Articles

Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study)

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Summary

Background The incidence of stroke is predicted to rise because of the rapidly ageing population. However, over the past two decades, findings of randomised trials have identified several interventions that are effective in prevention of stroke. Reliable data on time-trends in stroke incidence, major risk factors, and use of preventive treatments in an ageing population are required to ascertain whether implementation of preventive strategies can offset the predicted rise in stroke incidence. We aimed to obtain these data.

Methods We ascertained changes in incidence of transient ischaemic attack and stroke, risk factors, and premorbid use of preventive treatments from 1981–84 (Oxford Community Stroke Project; OCSP) to 2002–04 (Oxford Vascular Study; OXVASC).

Findings Of 476 patients with transient ischaemic attacks or strokes in OXVASC, 262 strokes and 93 transient ischaemic attacks were incident events. Despite more complete case-ascertainment than in OCSP, age-adjusted and sex-adjusted incidence of first-ever stroke fell by 29% (relative incidence 0·71, 95% CI 0·61–0·83, p=0·0002). Incidence declined by more than 50% for primary intracerebral haemorrhage (0·47, 0·27–0·83, p=0·01) but was unchanged for subarachnoid haemorrhage (0·83, 0·44–1·57, p=0·57). Thus, although 28% more incident strokes (366 *vs* 286) were expected in OXVASC due to demographic change alone (33% increase in those aged 75 or older), the observed number fell (262 *vs* 286). Major reductions were recorded in mortality rates for incident stroke (0·63, 0·44–0·90, p=0·02) and in incidence of disabling or fatal stroke (0·60, 0·50–0·73, p<0·0001), but no change was seen in case-fatality due to incident stroke (17·2% *vs* 17·8%; age and sex adjusted relative risk 0·85, 95% CI 0·57–1·28, p=0·45). Comparison of premorbid risk factors revealed substantial reductions in the proportion of smokers, mean total cholesterol, and mean systolic and diastolic blood pressures and major increases in premorbid treatment with antiplatelet, lipid-lowering, and blood pressure lowering drugs (all p<0·0001).

Interpretation The age-specific incidence of major stroke in Oxfordshire has fallen by 40% over the past 20 years in association with increased use of preventive treatments and major reductions in premorbid risk factors.

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Introduction

Stroke is the second leading cause of death worldwide[1] and the main cause of long-term neurological disability in adults, with more than half of survivors being left dependent on others for everyday activities.[2] It is also a major cause of depression, dementia, epilepsy, and falls, and patients with stroke account for more hospital and care-home bed days than any other disorder.[2] The burden of stroke is predicted to increase over the years ahead because of the rapid rise in the elderly population in both the developed and developing world. However, over the past two decades, findings of randomised trials have shown that several interventions are effective in both the primary and secondary prevention of stroke,[3–6] and researchers have estimated that full implementation of currently available preventive strategies could reduce stroke incidence by as much as 50–80%.[7,8] Country-specific data on time-trends in stroke incidence are required to assess whether implementation of these preventive strategies has been associated with any such change.

Stroke mortality rates fell from the 1950s to 1980s in North America and western Europe,[9,10] but this decline has since levelled off.[11–13] Although apparent trends in stroke mortality are very difficult to interpret because of changes over time in death certification practices and case-fatality, stroke incidence also seemed to diminish in the 1960s and 1970s in the USA,[14,15] Asia,[16] and Europe.[17–19] However, findings of most subsequent studies during the 1980s and 1990s, when effective preventive treatments had become more widely available, have shown either no change[20–24] or an increase in age-adjusted and sex-adjusted incidence.[25–31] Thus, as yet, no evidence is available that preventive strategies have reduced the incidence of stroke on a community level.

A population-based incidence study of stroke and transient ischaemic attack (the Oxfordshire Community Stroke Project; OCSP)[32,33] was undertaken in Oxfordshire, UK, 20 years ago. Because little change has taken place in either the racial mix of the population or in the organisation of the health-care system in the interim we had the opportunity to ascertain reliably the change in the incidence of stroke and transient ischaemic attack over the past 20 years. In collaboration with the original OCSP investigators, and using the same methods, we aimed to remeasure the incidence of stroke and transient ischaemic

attack in the same population in 2002–04 (Oxford Vascular Study) and to compare premorbid use of preventive treatments and risk factors.

Methods

Study population

The OXVASC study population comprised all individuals, irrespective of age, registered with 63 family doctors in nine general practices in Oxfordshire, UK. In the UK, most people register with a general practice, which provides their primary health care and holds a lifelong record of all consultations with the family doctor and secondary-care providers and details of medications, blood pressure, and investigations. OXVASC included all practices that had participated in OCSP apart from two (Thame and Deddington were excluded because they no longer refer all patients to Oxford hospitals). The remaining practices covered the same geographic areas as in OCSP, had the same referral patterns, held accurate age-sex registers of their patients, and were willing to refer any patient with a suspected cerebrovascular event to the study and allow regular searches of their computerised diagnostic coding systems. The OXVASC population was 94% white.[34] Census data suggest that this proportion has not changed since OCSP. To estimate social deprivation in the population served by our practices we used the index of multiple deprivation (IMD).[35] The electoral wards containing our practices were significantly less deprived than the rest of England (mean IMD score 8·69 *vs* 16·98, p<0·0001) but had a broad range of deprivation, with two of nine wards ranking in the lower third nationally. OXVASC was approved by our local research ethics committee.

Procedures

Diagnosis was designed to be as similar as possible to the OCSP. We used the same definitions of stroke and transient ischaemic attack.[36] Furthermore, since clinical opinion about which clinical syndromes represent transient ischaemic attack or stroke has evolved over the past 20 years, summaries of all potential cases were reviewed by the principal investigator of OCSP (CPW) to ensure that the application of definitions of events was comparable. Diagnosis was based on clinical findings and CT brain imaging as in OCSP. Furthermore, all CT scans were reviewed by a study neuroradiologist (PA) who was also involved in OCSP, and the same criteria were used for haemorrhagic infarction and primary intracerebral haemorrhage in both studies.

All events were categorised as first-ever incident or recurrent on the basis of clinical history rather than findings on brain imaging. As in OCSP, a first-ever stroke that happened in a patient with a previous transient ischaemic attack was coded as incident, but a first-ever transient ischaemic attack in a patient with a previous stroke was coded as recurrent.[33] The other OCSP requirements for definition of an incident transient ischaemic attack were also adhered to.[33] As in the OCSP, patients who had an event while temporarily away from Oxford were included, but visitors to Oxford who were not registered with one of the study family doctors were excluded.

After a 3-month pilot study to develop rapid and effective case-ascertainment, formal ascertainment began on April 1, 2002. This report concerns strokes and transient ischaemic attacks happening up until March 31, 2004. We used the five sources of ascertainment that were used in OCSP. (1) Collaborating family doctors reported cases to the study doctors by telephone, facsimile, or pager as soon as they became aware of a possible transient ischaemic attack or stroke. Patients not requiring immediate hospital admission were seen in a dedicated daily hospital clinic or at home if transfer to hospital was believed to be clinically inappropriate. (2) The study team maintained frequent personal contact with the general practices by regular visits, a quarterly newsletter, and via a liaison family doctor in every practice. (3) Computerised hospital diagnostic codes were reviewed regularly. In OCSP, the Oxford record linkage system[37] was used. In OXVASC, the coding department for the Oxford Radcliffe Hospitals Trust provided a monthly general practice-specific list of all patients with ICD10 (International Classification of Diseases, 10th revision) codes for transient ischaemic attack and stroke and all deaths in hospital. A similar list was obtained from the Oxford Eye Hospital and local community hospitals. (4) Hospital admission and emergency department registers were reviewed daily. (5) Deaths out of hospital were identified via the Coroner's Office, by review of all death certificates in the study practices, and by ICD10 vascular death codes from the local Department of Public Health. Three methods of case-ascertainment that were not used in OCSP were used in OXVASC. (1) Daily visits to the acute medical admissions unit, acute stroke unit, neurology wards, and stroke rehabilitation wards, and daily contact with hospital bereavement officers to identify all patients brought into hospital dead or who died soon after arrival. (2) A computer-generated list of all requests for brain and cerebral vascular imaging was reviewed on a monthly basis and all referrals for carotid doppler ultrasound were reviewed every week. (3) Patients with visual symptoms due to retinal or cerebral ischaemia were referred directly to the study from the eye emergency unit and department of ophthalmology, and lead clinical staff in the other departments (eg, paediatrics, obstetrics, etc) were contacted monthly to ascertain strokes in patients under their care.

We used two additional methods that were not used in OCSP to test the completeness of ascertainment by the methods listed above. First, all study general practice computer systems were searched every month for all patients coded with a cerebrovascular diagnosis. Second, we assessed a high-risk subset of our study population by ascertaining on a daily basis all patients admitted to hospital with an acute coronary syndrome or an acute peripheral vascular event (ruptured aortic aneurysm, acute limb or bowel ischaemia, etc) and all patients undergoing elective or emergency coronary, carotid, or peripheral vascular investigations or interventions (eg, angiography, angioplasty, endarterectomy, arterial bypass, etc). In these patients a detailed history was taken at baseline and at 1, 3, 6, and 12 months' follow-up to identify any transient ischaemic attacks or strokes happening during the study period.

A study clinician assessed patients as soon as possible after the event in hospital, in a daily dedicated clinic, or at home. Informed consent was sought, where possible, or assent was obtained from a relative. A standard clinical history and examination was done. As in OCSP, premorbid handicap and disability was assessed with the Rankin score.[38] If a patient died before assessment, we obtained an eyewitness account of the clinical event and reviewed any relevant records. We aimed to obtain CT brain imaging in every case. If death occurred outside hospital or before brain imaging, the autopsy result was reviewed. In view of the high rate (98%) of imaging and autopsy in OXVASC, strokes of unknown type were coded as ischaemic for this analysis. In OCSP, strokes

	Men		Women		Total	
	Number/number at risk	Rate (95% CI)	Number/number at risk	Rate (95% CI)	Number/number at risk	Rate (95% CI)
OXVASC (age, years)						
<35	0/22 910	..	0/20 063	..	0/42 973	..
35–44	4/7401	0·27 (0·07–0·69)	2/6360	0·16 (0·02–0·57)	6/13 761	0·22 (0·08–0·47)
45–54	9/6168	0·73 (0·33–1·38)	6/5577	0·54 (0·20–1·17)	15/11 745	0·64 (0·36–1·05)
55–64	17/4798	1·77 (1·03–2·84)	16/4574	1·75 (1·00–2·84)	33/9372	1·76 (1·21–2·47)
65–74	44/3403	6·46 (4·70–8·68)	28/3435	4·08 (2·71–5·89)	72/6838	5·26 (4·12–6·63)
75–84	35/1857	9·42 (6·56–13·10)	54/2570	10·51 (7·89–13·71)	89/4427	10·05 (8·07–12·37)
⩾85	17/431	19·72 (11·49–31·58)	30/995	15·08 (10·17–21·52)	47/1426	16·47 (12·10–21·91)
Total	126/46 968	1·34 (1·12–1·60)	136/43 574	1·56 (1·31–1·85)	262/90 542	1·45 (1·28–1·63)
OCSP (age, years)						
<35	2/25 034	0·03 (0·00–0·19)	4/22 587	0·06 (0·00–0·25)	6/47 621	0·04 (0·01–0·15)
35–44	7/5959	0·39 (0·16–0·81)	3/5777	0·17 (0·04–0·51)	10/11 706	0·28 (0·14–0·52)
45–54	10/4577	0·73 (0·35–1·34)	3/4467	0·22 (0·05–0·65)	13/9044	0·48 (0·26–0·82)
55–64	44/3986	3·68 (2·67–4·94)	22/4058	1·81 (1·13–2·74)	66/8044	2·73 (2·12–3·48)
65–74	68/2766	8·19 (6·36–10·39)	56/3108	6·01 (4·54–7·80)	124/5874	7·04 (5·85–8·39)
75–84	65/1223	17·72 (13·67–22·58)	92/2006	15·29 (12·32–18·75)	157/3229	16·21 (13·77–18·95)
⩾85	14/234	19·94 (10·90–33·46)	39/735	17·69 (12·58–24·18)	53/969	18·23 (13·66–23·85)
Total	210/43 749	1·60 (1·39–1·83)	219/42 738	1·71 (1·49–1·95)	429/86 487	1·65 (1·50–1·82)

Population denominators refer to the whole study population without exclusions.

Table 1: **Age and sex structure of the study populations and crude incidence per 1000 population of first-ever stroke**

that did not have brain imaging or autopsy (12%) were classified as haemorrhages only if clinical scoring systems indicated a high degree of certainty.[32] Otherwise they were coded as ischaemic for this analysis. Diagnosis of subarachnoid haemorrhage[32] and clinical subtyping of stroke[39] were the same as in OCSP.

Both OCSP and OXVASC recorded premorbid medication and vascular risk factors from the patient or relative, hospital records, and general practice records. The most recent measurement of blood pressure was recorded in both studies from the general practice records. Total cholesterol concentration was measured at the time of assessment after the transient ischaemic attack or stroke. All surviving cases were followed up by a research nurse or therapist at 1, 3, 6, and 12 months from the time of the stroke and the Rankin score was calculated. If a recurrent vascular event was suspected the patient was assessed by a study doctor.

Statistical analysis

OCSP ascertained strokes and transient ischaemic attacks initially from Nov 1, 1981, to Oct 31, 1984, and OXVASC from April 1, 2002, to March 31, 2004. The midpoints of these dates are exactly 20 years apart (April 1, 1983, and April 1, 2003) and these periods form our primary comparison. OCSP subsequently ascertained strokes again in 1986[32] and continued to record transient ischaemic attacks during 1985 and 1986.[33] Data from these periods were analysed separately. The original individual patient data and the 1981–84 and 1986 age-sex study population data from OCSP were used to recalculate the original incidences for the nine general practices in OXVASC. CIs for incidence were calculated assuming a Poisson distribution for the number of events. Poisson regression models, adjusted for the age and sex structures of the two populations, were used to calculate relative incidence for OXVASC versus OCSP. In neither OCSP nor OXVASC was there evidence of significant variation in incidence between general practices. Incidence of strokes of differing severity were calculated based on the Rankin score at 1 month and also in relation to the incidence of total anterior circulation strokes.[39] All incidences were standardised to the 2001 population of England and Wales. Changes between OCSP and OXVASC in premorbid risk factors and medication were ascertained and significance adjusted for differences in age and sex with regression models.

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or in the decision to submit for publication.

Results

476 individuals had at least one transient ischaemic attack or stroke during the study period. Of these,

	1981–84 (OCSP)	1986 (OCSP)	2002–04 (OXVASC)	Relative incidence† (95% CI)	p
Any first stroke					
Men	2·26 (1·95–2·57)	1·94 (1·45–2·42)	1·50 (1·24–1·77)	0·66 (0·53–0·82)	0·006
Women	2·28 (1·98–2·59)	2·07 (1·56–2·59)	1·74 (1·44–2·03)	0·76 (0·61–0·94)	0·04
Age ⩾85 years	18·31 (13·4–23·3)	19·99 (10·8–29·2)	16·36 (11·7–21·1)	0·89 (0·60–1·32)	0·67
Age <85 years	1·95 (1·76–2·15)	1·65 (1·34–1·96)	1·33 (1·15–1·51)	0·68 (0·58–0·80)	0·0002
Overall	2·27 (2·06–2·49)	2·01 (1·65–2·36)	1·62 (1·43–1·82)	0·71 (0·61–0·83)	0·0002
Pathological type					
Ischaemic stroke	1·93 (1·73–2·13)	1·73 (1·40–2·07)	1·42 (1·24–1·61)	0·73 (0·62–0·86)	0·0009
Primary intracerebral haemorrhage	0·22 (0·15–0·28)	0·22 (0·10–0·33)	0·10 (0·05–0·15)	0·47 (0·27–0·83)	0·01
Subarachnoid haemorrhage	0·11 (0·07–0·16)	0·05 (0·00–0·11)	0·09 (0·05–0·14)	0·83 (0·44–1·57)	0·57
Rankin score at 30 days					
0–1	0·52 (0·42–0·62)	0·49 (0·32–0·65)	0·55 (0·44–0·67)	1·04 (0·79–1·39)	0·75
2–3	0·75 (0·63–0·88)	0·78 (0·57–1·00)	0·47 (0·36–0·57)	0·61 (0·46–0·81)	0·002
4–6	1·00 (0·86–1·15)	0·74 (0·51–0·97)	0·60 (0·48–0·72)	0·60 (0·50–0·72)	0·0004

*To the 2001 census population of England and Wales. †For primary analysis of 1981–84 versus 2002–04.

Table 2: **Standardised* overall incidence per 1000 per year (95% CI) of first stroke in OCSP and OXVASC stratified by sex, age, pathological type, and degree of disability at follow-up 30 days after stroke**

262 were first-ever incident strokes (223 ischaemic strokes, 17 primary intracerebral haemorrhages, 16 subarachnoid haemorrhages, and six unknown) and 76 were recurrent strokes. 138 people presented to medical attention with at least one OCSP-compatible transient ischaemic attack during the study. Of these, 20 had a previous transient ischaemic attack, 17 had a previous stroke, and eight had both, leaving 93 individuals with an incident transient ischaemic attack. A further eight patients were ascertained retrospectively after presenting with a stroke but had not sought medical attention after their transient ischaemic attack. Such cases were not classified as incident events in the OCSP and were therefore excluded from this analysis. Nine of 355 incident events (2·5%, 95% CI 1·2–4·8) happened in non-whites, which was not significantly different (p=0·18) to the proportion in OCSP (nine of 728; 1·2%, 0·6–2·4)

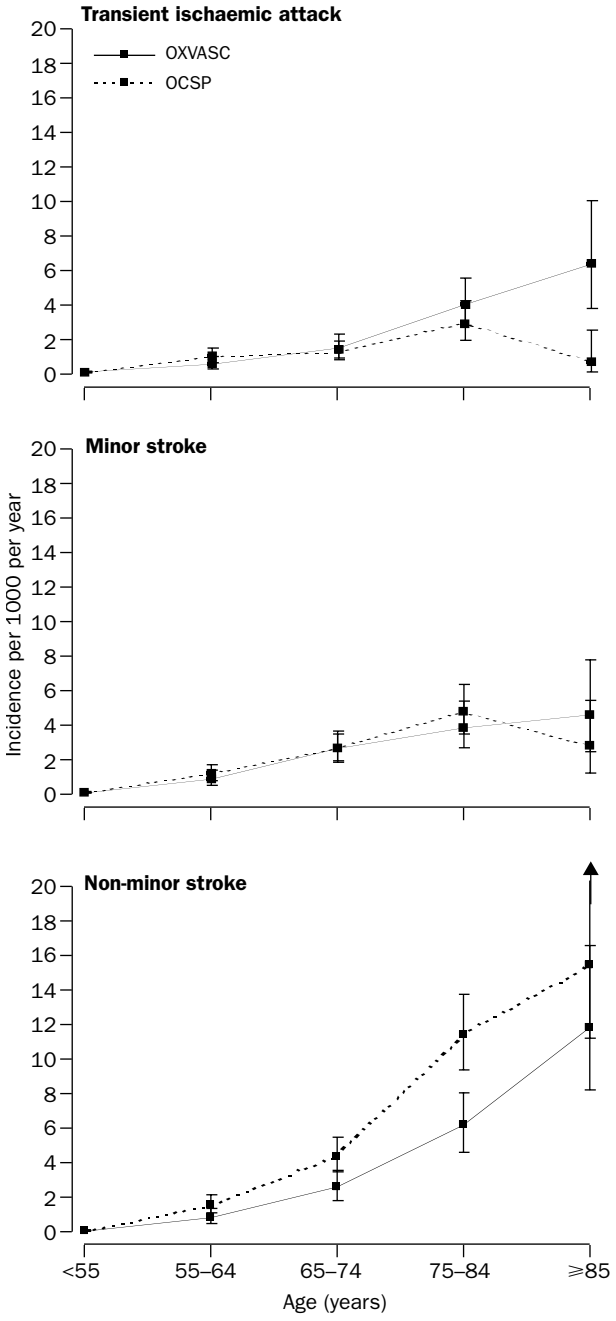

Figure 1: **Age-specific incidence of transient ischaemic attack, minor stroke, and non-minor stroke**
Error bars are 95% CI.

Table 1 compares the age and sex structure of the mid-study populations. In OXVASC, the proportion of individuals aged 75 years or older was increased by 33% and those aged 85 years or older by 41%. If the age-specific incidence of stroke had remained the same as in OCSP, the total number of incident strokes expected in OXVASC would be 28% greater than in OCSP (366 *vs* 286). In fact, the observed number of incident strokes in OXVASC was less than in OCSP (262 *vs* 286).

24 patients with incident stroke died before assessment by a study doctor and one had his event while abroad; he was fully investigated but refused assessment other than allowing access to his medical records. 239 (91%) of 262 patients with incident stroke were ascertained either in our daily clinic or during their admission to hospital. 147 (56%) were inpatients. A study doctor assessed all but two of the patients with incident transient ischaemic attack. The median (IQR) number of days from onset to assessment was 3 (1–9) for incident strokes and 5 (3–12) for incident transient ischaemic attacks compared with 4 (1–12) and 5 (3–11), respectively, in OCSP. The median (IQR) number of days from onset to brain imaging was 6 (2–13) in OXVASC and 8 (3–14) in OCSP.

Of the 262 incident strokes in OXVASC, 220 were ascertained by OCSP methods alone. However, the two methods of direct assessment of ascertainment suggested that this process in OXVASC was near complete. Only four incident strokes that had not been identified by our primary methods were identified by monthly searches of the primary care electronic patient records of the whole study population. Assessment and follow-up of 1103 high-risk individuals (all those who had an acute coronary or peripheral vascular event or a related elective investigation or intervention during the study period [5·5% of our study population ⩾60 years]) identified 16 incident strokes, all of which had already been ascertained by other methods.

The crude incidence per 1000 population in OXVASC was 1·87 (95% CI 1·67–2·08) for any stroke, 1·45 (1·28–1·63) for first-ever stroke, and 0·42 (0·33–0·53) for recurrent stroke. Recurrent events were not included in OCSP. Table 1 shows the number of incident strokes by age and sex in OXVASC and during 1981–84 in OCSP. Table 2 shows the overall incidence of first-ever stroke adjusted to the 2001 census population of England and Wales. There was a 29% reduction in incidence of any first stroke between 1981–84 and 2002–04 (relative incidence 0·71, 95% CI 0·61–0·83, p=0·0002). The incidence of stroke in OCSP in 1986 was non-significantly lower than in 1981–84, but incidence in OXVASC remained lower than in the two OCSP periods combined (0·73, 0·63–0·85, p=0·0003). The standardised rates (per 1000 population) for recurrent stroke and any stroke (recurrent or incident) in OXVASC were 0·48 (0·37–0·59) and 2·10 (1·88–2·33), respectively.

Table 2 shows incidence in 1981–84, 1986, and 2002–04 for types of stroke. Incidence in 2002–04 was reduced from that in 1981–84 for ischaemic stroke (0·73, 95% CI 0·62–0·86, p=0·0009) and primary intracerebral haemorrhage (0·47, 0·27–0·83, p=0·01) but not for subarachnoid haemorrhage (0·83, 0·44–1·57, p=0·57). Stratification of incident strokes by severity revealed no apparent reduction in incidence of minor stroke (Rankin 0–1 at 1 month; relative incidence 1·04, 95% CI 0·79–1·39, p=0·75) but a significant decline in disabling or fatal stroke (Rankin ⩾2; 0·60, 0·50–0·73, p<0·0001).

	Annual transient ischaemic attack incidence per 1000 (95% CI)		
	1981–84 (OCSP)	1985–86 (OCSP)	2002–04 (OXVASC)
Crude incidence			
Men	0·37 (0·28–0·49)	0·42 (0·30–0·58)	0·35 (0·24–0·49)
Women	0·29 (0·20–0·40)	0·32 (0·21–0·46)	0·69 (0·53–0·89)
Overall	0·33 (0·27–0·41)	0·37 (0·29–0·47)	0·51 (0·41–0·63)
Standardised incidence			
Men	0·49 (0·35–0·63)	0·59 (0·40–0·77)	0·37 (0·24–0·50)
Women	0·37 (0·25–0·49)	0·46 (0·29–0·63)	0·77 (0·57–0·96)
Overall	0·43 (0·34–0·52)	0·52 (0·40–0·65)	0·58 (0·46–0·69)
Standardised incidence by age			
⩾85 years	0·66 (0·00–1·56)	3·88 (1·01–6·76)	6·41 (3·45–9·38)
<85 years	0·42 (0·33–0·52)	0·45 (0·34–0·57)	0·46 (0·35–0·56)
<75 years	0·27 (0·20–0·34)	0·33 (0·23–0·43)	0·24 (0·17–0·32)

Direct standardisation to the 2001 census population of England and Wales was used.

Table 3: **Overall incidence of transient ischaemic attack in OXVASC and OCSP by sex and age**

Also, a 60% reduction from 1981–84 to 2002–04 was found in the adjusted incidence of total anterior circulation stroke syndromes (0·56/1000 [95% CI 0·54–0·67] *vs* 0·23/1000 [0·15–0·30]; relative incidence 0·40, 95% CI 0·31–0·65, p=0·0003). Adjusted mortality rates due to incident stroke (based on survival at 1 month) also fell from 0·44/1000 (0·35–0·54) during 1981–84 to 0·28/1000 (0·20–0·37) during 2002–04 (0·63, 0·44–0·90, p=0·02). However, 30-day case-fatality remained the same: 17·2% (45/262) in 2002–04 versus 17·8% (99/557) in 1981–84 (age and sex-adjusted relative risk 0·85, 95% CI 0·57–1·28, p=0·45).

By contrast with the reduction in stroke incidence, adjusted incidence of transient ischaemic attack rose slightly in OXVASC (relative incidence 1·27, 95% CI 0·95–1·71, p=0·12); however, changes in men and women were significantly different (p=0·0006), with slightly reduced incidence in men (0·76, 0·49–1·19, p=0·25) but an increase in women (1·98, 1·32–2·99, p=0·003, table 3). However, these findings could be biased by under-ascertainment of transient ischaemic attack in OCSP. Figure 1 compares the age-specific incidence curves for transient ischaemic attack in OXVASC and OCSP. The increase in incidence with age was less steep in OCSP than in OXVASC at age 65 or older and incidence seemed to fall at age 85 or older in OCSP. A slightly reduced incidence of transient ischaemic attack was noted in OXVASC compared with 1981–84 and 1985–86 in individuals younger than 75 years, and the sex difference was less pronounced (p=0·05): males, relative incidence 0·63, 95% CI 0·36–1·09; females 1·47, 0·79–2·74.

To identify any similar under-ascertainment of stroke in the elderly, we compared the incidence of minor stroke by age in 1981–84 and 2002–04 (figure 1). Premorbid Rankin scores in elderly people are sometimes 2 or more

	1981–84 (n=429)	1986 (n=128)	2002–04 (n=262)	p*
Baseline characteristic				
Male sex	210 (49·0%)	62 (48·4%)	126 (48·1%)	0·83
Mean (SD) age	72·3 (12·7)	70·6 (15·3)	73·6 (11·9)	0·18
Premorbid medication				
Treated hypertension	85 (19·8%)	26 (20·3%)	124 (47·3%)	<0·0001
One drug	52 (12·1%)	19 (14·8%)	61 (23·3%)	
Two drugs	31 (7·2%)	6 (4·7%)	45 (17·2%)	
Three drugs	2 (0·5%)	1 (0·8%)	18 (6·9%)	
Antiplatelet agent	16 (2·9%)	6 (4·7%)	88 (33·6%)	<0·0001
Anticoagulant	5 (1·1%)	0 (0%)	10 (3·8%)	0·02
Lipid-lowering drug	0 (0%)	0 (0%)	29 (11·1%)	<0·0001
Premorbid risk factor				
Total cholesterol (mmol/L)				
Mean (95% CI) baseline concentration	6·24 (6·10–6·39)†	6·21 (5·95–6·47)‡	5·40 (5·26–5·54)§	<0·0001
Proportion ⩾6·0 mmol/L	203 (57·5%)	64 (58·7%)	70 (29·5%)	<0·0001
Systolic blood pressure (mm Hg)				
Mean (95% CI) most recent measurement	156·3 (153·6–159·0)¶	152·9 (147·9–157·9)‖	147·6 (144·8–150·4)**	<0·0001
Proportion ⩾150 mm Hg	221 (60·9%)	67 (56·3%)	118 (45·7%)	0·0002
Proportion ⩾160 mm Hg	185 (51·0%)	48 (40·3%)	69 (26·7%)	<0·0001
Diastolic blood pressure (mm Hg)				
Mean (95% CI) most recent measurement	88·0 (86·7–89·3)¶	87·3 (85·0–89·6)‖	82·0 (80·5–83·5)**	<0·0001
Proportion ⩾85 mm Hg	214 (59·0%)	67 (56·3%)	104 (40·3%)	<0·0001
Proportion ⩾90 mm Hg	190 (52·3%)	58 (48·7%)	67 (26·0%)	<0·0001
Smoking				
Current	123 (32·6%)††	36 (29·8%)‡	47 (18·1%)‡‡	<0·0001
Ex	147 (37·4%)	42 (34·7%)	96 (36·9%)	
Never	123 (31·3%)	47 (38·8%)	117 (45·0%)	
Diabetes	45 (10·5%)	12 (9·4%)	25 (9·5%)	0·69
Previous transient ischaemic attack	52 (12·1%)	16 (12·5%)	41 (15·6%)	0·19
Known previous atrial fibrillation	41 (9·6%)	17 (13·3%)	44 (16·8%)	0·005
Previous myocardial infarction	78 (18·2%)	14 (10·9%)	33 (12·6%)	0·05
Angina	67 (15·6%)	22 (17·2%))	32 (12·2%)	0·21
Peripheral vascular disease	50 (11·7%)	10 (7·8%)	22 (8·8%)	0·23

Data are number of patients (%) unless otherwise indicated. *1981–84 versus 2002–04. Unavailable in: †76 (17·7%) cases; ‡19 (14·8%); §25 (9·5%); ¶66 (15·4%); ‖nine (7·0%); **four (1·5%); ††36 (8·1%); ‡‡two (0·8%).

Table 4: **Premorbid risk factors and medication in patients with incident stroke**

	1981–84 (n=87)	1985–86 (n=67)	2002–04 (n=93)	p*
Baseline characteristic				
Male sex	49 (56·3%)	39 (58·2%)	33 (35·5%)	0·005
Mean (SD) age	67·4 (13·2)	69·8 (12·2)	74·1 (13·0)	0·0007
Premorbid medication				
Treated hypertension			43 (46·2%)	
One drug	..	..	17 (18·3%)	..
Two drugs	..	..	17 (18·3%)	..
Three drugs	..	..	9 (9·7%)	..
Antiplatelet agent	4 (4·6%)	1 (1·5%)	35 (37·6%)	<0·0001
Anticoagulant	2 (2·3%)	2 (3·0%)	6 (6·5%)	0·28
Lipid-lowering drug	0 (0%)	1 (1·5%)	20 (21·5%)	<0·0001
Premorbid risk factor				
Total cholesterol (mmol/L)				
Mean (95% CI) baseline concentration	6·91 (6·54–7·28)†	6·86 (6·53–7·19)	5·61 (5·35–5·87)‡	<0·0001
Proportion ⩾6·0 mmol/L	57 (68·7%)	47 (70·1%)	32 (36·0%)	<0·0001
Systolic blood pressure (mm Hg)				
Mean (95% CI) most recent measurement	159·1 (156·8–164·4)§	153·9 (147·3–160·5)¶	146·5 (141·8–151·1)‖	0·002
Proportion ⩾150 mm Hg	53 (67·1%)	40 (61·5%)	41 (44·6%)	0·003
Proportion ⩾160 mm Hg	42 (53·2%)	26 (40·0%)	27 (29·3%)	0·002
Diastolic blood pressure (mm Hg)				
Mean (95% CI) most recent measurement	87·4 (84·6–90·2)§	85·3 (82·6–88·0)¶	80·4 (78·0–82·8)‖	0·0002
Proportion ⩾85 mm Hg	44 (55·7%)	35 (53·8%)	32 (34·8%)	0·006
Proportion ⩾90 mm Hg	37 (46·8%)	29 (44·6%)	23 (25·0%)	0·003
Smoking				
Current	27 (31·0%)	16 (23·9%)	14 (15·1%)	0·03
Ex	34 (39·1%)	33 (49·3%)	39 (41·9%)	
Never	26 (29·9%)	18 (26·9%)	40 (43·0%)	
Diabetes	8 (9·2%)	3 (4·5%)	9 (9·7%)	0·91
Known previous atrial fibrillation	9 (10·3%)	6 (9·0%)	14 (15·1%)	0·34
Previous myocardial infarction	7 (8·1%)	5 (7·5%)	10 (10·8%)	0·53
Angina	13 (14·9%)	18 (26·9%)	14 (15·1%)	0·98
Peripheral vascular disease	8 (9·2%)	10 (14·9%)	6 (6·5%)	0·49

Data are number of patients (%) unless otherwise indicated. *1981–84 versus 2002–04. Unavailable in: †four cases; ‡five; §eight; ¶two; ‖one.

Table 5: **Premorbid risk factors and medication in patients with incident transient ischaemic attack**

and thus a crude analysis of incidence of non-disabling stroke by age (based on post-stroke Rankin score) would lead to an artifactual reduction in incidence with age. We therefore analysed the incidence of any stroke with a Rankin score of less than 2 at 1 month or any stroke in a patient with a premorbid Rankin score of 2 or more in which the post-stroke Rankin score was unchanged. A fall was recorded in incidence of minor stroke at age 85 or older in OCSP but not in OXVASC. The age-sex incidence curves were, however, similar for non-minor stroke (figure 1). The change in incidence of non-minor stroke (relative incidence 0·61, 95% CI 0·50–0·75, p<0·0001) is likely, therefore, to provide the best estimate of the true change in stroke incidence between 1981–84 and 2002–04.

Table 4 shows data for premorbid risk factors and vascular preventive medication for patients with incident first-ever stroke in OCSP and OXVASC, and table 5 shows data for patients with incident first-ever transient ischaemic attack. Similar changes were present in both analyses. Significant reductions were recorded in mean values for the most recent premorbid measurements of systolic and diastolic blood pressure and for mean total cholesterol concentration on admission or assessment in 2002–04 compared with 1981–84. For example, in patients with transient ischaemic attack, we recorded a 12·6/7·0 mm Hg reduction in blood pressure and a 40% decrease in the proportion of patients with diastolic blood pressure 90 mm Hg or more and with systolic blood pressure 160 mm Hg or more. The median (IQR) time from most recent premorbid blood pressure measurement was 7 months (2–23) in OXVASC and 11 months (3–34) in OCSP (p=0·007). Also, a 1·3 mmol/L reduction was noted in mean total cholesterol concentration between 1981–84 and 2002–04 and a nearly 50% reduction in patients with values of 6·0 mmol/L or greater. A significant reduction in the number of patients who were regular smokers before the event was also seen. In both incident transient ischaemic attacks and strokes, the proportions of patients taking antiplatelet drugs, blood pressure lowering drugs and lipid-lowering drugs were all significantly greater. All the above changes were independent of differences in age and sex between OCSP and OXVASC cases.

A lower frequency of symptomatic arterial disease was recorded in other vascular territories in 2002–04 incident strokes than in 1981–84 (table 4). This difference was less obvious in the transient ischaemic attacks (table 5) but the OXVASC patients were significantly older. Figure 2 shows data for premorbid preventive medication in patients with incident transient ischaemic attacks and with incident stroke combined and stratified according to whether or not the individual had any previous symptomatic vascular disease—ie, primary prevention versus secondary prevention. Secondary prevention patients had a previous transient ischaemic attack (in stroke cases), acute coronary syndrome, angina, or symptomatic peripheral vascular disease.

Discussion

We have shown a major reduction in the age and sex specific incidence of stroke in Oxfordshire, UK, over the past 20 years. As a result, the absolute number of strokes has fallen despite a 33% rise in the population older than 75 years of age and improved ascertainment of stroke in elderly people. This decline was associated with increased use of preventive treatment and better control of vascular risk factors.

Hospital-based studies are prone to bias because changes in patterns of referral, admission, or both can significantly distort longitudinal trends, and major international studies of cardiovascular disease, such as

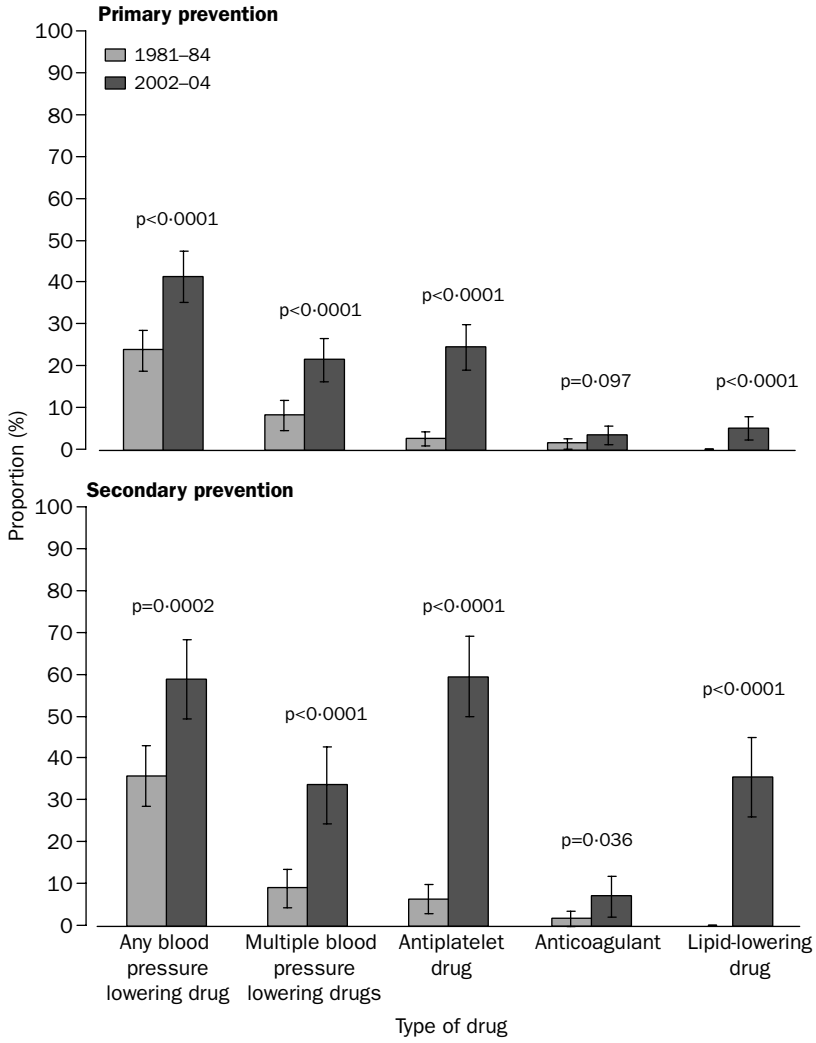

Figure 2: **Premorbid medication in patients with incident first-ever transient ischaemic attack or stroke**

Error bars are 95% CI. Patients stratified according to whether they had no previous evidence of symptomatic vascular disease (primary prevention) or had a previous transient ischaemic attack (in stroke cases), acute coronary syndrome, angina, or symptomatic peripheral vascular disease (secondary prevention).

MONICA,[11] are confined to populations younger than 75 years, thereby excluding half of all strokes (52% in OXVASC) and the age-group of greatest current interest. OCSP was one of the first population-based studies to measure the incidence of transient ischaemic attack and stroke, and OXVASC has had more rigorous case-ascertainment and a higher brain imaging and autopsy rate than any previous population-based stroke incidence study.

Studies of time-trends in disease incidence can be undermined by changes in diagnosis and investigations. To ensure comparability, we used the same criteria as in OCSP, and had diagnosis and inclusion reviewed by both the original OCSP principal neurologist and one of the study neuroradiologists. However, our estimates of the reduction in incidence of stroke are probably conservative because of under-ascertainment of minor stroke in OCSP, particularly in elderly people. The apparent fall in incidence of transient ischaemic attack and minor stroke in elderly patients in OCSP is contrary to all other reliable data, and is highly likely to represent under-ascertainment.

To quantify exactly the difference in completeness of ascertainment between OXVASC and OCSP is difficult. Indirect statistical modelling methods, such as capture-recapture, are poorly validated in stroke incidence studies and are unstable or inappropriate in other similar situations.[40–42] We therefore used two direct methods to assess completeness of ascertainment in OXVASC, both of which suggested that it was near complete. However, only 84% of incident strokes ascertained in OXVASC were identified by methods that had been used in OCSP. Also, some evidence suggested that the public might now be more likely to seek medical attention after stroke-like symptoms than they were at the time of the OCSP. First, in OCSP, 28 patients were identified who presented with a stroke and who had had a previous incident transient ischaemic attack during the study period but had not sought medical attention.[33] In OXVASC, only eight such patients were identified (relative proportion 0·60, 95% CI 0·28–1·27). Second, in our large cohort of patients presenting with non-cerebrovascular disease (5·5% of our total study population aged ⩾60 years) we recorded no patients with symptoms suggestive of transient ischaemic attack or stroke during the study period who had not presented to medical attention.

The true reduction in age-specific incidence of stroke between OCSP and OXVASC is best determined with events for which completeness of ascertainment is likely to have been comparable, such as moderately disabling stroke (Rankin 2–3; 39% reduction), major disabling or fatal stroke (Rankin 4–6; 40% reduction), and fatal stroke (37% reduction), the reductions in which were highly consistent. The fall in total anterior circulation ischaemic stroke syndromes was even greater but had wide confidence intervals (35–69%). Some of this reduction might indicate improvements in management of acute stroke since OCSP, but any such effect is likely to have been small for several reasons. First, most stroke patients in Oxfordshire hospitals are still not currently cared for on dedicated stroke units. Second, the number of patients with severe strokes on initial assessment (before treatment), particularly total anterior circulation stroke syndromes and primary intracerebral haemorrhages, suggests a genuine reduction in the incidence of major stroke. Third, a decline in incidence of major stroke is also consistent with the fall in mortality due to incident fatal stroke in the absence of a reduction in case-fatality of incident stroke.

The 53% reduction in incidence of primary intracerebral haemorrhage confirms the suggestion of a fall of this magnitude in UK mortality and hospital discharge data.[43] A few strokes that did not have brain imaging or autopsy were classified as haemorrhages in OCSP using clinical scoring systems, but this was only done when the score indicated a high degree of certainty.[32] The identification of less clinically obvious haemorrhages due to the higher rate on imaging and autopsy in OXVASC will, if anything, have underestimated the

reduction in incidence. A similar fall in the incidence of intracerebral haemorrhage has been reported in Sweden, as well as an increase in minor ischaemic strokes.[44]

We noted major reductions between OXVASC and OCSP in premorbid systolic and diastolic blood pressure, total cholesterol concentration, and smoking. Some data were missing in patients with incident strokes, attributable partly to deaths before assessment, but the results were very similar in patients with transient ischaemic attack, in whom data were virtually complete. The changes do not seem to be due to any systematic change in methods of measurement. Moreover, the measured reductions in blood pressure and cholesterol concentration are consistent with the measured increases in use of blood pressure and cholesterol lowering drugs.

We could not study changes in premorbid risk factors and medication in the whole of our study population, but the findings in patients with incident transient ischaemic attack and stroke are arguably more relevant because they show the changes in a section of the population that was clearly at risk. However, they are likely to underestimate the changes in the at-risk population as a whole because we could not include those patients in whom an incident transient ischaemic attack or stroke was successfully prevented. Nevertheless, our data provide a useful conservative measure of the changes in risk factors and medication in patients at risk of stroke over the past 20 years. The proportion of the reduction in stroke incidence that is due to these improvements in risk factor control and other preventive treatments is uncertain. Although the changes that we measured, particularly in premorbid blood pressure, are sufficient to account for the reduction in incidence, and might even be expected to produce a greater reduction if representative of changes in the wider at-risk population,[45] we cannot prove that the association is causal and other changes in diet, environment, or behaviour could also be responsible.

The reduction in stroke incidence over the past 20 years should be qualitatively generalisable to other health-care systems that have achieved similar risk factor modification and improvements in preventive treatment. These improvements have been fairly recent in most countries, which could explain why reductions in stroke incidence have not been reported in other studies done in the 1980s and early 1990s.[20–31] The only exception in a population-based study is the fall in stroke incidence in Perth, Australia, between 1989–90 and 1995.[46]

Our quantitative findings will be less generalisable to other settings. Even within the UK, mortality due to stroke varies by nearly 50%, with fairly low rates in Oxfordshire. However, nearly all this variation can be accounted for by differences in the frequency of major risk factors,[47] and therefore lends support to our general conclusions. Moreover, the stroke incidence originally reported in OCSP was consistent with other studies of comparable quality elsewhere in Europe, North America, and Australia.[24]

In conclusion, there has been a major reduction in the age-specific and sex-specific incidence of stroke in Oxfordshire, UK, over the past 20 years. Although we cannot prove that the fall in stroke incidence is a direct result of the measured changes in established risk factors, the size of the changes is consistent and the measured increase in use of preventive medication would be expected to produce a significant reduction in stroke incidence. If the decline in stroke incidence is due in part to risk factor modification and preventive treatment then further reductions are possible with more widespread stroke prevention.

Contributors

P M Rothwell designed OXVASC and obtained funding, supervised the day-to-day running of the study, reviewed all potential transient ischaemic attacks and strokes, analysed data, and wrote the manuscript. A J Coull and M F Giles ascertained and assessed patients with transient ischaemic attack and stroke and those with vascular disease in other territories. L E Silver ascertained and assessed patients with vascular disease in other territories. L M Bull followed up patients with transient ischaemic attack and stroke at 1 month, liaised with the general practices, and obtained data on premorbid risk factors and medication. S A Gutnikov and S C Howard were responsible for data management and statistical analysis, respectively. P Edwards was the study administrator for OXVASC. D Mant, C M Sackley, and A Farmer obtained part of the funding for initial follow-up of patients in OXVASC, supervised initial follow-up of some of the patients, and contributed to discussions about study design. C P Warlow was the principal investigator of OCSP and checked the inclusion of potential transient ischaemic attack and stroke patients in OXVASC. P A G Sandercock, M S Dennis, and J M Bamford undertook OCSP. P Anslow assessed all CT brain scans of patients with transient ischaemic attack and stroke in OXVASC.

Conflict of interest statement

None declared.

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