45:849-60.
5 Shepherd J, Cobbe SM, Ford I, Isles C, Lorimer AR, Macfarlane PW, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med* 1995;333:1301-7.
6 Cook RJ, Sackett DL. The number needed to treat: a clinically useful measure of treatment effect. *BMJ* 1995;310:452-4.
7 Registrar General Scotland. *Annual report 1994.* Edinburgh: HMSO, 1995.
8 Kendrick S, Clarke J. The Scottish record linkage system. *Health Bull (Edin)* 1993;51:72-9.
9 Tsevat J, Goldman L, Soukup JR, Lamas GA, Connors KF, Chapin CC, et al. Stability of time-tradeoff utilities in survivors of myocardial infarction. *Med Decis Making* 1993;13:161-5.
10 Rose G, McCartney P, Reid DD. Self administration of a questionnaire on chest pain: intermittent claudication. *Br J Prev Soc Med* 1977;31:42-8.
11 Pyörälä K, De Backer G, Graham I, Poole-Wilson P, Wood D. Prevention of coronary heart disease in clinical practice. Recommendations of the task force of the European Society of Cardiology, European Atherosclerosis Society and European Society of Hypertension. *Eur Heart J* 1994;15:1300-31.
12 O'Brien JA, Caro JJ, Klittich WS. Beyond acute care: the true cost of stroke. *Clin Therapeut* 1996;149:21.
13 Pharoah PDP, Hollingworth W. Cost effectiveness of lowering cholesterol concentration with statins in patients with and without pre-existing coronary heart disease: life table method applied to health authority population. *BMJ* 1996;312:1443-8.
14 Stinnet AA, Mittleman MA, Weinstein MC, Kuntz KM, Cohen DJ, Williams LW, et al. Appendix C: the cost-effectiveness of dietary and pharmacologic therapy for cholesterol reduction in adults. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-effectiveness in health and medicine.* New York:Oxford University Press, 1996:349-91.
15 Jönsson B, Johannesson M, Kjekshus J, Olsson AG, Pedersen TR, Wedel H. Cost-effectiveness of cholesterol lowering. Results from the Scandinavian simvastatin survival study (4S). *Eur Heart J* 1996;17:1001-7.

(Accepted 29 July 1997)

Epileptic seizures after a first stroke: the Oxfordshire community stroke project

John Burn, Martin Dennis, John Bamford, Peter Sandercock, Derick Wade, Charles Warlow

Rehabilitation Research Unit, Southampton General Hospital, Southampton SO9 4XY

John Burn, *consultant in rehabilitation medicine*

continued over

BMJ 1997;315:1582–7

Abstract

Objective: To describe the immediate and long term risk of epileptic seizures after a first ever stroke.
Design: Cohort study following up stroke survivors for 2 to 6.5 years; comparison with age specific incidence rates of epileptic seizures in the general population.
Setting: Community based stroke register.
Subjects: 675 patients with a first stroke, followed up for a minimum of 2 years.
Main outcome measures: Occurrence of single and recurrent seizures.
Results: 52 patients had one or more post stroke seizures; in 25 the seizures were recurrent. The 5 year actuarial risk of a post stroke seizure in survivors (excluding19 patients with a history of epilepsy and 3 patients in whom the seizure occurred shortly before death from another cause) was 11.5% (95% confidence interval 4.8% to 18.2%). The relative risk of seizures, in comparison with the general population, was estimated at 35.2 in the first year after stroke and 19.0 in year 2. The risk of seizures was increased in survivors of subarachnoid and intracerebral haemorrhage (hazard ratio for intracranial haemorrhage *v* cerebral infarction 10.2 (3.7 to 27.9)). The risk of seizures after ischaemic stroke was substantial only in patients presenting with severe strokes due to total anterior circulation infarction. Only 9 of 295 patients (3%) independent one month after stroke suffered a seizure between 1 month and 5 years (actuarial risk 4.2% (0.1% to 8.3%)).
Conclusion: Stroke patients have about an 11.5% risk of single or recurrent seizures in the first 5 years after a stroke. Patients with more severe strokes or haemorrhagic strokes are at higher risk.

Introduction

Cerebrovascular disease is an important cause of epilepsy,[1] particularly in elderly people.[2] When seizures complicate a clinical stroke they have a devastating

effect on morale and further impair an already compromised quality of life. Precise estimates of the risk of developing epilepsy would be helpful not only to patients but also to those who give advice on returning to work or driving. Data from hospital based studies may give falsely high estimates of risk since patients with severe strokes, or strokes presenting with seizures, may be more likely to be admitted to hospital.[3] In this study we had three aims: to describe the immediate and long term risk of epileptic seizures after a first stroke among patients in a community stroke register; to analyse the occurrence of seizures in relation to the pathological and clinical subtype of first stroke; and to compare the risk of a first epileptic seizure in these stroke patients with the risk in the general population.

Method

The cohort

The Oxfordshire community stroke project registered 675 patients with a first stroke, 357 (53%) women and 318 (47%) men, from a study population of about 105 000 over 4 years. Patients of all ages were included: 163 (24%) were under 65 years, 195 (29%) 65-74 years, 228 (34%) 75-84 years, and 89 (13%) over 84 years (mean age 72.2 years). Patients were recruited between 1981 and 1986 and were followed up until 1988, when the project finished (minimum follow up 2 years). The methods used to identify and assess cases have been described elsewhere.[4 5] A total of 545 patients (81%) had cerebral infarction, 66 (10%) primary intracerebral haemorrhage, and 33 (5%) subarachnoid haemorrhage. In 31 (4%) cases the type of stroke could not be determined.

Ten patients had intracranial operations for aneurysm, and five of these patients received prophylactic phenytoin for 18 months to 2 years. Prophylactic anticonvulsant treatment was not offered to any other patients. One patient with primary intracerebral haemorrhage (not complicated by seizures) had intracranial surgery.

All but two of the 545 patients with cerebral infarction could be classified into subtypes according to their clinical presentation[6]: 92 patients had total anterior circulation infarction (cortical and subcortical ischaemia likely to be due to occlusion of the main stem of the middle cerebral artery or of the internal carotid artery); 185 patients had partial anterior circulation infarction (predominantly cortical ischaemia likely to be due to occlusion of a branch of the middle cerebral or anterior cerebral artery); 137 patients had lacunar infarction (a lacunar syndrome likely to be due to intracerebral small vessel occlusion[7]); and 129 patients had posterior circulation infarction (ischaemia in the brainstem, cerebellum or occipital cortex likely to be due to either small or large vessel occlusion).

Follow up

Survivors were interviewed by a study nurse at 1 month, 6 months, 12 months, and then annually around the anniversary of their first stroke. At each follow up the nurse asked the patient and caregivers specifically about whether any possible seizure had occurred. As a check the nurse also reviewed the records kept by the primary healthcare team. Patients with suspected seizures were reassessed clinically by the study neurologist. Long term survivors were visited at the close of the study by one of the study neurologists (JPSB), and all available information about possible seizures was reviewed again with the patient. The hospital and primary care records of patients who died before this final visit were reviewed by one of the study neurologists (JPSB), and data relating to possible seizures were discussed at regular consensus meetings of the study team. Generalised seizures were diagnosed with reference to statements of witnesses. Focal seizures were distinguished clinically from clonus, spasms, and recurrent strokes.[8 9] Electroencephalograms were not routinely performed. Each visit included an assessment of functional ability using the Oxford handicap scale[10]; in this report patients in grades 0-2 were described as independent and patients in grades 3-5 as dependent.

The Oxfordshire community stroke project followed up every patient for 2 years or until death. Patients recruited earlier in the study were followed for longer, and no patient was lost to follow up. Seventeen patients died on day 1, 129 by 30 days, 208 by 1 year, and 254 by 2 years. A total of 421 patients were followed up at 2 years, 274 were seen at 3 years, 182 at 4 years, and 92 at 5 years; 324 patients survived to a final examination by a study neurologist between August 1987 and November 1988.

Classification of seizures

Onset seizures were defined as occurring within 24 hours of the onset of stroke. This definition (see appendix) is based on that used in a population based study of acute seizures after head injury.[11] Seizures occurring later were classified as post stroke seizures, except in two cases where evolution of stroke was prolonged.

Comparison with the general population

The incidence of post stroke seizures was compared with the estimated rate of epileptic seizures in the general population, using data from the VAMP research bank, a large British primary care database.[12 13] Eighty two practices had sent in data on the medical and prescribing history of 369 819 patients. The data were checked for completeness and internal consistency,[13] and practices supplying unreliable data were excluded.

Statistical methods

Actuarial analysis was used for cohort data involving the follow up of patients for varying lengths of time. Kaplan-Meier survival curves were constructed in which patients who died or were no longer being followed up (after 2 years) were censored. The occurrence of a post stroke seizure qualified as an end point, and these were graphically represented as a cumulative seizure rate. Different pathological types, age stratifications, and clinical subtypes of stroke were compared by using the log rank method.[14] The incidence of epileptic seizures was compared between stroke survivors and the general population and expressed as a ratio of the observed to the expected frequency with confidence intervals calculated from the Poisson distribution.[15] Calculations were made for year 1 and year 2 separately; there were insufficient events to continue this comparison in years 3-5. Confidence intervals of small samples were calculated by using an exact test.[15]

Department of Clinical Neurosciences, Western General Hospital, Edinburgh EH4 2XU
Martin Dennis, *senior lecturer in stroke medicine*
Peter Sandercock, *reader in medical neurology*
Charles Warlow, *professor of medical neurology*
Department of Neurology, St James's University Hospital, Leeds LS9 7TF
John Bamford, *consultant neurologist*
Rivermead Rehabilitation Centre, Oxford OX1 4XD
Derick Wade, *consultant neurologist*
Correspondence to: Dr Burn
rehab@soton.ac.uk

Table 1 Frequency of onset seizures and development of post stroke seizures by type of first stroke

Type of first stroke	No (%; 95% CI) of patients with onset seizures	Number (%) of patients with onset seizures who developed post stroke seizures
Cerebral infarction (n=545)	10 (2; 0.9 to 3.4)	4 (40)
Primary intracerebral haemorhage (n=66)	2 (3; 0.4 to 10.5)	1 (50)
Subarachnoid haemorrhage (n=33)	2 (6; 0.7 to 20.2)	0
Unknown (n=31)	0 (0; 0 to 11.2)	0
Total (n=675)	14 (2; 1.1 to 3.5)	5 (36)

Table 2 Number (% of cohort; 95% confidence interval) of patients with single and recurrent seizures after first stroke (four patients who had seizures within a few hours of death as part of a terminal illness, or seizures that started before the stroke, were excluded)

Classification of first stroke	Single post stroke seizure	Recurrent post stroke seizures	Total
Cerebral infarction (n=545):	17 (3)	18 (3)	35 (6; 4 to 9)
Total anterior circulation infarction (n=92)	5 (5)	10 (11)	15 (16)
Partial anterior circulation infarction (n=185)	5 (3)	3 (2)	8 (4)
Lacunar infarction (n=137)	3 (2)	2 (1)	5 (3)
Posterior circulation infarction (n=129)	4 (3)	3 (2)	7 (5)
Primary intracerebral haemorrhage (n=66)	3 (5)	4 (6)	7 (11; 3 to 18)
Subarachnoid haemorrhage (n=33)	3 (9)	3 (9)	6 (18; 5 to 31)
Unknown (n=31)	0	0	0
Total (n=675)	23 (3)	25 (4)	48 (7; 6 to 9)

Table 3 Cumulative actuarial risks (95% confidence intervals) of experiencing a seizure after stroke by type of first stroke (19 patients with a history of prestroke seizures were excluded)

Time after stroke	Cerebral infarction	Primary intracerebral haemorrhage	Subarachnoid haemorrhage	Total
1 year	4.2 (2.2 to 6.2)	19.9 (1.5 to 38.3)	22.0 (2.6 to 41.8)	5.7 (3.5 to 7.9)
2 years	6.7 (4.1 to 9.3)	19.9 (1.5 to 38.3)	27.8 (5.3 to 50.7)	8.2 (5.4 to 11.0)
3 years	7.4 (4.0 to 10.8)	26.1 (2.2 to 50.0)	34.3 (8.0 to 62.0)	9.5 (5.8 to 13.2)
4 years	8.6 (4.5 to 12.7)	26.1 (1.3 to 50.9)	34.3 (2.0 to 68.1)	10.5 (6.0 to 15.0)
5 years	9.7 (3.7 to 15.7)	26.1 (0 to 54.8)	34.3 (0 to 100)	11.5 (4.8 to 18.2)

Results

Seizures preceding stroke

Nineteen of the 675 patients (3%) registered with the Oxfordshire community stroke project gave a history of one or more seizures before their first stroke or had documentation of past seizures in their medical record. In one patient the seizures were secondary to a craniotomy for a benign tumour; in one they occurred in the context of eclampsia; and in two they were related to alcohol abuse. The remaining seizures were considered idiopathic, and some may have been caused by otherwise asymptomatic cerebrovascular disease. Eleven of the 19 patients had had a seizure in the year before the stroke: in seven this was a first seizure, and four of these seven patients had partial motor seizures in the same limb as was subsequently affected by the stroke.

Seizures at the onset of the first stroke

Fourteen patients (2%) had an onset seizure, none of whom had a previous history of seizures. In seven the seizure was generalised, in six it was a simple partial seizure, and in one it was a complex partial seizure.

The occurrence of an onset seizure was not, in this cohort, associated with a worse outcome. The 30 day case fatality rate of patients with onset seizures was not raised. Two patients (14%) with onset seizures died compared with 127 of the 661 without onset seizures (19.2%, 95% confidence interval 16.2% to 22.2%). There was also no suggestion that patients with onset seizures had a worse functional prognosis. Three of ten previously independent patients with onset seizures were dependent at one month compared with 179 of those without onset seizures (38.3%, 33.9% to 42.7%).

The occurrence of an onset seizure was, however, associated with an increased risk of having further seizures. Five (36%) of the 14 patients with onset seizures went on to have one or more post stroke seizures compared with 43 (6.9%) of 625 patients who survived the first day without a history of pre-stroke or onset seizures (odds ratio 7.52, 2.46 to 22.98).

Patients with subarachnoid haemorrhage had an excess of onset seizures but this was not statistically significant. Four (4%) of the 99 patients with intracranial haemorrhage had an onset seizure compared with 10 (1.8%) of the 545 patients with cerebral infarction (odds ratio 2.25, 0.69 to 7.33) (table 1).

Post stroke seizures

Fifty two (8%) of 658 patients who survived the first day had one or more post stroke seizures. Three patients had their first seizure only a few hours before death as part of the terminal illness and one patient had had seizures before the stroke. Most analyses were restricted to the remaining 48 patients. Twenty three patients had only a single post stroke seizure; 25 patients had recurrent post stroke seizures as defined in the appendix (table 2), but these generally occurred infrequently; only eight patients had more than one seizure a month over a period of two months or more. Only two of the five patients who had previously had an onset seizure went on to develop recurrent seizures.

Twenty four (50%) of the 48 patients were treated with anticonvulsant drugs; six of these had had only one post stroke seizure. Forty (83%) patients had at least one generalised seizure. Partial seizures occurring alone were less common than at the onset of the stroke.

Risk of post stroke seizure

A Kaplan-Meier survival curve was constructed in which the occurrence of a first post stroke seizure was recorded as an end point and deaths were censored (table 3, fig 1). Patients with a history of epilepsy before the stroke (n = 19) or who died in the first day after the stroke (n = 17) were excluded from these analyses. The probability of having a post stroke seizure was 5.7% (3.5% to 7.9%) within the first year and 11.5% (4.8% to 18.2%) within 5 years. The incremental risk averaged about 1.5% a year after the first 12 months. Five of the 10 patients who had a first seizure more than 2 years after the stroke had had another stroke more recently, and two had taken prophylactic phenytoin for two years after a subarachnoid haemorrhage.

The probability of a post stroke seizure was higher among patients aged over 84 years (observed/expected 2.0) but there was no significant trend on log rank analysis for an increasing risk with age ($\chi^2 = 0.91$, df = 1, $P > 0.25$). Subsequent analyses were not adjusted for age.

Patients who had had a haemorrhagic first stroke were more at risk of post stroke seizures than patients who had cerebral infarction (hazard ratio 10.2, 3.7 to 27.9) (table 3; fig 2). However, the lower risk after cerebral infarction concealed a significant hetero-

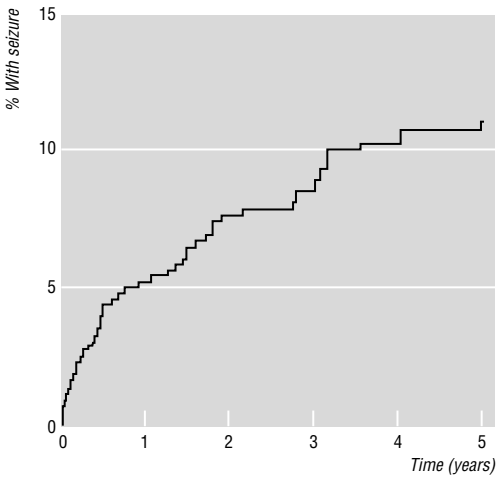

Fig 1 Kaplan-Meier estimate of the risk of post stroke seizures after first stroke; bars indicate 95% confidence intervals. Patients with a history of prestroke seizures (n=19) were excluded and deaths censored. Number of patients still being followed up at 1-5 years who had not had a seizure are indicated. Six of the 92 patients still being followed up at 5 years had had a previous seizure

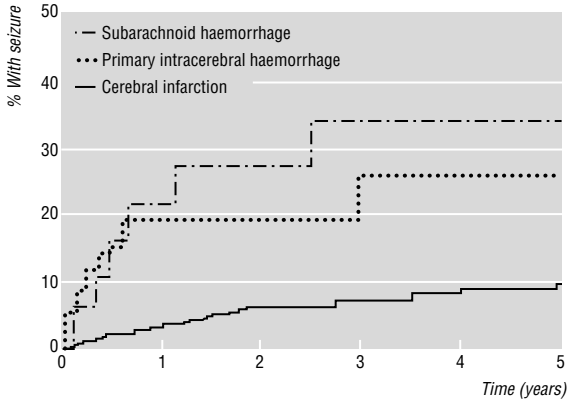

Fig 2 Kaplan-Meier estimate of post stroke seizures subdivided by type of stroke

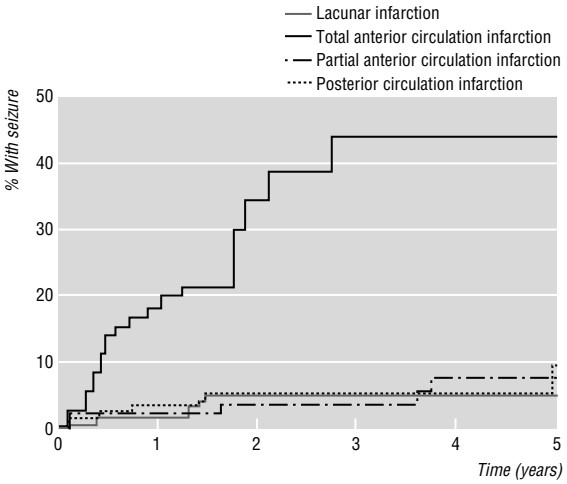

Fig 3 Kaplan-Meier estimates of post stroke seizures after cerebral infarction, subdivided by clinical subtype

geneity between different subtypes ($\chi^2 = 34.0$, df = 3, $P < 0.001$) (table 2; fig 3).

Survivors of total anterior circulation infarction had a markedly increased risk of post stroke seizures when compared with the survivors of other subtypes of cerebral infarction.

The good prognosis for survivors of partial anterior circulation infarction, lacunar infarction, and posterior circulation infarction was reflected in the low probability of future post stroke seizures among independent stroke survivors (those with Oxford handicap scale score 0-2). A further Kaplan-Meier curve restricted to patients alive and independent at 1 month revealed an incremental risk of suffering a post stroke seizure of about 0.9% a year and an actuarial risk at 5 years of 4.2% (0.1% to 8.3%). If only survivors independent at 6 months were included the 5 year actuarial risk was 2.7% (0 to 6.0%).

Comparison with the general population

Forty eight patients had at least one post stroke seizure recorded in a total follow up period (for patients without a history of epilepsy) of 1641 patient years—an incidence of 29.3 patients developing post stroke seizures per 1000 patient years, or 23.5 per 1000 patient years when patients with intracerebral infarction, subarachnoid haemorrhage, or unknown pathology were excluded. This incidence was compared year by year for the first 2 years after stroke with the age specific incidence in the general population, as recorded by the VAMP research data bank over the 12 months between 1 February 1989 and 31 January 1990. Stroke survivors had a 35-fold increased risk of seizures in the first year (table 4). The increase in risk was particularly evident for patients under 65 years.

Discussion

An earlier, community based study of seizures after stroke reported that 9.5% of 518 survivors suffered a seizure 2-5 years after stroke, but no mention was made of subjects who were not followed up or who had died before the assessment.[16] Such problems can be addressed by an actuarial analysis which censors patients who die or who are lost to follow up. This method of analysis has been used in hospital based studies of epilepsy after stroke in New York[17] and Sweden[18] and in a population based study of seizures after cerebral infarction in Rochester, Minnesota.[19] The 5% risk of developing recurrent seizures by 5 years after the stroke found in the Swedish study[18] is similar to the risk observed in the Oxfordshire community stroke project (5.4%, 0.3% to 10.5%). The New York study reported a 19% risk of single or recurrent seizures by six years after an ischaemic stroke[17]; much higher than the risk we observed after cerebral infarction. This study, reported only in abstract, was retrospective and patients with post stroke seizures may have been preferentially followed up. An admission bias towards more patients with severe strokes[20] may also have raised the rate of seizures.

Seizures before stroke

The identification of seizures occurring shortly before the stroke offers support for the concept of vascular precursor epilepsy.[21] Eleven (2%) patients in the Oxfordshire study had a seizure in the year before the

Key messages

- Cerebrovascular disease is an important cause of epilepsy but the risk of seizures after stroke may be overestimated by hospital based studies
- From a community based register, patients with a first ever stroke had a 2% risk of having a seizure at stroke onset and an 11% risk of having a later seizure in the first 5 years of follow up
- Patients with intracerebral and subarachnoid haemorrhage were at higher risk of seizures after stroke
- Survivors who were independent at 1 month were at very low risk of future seizures

stroke. This was three times the number expected in the general population.[22] A case-control study has shown an eightfold increased risk of epilepsy preceding stroke but was confounded by admission bias and the use of elective surgical admissions as controls,[23 24] and a study of patients investigated with computed tomography at the time of their first clinical stroke has confirmed evidence of preceding asymptomatic cerebral infarctions in 11% of patients; half of these involved the cerebral cortex.[25] Prestroke seizures could have arisen from such areas.

Seizures at onset of stroke

The Oxfordshire community stroke project recorded a lower rate of onset seizures than other studies which used a similar definition but in which a selection bias may have raised the rate.[26–28] These studies, which found rates in excess of 4%, were restricted to patients admitted to hospital, and the much quoted study by Aring and Merritt included only cases coming to necropsy.[28] This overrepresentation of fatal cases would have led to an excess of haemorrhagic strokes that were both epileptogenic and fatal.

A more representative hospital series of 1000 consecutive patients admitted to an Australian hospital with acute stroke identified 4.4% of patients with onset seizures and 3.5% with seizures after cerebral infarction.[29] The incidence among patients in the Oxfordshire study was lower, but the Australian series used an extended definition of onset seizures, including events that occurred up to 2 weeks from stroke onset. With the same definition, four more Oxfordshire patients with ischaemic stroke would be included and the incidence of onset seizures after cerebral infarction would rise to 2.7% (1.5% to 3.9%), similar to the Australian result.

In the population based study from Rochester 4.8% of patients had an onset seizure within 24 hours of cerebral infarction,[19] a higher rate than in the Oxfordshire study. The Rochester series may have included patients with haemorrhagic lesions as these subjects had sustained their first stroke between 1960 and 1969, before the use of computed tomography scanning. A more recent series of 1195 hospital patients with both ischaemic and haemorrhagic stroke, which used the same two week definition of onset seizures, reported an incidence of 4.2%.[30] The occurrence of onset seizures in this study was associated, in a multiple regression analysis, with severity of the initial stroke, but the occurrence of an onset seizure did not in this study, or in the Oxfordshire study, necessarily indicate a worse outcome.

Onset seizures after stroke had features in common with acute seizures occurring after traumatic brain injury: the frequency of seizures occurring within 24 hours of the event was similar[11 31]; onset seizures were more often partial[31–33]; and the occurrence of an onset seizure increased the risk of later seizures.[31] These similarities suggest that onset seizures after stroke and traumatic brain injury may have a common pathogenesis.[34 35] The risk of later seizures is, if anything, higher after stroke,[19] but such seizures are less likely to recur.[31]

Post stroke seizures

The risk of post stroke seizures was lower after cerebral infarction than after primary intracerebral haemorrhage or subarachnoid haemorrhage except among patients surviving total anterior circulation infarction, who had a 34% (12% to 57%) risk at 2 years. This estimated risk has broad confidence intervals because only 56 of these patients survived beyond the first 30 days, but it is significantly higher than after other subtypes of cerebral infarction. Post stroke seizures have previously been associated with severe paralytic stroke,[36] particularly when the cerebral cortex has been involved.[29] The increased incidence after total anterior circulation infarction may reflect the extensive damage frequently sustained to the frontal and temporal cortex, the most epileptogenic areas of the brain.[37]

Some patients in the Oxfordshire study developed post stroke seizures without any clinical or computed tomography evidence of cortical damage. Five patients developed post stroke seizures after lacunar infarction. One of these patients had a history of alcohol misuse and another had a dementing illness with evidence on postmortem examination of previous asymptomatic cerebral infarction. In the remaining three patients no other cause was found apart from the lacunar stroke. Other reports of seizures complicating basal ganglionic haemorrhage[38 39] and lacunar infarction[40] suggest that the association between post stroke seizures and cortical damage may not to be as exclusive as previously thought.[36]

The relative and cumulative risks of seizures after cerebral infarction were greater in the Oxfordshire community stroke project than in the one comparable study from Rochester,[19] but both these studies showed a significant excess risk in the first year after stroke and a similar reduction in relative risk with increasing age. The differences may be due to chance alone (the

Table 4 Post stroke seizures observed in the Oxfordshire community stroke project cohort over the first 2 years compared with the number expected to occur in the general population[10]

	All strokes		Cerebral infarction	
Age (years)	No observed	Observed/expected (95% CI)	No observed	Observed/expected (95% CI)
First year after stroke				
<65 (n=163)	9	104.2 (47.7 to 197.9)	5	75.9 (24.7 to 177.2)
65-74 (n=195)	5	22.6 (7.3 to 52.6)	5	27.3 (8.9 to 63.8)
>74 (n=317)	14	28.7 (15.7 to 48.2)	9	22.3 (10.2 to 42.4)
Total (n=675)	28	35.2 (23.4 to 50.9)	19	29.2 (17.6 to 45.5)
Second year after stroke				
<65 (n=129)	1	14.8 (0.4 to 82.6)	1	17.2 (0.4 to 95.8)
65-74 (n=154)	3	17.1 (3.5 to 50.1)	3	18.5 (3.8 to 54.0)
>74 (n=184)	6	21.2 (7.8 to 46.2)	6	23.2 (8.5 to 50.5)
Total (n=467)	10	19.0 (9.1 to 35.0)	10	21.0 (10.0 to 38.4)

Rochester results are all within the 95% confidence intervals of the estimates from the Oxfordshire study), but it is possible that the Oxfordshire study detected seizures that did not come to medical attention and so would not be included in the Rochester records.

Implications

Although the Oxfordshire study recorded an 11.5% risk of having a post stroke seizure by 5 years, a much higher risk than in the general population, almost half of these patients had only a single seizure, and of the 25 who had recurrent seizures only eight were having them frequently. It is unusual for epilepsy to be a major problem among stroke survivors,[29 32] and the risk of seizures in this study was significant only after a haemorrhagic or severe ischaemic stroke. Stroke survivors who were functionally independent at 1 or 6 months after the stroke had a very low risk of future seizures. The results suggest a cautious approach to instituting anticonvulsant treatment and support the current British licensing regulations which allow stroke patients who are functionally competent to return to driving after 30 days.

Appendix

A *single seizure* includes a single episode of status epilepticus or multiple seizures with less than 2 weeks between events. Seizures which were "provoked" by a stroke recurrence, occurring at the onset of a new cerebrovascular event, were included as post stroke seizures but were not included in the definition of recurrent seizures.

Recurrent seizures—two or more unprovoked seizures with at least two weeks between events.[29]

Prestroke seizure—single or recurrent seizures occurring before the day of the first stroke.

Onset seizures—seizures occurring within 24 hours of stroke onset or, in two cases, at three and four days during the evolution of a progressive stroke while it was still getting worse.

Post stroke seizures—seizures occuring more than 24 hours after stroke onset or after a stable deficit had been established.

We gratefully acknowledge support from the Medical Research Council (UK) and the Stroke Association. We also thank Lesley Jones, computer programmer, for her work in data management and statistical analysis, and the study nurses Sue Price, Liz Mogridge, and Claire Clifford. The project would not have been possible without the cooperation of the following general practices (liaison partners): Beaumont Street, Oxford (Dr A MacPherson); East Oxford Health Centre (Dr D Leggate); Thame (Dr A Marcus); Berinsfield (Dr M Agass); Stert Street, Abingdon (Dr N Crossley); Marcham Road, Abingdon (Dr R Pinches); Malthouse, Abingdon (Dr D Otterburn); Kidlington (Dr S Street); Wantage (Dr V Drury); Deddington (Dr H O'Donell). We also thank Mr Jim Slattery for statistical advice.

Funding: MRC and the Stroke Association.

Conflict of interest: None.

1 Roberts R, Shorvon S, Cox T, Gilliatt R. Clinically unsuspected cerebral infarction revealed by CT scanning in late onset epilepsy. *Epilepsia* 1988;29:190-4.
2 Roberts M, Godfrey J, Caird F. Epileptic seizures in the elderly: aetiology and type of seizure. *Age Ageing* 1982;11:24-8.
3 Bamford J, Sandercock P, Warlow C, Gray M. Why are patients with acute stroke admitted to hospital. *BMJ* 1986;292:1369-72.
4 Bamford J, Sandercock P, Dennis M, Warlow C, Jones L, McPherson K, et al. A prospective study of acute cerebrovascular disease in the community: the Oxfordshire community stroke project 1981-1986. *J Neurol Neurosurg Psychiatry* 1988;51:1373-80.
5 Bamford J, Sandercock P, Dennis M, Burn J , Warlow C. A prospective study of acute cerebrovascular disease in the community: the Oxfordshire community stroke project 1981-1986. Part 2. Incidence, case fatality rates and overall outcome at one year of cerebral infarction, primary intracerebral haemorrhage and subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* 1990;53:16-22.
6 Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet* 1991;337:1521-6.
7 Bamford J, Warlow C. Evolution and testing of the lacunar hypothesis. *Stroke* 1988;19:1074-82.
8 Baquis GD, Pessin MS, Scott RM. Limb shaking—a carotid TIA. *Stroke* 1985;16:444-8.
9 Ropper AH. "Convulsions" in basilar artery occlusion. *Neurology* 1988;38:1500-1.
10 Bamford JM, Sandercock PAG, Warlow CP, Slattery J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke* 1989;20:828.
11 Annegers JF, Grabow JD, Groover RV, Laws ER, Elveback LR, Kurland LT. Seizures after head trauma: a population study. *Neurology* 1980;30: 683-9.
12 Tallis R, Hall G, Craig I, Dean A. How common are epileptic seizures in old age? *Age Ageing* 1991;20:442-8.
13 Hall GC, Luscombe DK, Walker SR. Post-marketing surveillance using a computerised general practice database. *Pharm Med* 1988; 2:345-51.
14 Peto R, Pike MC, Armitage P, Breslow NE, Cox DR, Howard SV, et al. Design and analysis of randomised clinical trials requiring prolonged observation of each patient. 2. Analysis and examples. *Br J Cancer* 1977;35:1-39.
15 Gardner MJ, Altman DG, eds. *Statistics with confidence.* London: BMJ, 1989.
16 Moskowitz E, Lightbody FEH, Freitag NS. Long term follow up of the poststroke patient. *Arch Phys Med Rehabil* 1972;53:167-72.
17 Hauser WA, Ramirez-Lassepas H, Rosenstein R. Risk for seizures and epilepsy following cerebrovascular insults [abstract]. *Epilepsia* 1984;25:666.
18 Viitanen M, Erikson S, Asplund K. Risk of recurrent stroke, myocardial infarction and epilepsy during long term follow up after stroke. *Eur Neurol* 1988;28:227-31.
19 So E, Annegers J, Hauser W, O'Brien P, Whisnant M. Population-based study of seizure disorders after cerebral infarction. *Neurology* 1996;46:350-5.
20 Bamford J, Sandercock P, Warlow C, Gray M. Why are patients with acute stroke admitted to hospital? *BMJ* 1986;292:1369-72.
21 Barolin GS, Scherzer E, Schnaberth G. Epileptische Manifestationen als Vorboten von Schlaganfällen. "Vaskuläre Präkursiv Epilepsie." *Fortschr Neurol Psychiatr* 1971;39:199-216.
22 Goodridge DMG, Shorvon SD. Epileptic seizures in a population of 6000. 1. Demography, diagnosis, and classification and role of the hospital services. *BMJ* 1983;287:641-4.
23 Shinton RA, Gill JS, Zezulka AV, Beevers DG. The frequency of epilepsy preceding stroke. *Lancet* 1987;1:11-3.
24 Starkey IR, Warlow CP. Epilepsy preceding stroke [letter]. *Lancet* 1987;1:742-3.
25 Kase CS, Wolf PA, Chodosh EH, Zacker HB, Kelly-Hayes M, Kannel WB, et al. Prevalence of silent stroke in patients with initial stroke: the Framingham study. *Stroke* 1989;20:850-2.
26 Shinton RA, Gill JS, Melnick SC, Gupta AK, Beevers DG. The frequency, characteristics and prognosis of epileptic seizures at the onset of stroke. *J Neurol Neurosurg Psychiatry* 1988;51:273-6.
27 Davalos A, Cendra E, Genis D, Lopez-Pousa S. The frequency, characteristics and prognosis of epileptic seizures at the onset of stroke [letter]. *J Neurol Neurosurg Psychiatry* 1988;51:1464.
28 Aring CD, Merrit HH. Differential diagnosis between cerebral haemorrhage and cerebral thrombosis. *Arch Intern Med* 1935;56:435-56.
29 Kilpatrick CJ, Davis SM, Tress BM, Rossiter SC, Hopper JL, Vandendriesen ML. Epileptic seizures in acute stroke. *Arch Neurol* 1990;47:157-60.
30 Reith J, Jorgensen HS, Nakayama H, Raascha HO, Olsen TS. Early seizures do not worsen rehabilitation outcome. The Copenhagen stroke study [abstract]. *Eur J Neurol* 1996; 3(suppl 2):93.
31 Jennet B. *Epilepsy after non-missile head injury.* London: Whitefriars Press, 1975.
32 Gupta SR, Naheedy MN, Elias D, Rubino FA. Postinfarction seizures: a clinical study. *Stroke* 1988;19:1477-81.
33 De Carolis P, D'Alessandro RD, Ferrara R, Andreoli A, Saquegna T, Lugaresi E. Late seizures in patients with internal carotid artery and middle cerebral artery occlusive disease following ischaemic events. *J Neurol Neurosurg Psychiatry* 1984;47:1345-7.
34 Dodge PR, Richardson EP, Victor M. Recurrent convulsive seizures as a sequel to cerebral infarction: a clinical and pathological study. *Brain* 1954;77:610-38.
35 Evans JH. The significance of early post-traumatic epilepsy. *Neurology* 1963;13:207-12.
36 Olsen TS, Hogenhaven H, Thage O. Epilepsy after stroke. *Neurology* 1987;37:1209-11.
37 French JD, Gernandt BE, Livingstone RB. Regional differences in seizure susceptibility in monkey cortex. *Arch Neurol Psychiatr* 1956;75:260-74.
38 Faught E, Peters D. Seizures in intracerebral haemorrhage [abstract]. *Epilepsia* 1984;25:666.
39 Sung C-Y, Chu N-S. Epileptic seizures in intracerebral haemorrhage. *J Neurol Neurosurg Psychiatry* 1989;52:1273-6.
40 Avrahami A, Drury VE, Rabey MJ, Cohn DF. Generalised epileptic seizures as the presenting symptom of lacunar infarction in the brain. *J Neurol* 1988;235:472-4.

(Accepted 8 July 1997)