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Declining 1-year case-fatality of stroke and increasing coverage of vascular risk management: population-based cohort study

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ABSTRACT

Background The authors estimated trends in 1-year case-fatality of stroke in relation to changes in vascular risk management from 1997 to 2005.

Methods A cohort study was implemented using data for 407 family practices in the UK General Practice Research Database, including subjects with first acute strokes between 1997 and 2005. One-year case-fatality was estimated by year and sex. Rate ratios were estimated using Poisson regression.

Results There were 19 143 women and 16 552 men who had first acute strokes between 1997 and 2005. In women, the 1-year case-fatality declined from 41.2% in 1997 to 29.2% in 2005. In men, the decline was from 29.2% in 1997 to 22.2% in 2005. The proportion of general practices that prescribed antihypertensive drugs to two-thirds or more of new patients with stroke increased from 6% in 1997 to 48% in 2005, for statins from 1% to 39% and for antiplatelet drugs from 11% to 39%. The rate ratio for 1-year mortality in 2005, compared with 1997–1998, adjusted for age group, sex, prevalent coronary heart disease, prevalent hypertension and deprivation quintile was 0.79 (0.74 to 0.86, $p < 0.001$). After adjustment for antihypertensive, statin and antiplatelet prescribing, the rate ratio was 1.29 (1.17 to 1.42).

Conclusions Reducing 1-year case-fatality after acute stroke may be partly explained by increased prescribing of antihypertensive, statin and antiplatelet drugs to patients with recent strokes. However, these analyses did not include measures of possible changes over time in stroke severity or acute stroke management.

INTRODUCTION

Stroke is a major contributor to the global burden of disease. Approximately 15.3 million strokes occur worldwide each year, and stroke accounts for approximately 10% of all deaths.¹ In high-income countries, mortality from stroke has been declining for a number of years. In the UK, stroke mortality halved over a 25-year period between 1979 and 2004.²

Changes in stroke incidence, as well as changes in case-fatality, may be contributing to decreasing stroke mortality.³ In high-income countries, stroke incidence showed a general decline up to the early 1980s. Some studies suggest that stroke incidence may have stabilised or increased since the late 1980s,⁴ but age-standardised data from the UK suggest that the incidence of stroke continues to decline.⁵ Stroke case-fatality is also decreasing. This

is evident in results from the WHO Monica study of people aged 35–64 years, which found that changes in stroke mortality appeared to result primarily from changes in the case-fatality of stroke.^{6,7} A report from Auckland, New Zealand found that 1-year case-fatality following stroke declined from 45.6% in 1981–1982 to 30.2% in 2002–2003.³

Over the last two decades, there have been important developments in the care of patients with stroke. In the acute phase, the management of acute stroke has been concentrated in stroke units which may facilitate better outcomes.⁸ Management of vascular risk contributes to preventing of stroke, as well as reducing mortality and recurrent vascular events subsequent to stroke onset. The value of antihypertensive therapy,⁹ statin therapy¹⁰ and aspirin and antiplatelet therapy¹¹ for reducing recurrent vascular events and mortality has been demonstrated in large randomised trials and meta-analyses. These developments have been accompanied by systematic attempts to improve the quality of chronic illness care,¹² and promote evidence-based practice,¹³ leading to increased coverage of the at-risk population with effective therapies.¹⁴ However, there is also evidence of poor-quality practice and inadequate coverage of some groups at risk.^{15,16}

In the present study, we aimed to evaluate the significance of vascular risk management for trends in stroke survival in a sample with high geographical coverage and large numbers of cases. In this study, we utilised data from electronic patient records from UK family practices. We aimed to estimate trends in 1-year survival following acute stroke, to evaluate trends in prescribing for vascular risk management and to determine whether increasing coverage of vascular risk management might be associated with trends in case-fatality.

METHODS

Ethics

The study represented an analysis of anonymised data. The study protocol was approved by the Independent Scientific Advisory Committee (ISAC) of the Medicines and Healthcare products Regulatory Agency (MHRA) (ISAC Protocol No 07_027R).

Data source and subjects

The General Practice Research Database (GPRD) is a large database that comprises the electronic patient records from approximately 5% of UK family practices.¹⁷ Practices contributing to the GPRD are spread across the UK, including England,



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Wales, Scotland and Northern Ireland. There may be some under-representation practices in the inner cities and in the most affluent areas.¹⁷ However, the age and sex distributions of the GPRD population are similar to those of the UK general population.¹⁸ GPRD data are subject to quality checks and are referred to as up to standard (UTS) when the data are of sufficiently high quality to be used for research. Several studies have shown that data for medical diagnoses recorded in GPRD have satisfactory validity.^{19–20} Estimates for rates from GPRD are consistent with those obtained from dedicated data collection systems.²¹

For the present analyses, we selected subjects who had first diagnoses of stroke between 1 January 1997 and 31 December 2006, and who had a minimum of 24 months UTS record prior to the index stroke event. We did not evaluate recurrent strokes. Initially, we utilised a set of 202 medical codes for stroke, derived from the UK Office for National Statistics publication, Key Health Statistics from General Practice.¹⁷ However, initial analysis of the resulting sample of subjects revealed important secular changes in the utilisation of specific codes. In particular, there was a selective increase in the use of codes for 'stroke annual review' and 'stroke monitoring' after 2003.²² This was thought to be associated with contractual changes to family practices associated with the Quality and Outcomes Framework.²³ The codes used in this paper were therefore reviewed and restricted to 121 codes for cerebral infarction, cerebral haemorrhage, subarachnoid haemorrhage, 'cerebral vascular accident' and hemiplegia.²² The most frequently utilised index codes were for 'cerebral vascular accident,' and it was not possible to distinguish infarction from haemorrhage in the majority of subjects. Data were extracted in August 2007, and as the 12-month follow-up was not complete for all subjects, subjects diagnosed in 2006 were excluded.

Analysis

Numbers of strokes were tabulated by index year and gender. The mean age at stroke onset date was estimated, as were the proportions of subjects with coronary heart disease or hypertension ever recorded before the stroke index date. Numbers of deaths within 365 days of the stroke index date were enumerated. The 1-year case-fatality was estimated from a time to event analysis which allowed for the censoring that resulted from patients transferring out of the practice or the end of the study period being reached. Standardised case-fatality ratios (SCFR) were estimated for quintiles of deprivation using all years for reference.

Drug utilisation was estimated using information included on all prescriptions issued to patients recorded in the GPRD Therapy file. We evaluated three sets of drugs: antihypertensive drugs including thiazide diuretics (British National Formulary, BNF, section 2.2.1), potassium sparing diuretics (2.2.3) and their combinations (2.2.4), β blockers (2.4), vasodilators (2.5.1), centrally acting drugs (2.5.2), adrenergic neuron inhibiting drugs (2.5.3), α -blockers (2.5.4), ACE inhibitors (2.5.5.1) and angiotensin receptor blockers (2.5.5.2) and calcium-channel blockers (2.6.2); statins; and aspirin and antiplatelet drugs (BNF 2.9). For each class of drugs, we evaluated whether the drugs were ever prescribed before the stroke index date, or prescribed in the first 12 months after the stroke index date. We recognised that an analysis at the individual patient level presented difficulties because of confounding by indication, as well as length bias with longer surviving subjects having a greater opportunity of being prescribed drugs. We therefore implemented an analysis at the level of the general practice. For each family practice and study

year, we estimated the proportion of patients with acute stroke who were prescribed antihypertensive drugs, statins or antiplatelet drugs. We classified practices by year, using an arbitrary a priori classification, into those that prescribed the drug class of interest to fewer than 33% of its patients with stroke, to between 33% and less than 66% of its patients with stroke, or to 66% of its patients with stroke or greater.

We evaluated the association between drug utilisation and case-fatality. We then fitted random-effects Poisson models, using the 'xtpoisson' command in Stata V.10,²⁴ deaths in the first year following stroke were the dependent variables, survival time to death, 1 year or end of study was the exposure, with family practice as a random effect. We evaluated the association of study year with 1-year case-fatality after adjusting for fixed effects of age group, sex, deprivation quintile, prevalent coronary heart disease or hypertension, and proportions of subjects at each practice that were prescribed antihypertensive drugs, statins or antiplatelet drugs.

RESULTS

There were 48 239 subjects, initially identified using 202 codes for prevalent stroke with a minimum of 24 months' stroke-free record before the index date. From this set of cases, we selected 39 424 (82%) cases with restricted codes for acute stroke on the index date as well as 293 (0.6%) cases in whom the index code was not for acute stroke but in whom a code for acute stroke was recorded within 30 days of the index date. After excluding 3708 subjects whose stroke diagnosis was in 2006, 276 whose death date was recorded before the index date and 38 with uncertain vital status, there were 35 695 subjects, including 19 143 women and 16 552 men, for further analysis. The subjects were drawn from 407 general practices; these included 239 contributing in 1997, increasing to 373 in 2005.

Table 1 shows the distribution of cases by gender and year of study. The mean age at stroke was 70 years in men and 76 years in women. There was weak evidence of a slight decline in age at stroke in women and men. The proportion of stroke cases with prevalent coronary heart disease was approximately 20% in women and 26% in men with no trend over time. The proportion of subjects previously diagnosed as having hypertension increased between 1997 and 2005, increasing from 40% to 56% in women and from 37% to 48% in men. The 1-year case-fatality after acute stroke declined between 1997 and 2005, from 41% to 29% in women and from 29% to 22% in men. There was strong evidence of a linear trend by study year in both men and women.

Table 2 shows the SCFR for stroke by year and deprivation quintile using data for all years as reference. In 1997, the SCFR was 114 in the least deprived quintile and 118 in the most deprived quintile. A decline in SCFR was observed across all deprivation categories ($p < 0.001$), and in 2005 the SCFR was 83 in the least deprived and 95 in the most deprived quintile. This decline in SCFR was generally similar across all deprivation quintiles.

Figure 1 shows the proportion of men and women in whom the three classes of medications for vascular risk management were prescribed by study year. Upper panels show the percentage ever prescribed the drug class before stroke, while the lower panels show the percentage prescribed drug class in the first 12 months after stroke. The proportion of subjects who were prescribed antihypertensive medicines before stroke increased from 65% in women and 54% in men in 1997, to 74% in women and 64% in men in 2005. Prescribing of antihypertensive drugs in the first 12 months after stroke increased from 53% of women and 54% of men in 1997 to 74% of men and women in 2005.

Table 1 Characteristics of stroke subjects with 1-year case-fatality by year and gender

Year	Strokes N	Age (years)		Coronary heart disease		Hypertension		Deaths	1-year case-fatality		Standardised case- death ratios
		Mean	SD	n	%	n	%		%	95% CI	
Female											
1997	1730	76.7	13.40	348	20.12	692	40.00	700	41.16	38.86 to 43.55	122 (113 to 131)
1998	1893	76.5	14.22	391	20.66	781	41.26	709	37.93	35.77 to 40.18	111 (103 to 119)
1999	2061	76.7	13.55	406	19.70	864	41.92	755	37.24	35.17 to 39.40	108 (101 to 116)
2000	2101	76.3	14.35	436	20.75	974	46.36	690	33.45	31.45 to 35.54	98 (91 to 105)
2001	2306	75.8	14.92	524	22.72	1100	47.70	726	32.16	30.27 to 34.14	95 (88 to 102)
2002	2371	75.4	14.83	490	20.67	1142	48.17	748	31.99	30.14 to 33.93	97 (90 to 104)
2003	2383	75.0	14.80	484	20.31	1196	50.19	727	30.85	29.02 to 32.76	96 (89 to 103)
2004	2212	74.8	15.54	437	19.76	1162	52.53	639	29.29	27.43 to 31.26	90 (83 to 97)
2005	2086	75.1	14.88	399	19.13	1175	56.33	602	29.24	27.33 to 31.26	89 (82 to 96)
p Value		<0.001			0.519		<0.001		<0.001		
Male											
1997	1424	70.9	13.56	388	27.25	523	36.73	409	29.16	26.86 to 31.62	114 (103 to 125)
1998	1610	71.3	13.46	405	25.16	613	38.07	458	28.81	26.65 to 31.11	112 (102 to 122)
1999	1683	70.3	13.93	400	23.77	655	38.92	443	26.75	24.68 to 28.95	106 (96 to 116)
2000	1760	70.9	13.58	483	27.44	729	41.42	453	26.14	24.13 to 28.28	102 (93 to 112)
2001	1976	70.6	13.66	535	27.07	815	41.24	478	24.59	22.74 to 26.58	97 (89 to 106)
2002	2109	71.0	13.88	549	26.03	919	43.58	501	24.09	22.30 to 25.99	94 (86 to 102)
2003	2122	70.6	13.97	543	25.59	971	45.76	534	25.50	23.69 to 27.43	102 (94 to 111)
2004	2043	70.2	14.59	515	25.21	913	44.69	452	22.38	20.62 to 24.27	89 (81 to 98)
2005	1825	69.6	14.82	424	23.23	868	47.56	399	22.17	20.31 to 24.16	89 (80 to 98)
p value		0.036			0.261		<0.001		<0.001		<0.001

N, row total; n, frequency; p value, test for linear trend by study year.

Statin prescribing before stroke increased, between 1997 and 2005, from 1% to 28% in women and from 4% to 30% in men. Statin prescribing after stroke increased from 6% to 67% in women and from 10% to 75% in men. Prescribing of antiplatelet drugs before stroke increased from 33% to 49% in women and from 35% to 48% in men. After stroke, prescribing of antiplatelet drugs increased from 58% to 72% in women and from 62% to 73% in men. There was strong evidence of an increasing linear trend for each drug class, in both sexes, before and after stroke ($p=0.001$ or smaller).

Table 3 shows the results of the practice-level analysis. Prescribing of drug classes of interest to patients with recent strokes varied widely between practices, with percentage prescribed ranging from 0 to 100% at different practices in each study year. Over the study period, there were substantial increases in coverage of treatment with all three classes of drugs. In 1997, 27% of practices prescribed antihypertensive drugs to fewer than one-third of their patients with new

strokes, while only 6% prescribed antihypertensive drugs to two-thirds or more of their new patients with stroke. By 2005, 48% of practices prescribed antihypertensive drugs to two-thirds or more of their new patients with stroke, while only 6% of practices prescribed antihypertensive drugs to fewer than one-third of their new patients with stroke. In 1997, 97% of practices prescribed statins to fewer than one-third of their new patients with stroke; by 2005, 39% of practices prescribed statins to more than two-thirds of their new patients with stroke and 51% prescribed statins to between one and two-thirds of new patients with stroke. For antiplatelet drugs, practices prescribing to fewer than one-third of new patients with stroke amounted to 24% of the sample in 1997 but only 7% in 2005; practices prescribing to more than two-thirds of new patients with stroke increased from 11% in 1997 to 39% in 2005. Over all years, there was no association of deprivation quintile with low prescribing of any drug class.

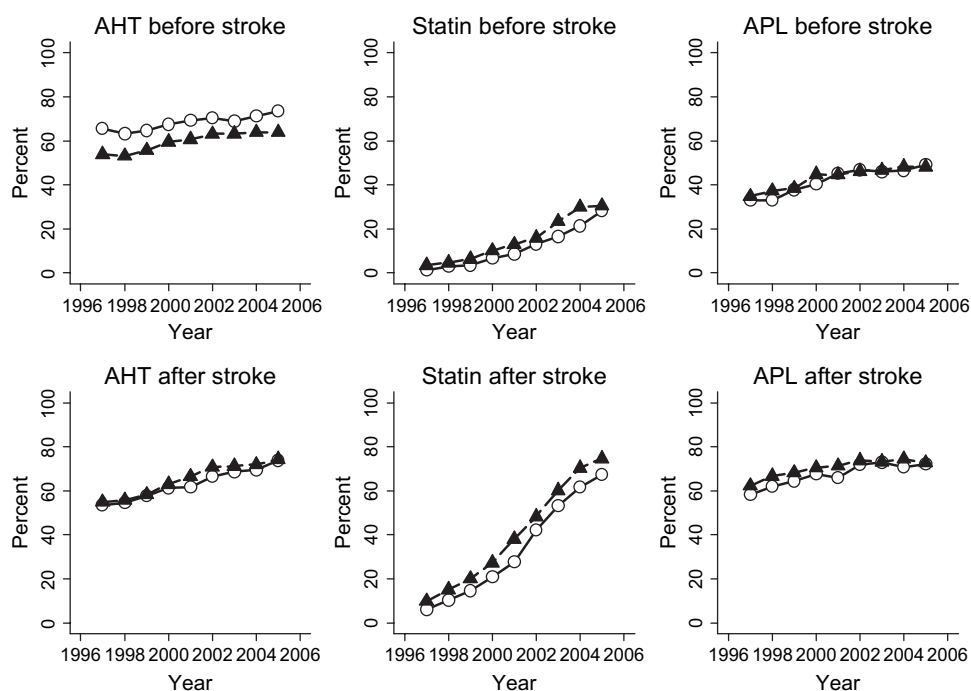
Table 4 shows the results of a Poisson regression analysis using individual subject data. After adjusting for age group and sex, the rate ratio for 1-year case-fatality in 2005, compared with 1-year case-fatality in 1997–1998, was 0.73 (0.68 to 0.79, $p<0.001$). Additional adjustment for deprivation quintile had negligible influence on estimated associations. Further adjustment for previously diagnosed hypertension and coronary heart disease reduced the rate ratio to 0.79 (0.74 to 0.86, $p<0.001$). As there was no trend in coronary heart disease, this observation suggests that approximately 36% of the effect may be accounted for by increased diagnosis of hypertension in primary care. After adjusting for whether the patient was registered at a family practice that prescribed antihypertensive drugs to a high proportion of its patients with stroke, there was no association of study year with 1-year survival. Further adjustment for proportion prescribed statins or antiplatelet drugs yielded a positive association of study year with increasing case-fatality.

Table 2 Standardised case-fatality ratio by year and practice deprivation quintile

Year	Practice deprivation quintile				
	Least deprived	2	3	4	Most deprived
1997	114	118	121	122	118
1998	100	105	111	120	113
1999	106	103	100	116	108
2000	95	98	97	109	98
2001	88	103	89	99	101
2002	92	96	92	103	98
2003	96	98	97	106	96
2004	88	81	93	93	90
2005	83	88	85	95	95

Figures are standardised case-fatality ratios. Data for all years were used for reference.

Figure 1 Prescription of antihypertensive drugs, statins or antiplatelet drugs ever prescribed before stroke or in the first year after stroke by year and sex. AHT, antihypertensive drugs; APL, antiplatelet drugs. Circles, women; triangles, men.



DISCUSSION

Main findings of this study

This study reveals a striking decrease in the 1-year case-fatality of subjects diagnosed as having acute stroke in UK primary care between 1997 and 2005. There was an absolute decrease in 1-year case-fatality of 11.8% for women and 6.7% for men, but the relative decrease since 1997 was 28.8% for women and 23.2% for men. There were only minor changes in case mix, including age and prevalent coronary heart disease, during the period. However, there were major changes in prescribing of medicines that modify vascular risk including antihypertensive drugs, statins and aspirin and antiplatelet therapy. The decline in case-fatality appeared to be explained by an increase in the numbers of practices entering the higher prescribing categories over time. While we cannot exclude bias from confounding, these observations suggest that increasing coverage of the population at risk with effective therapies that reduce vascular risk may be one factor contributing to the decline in 1-year case-fatality of acute stroke. These results provide indirect evidence to support strategies that encourage more intensive management of vascular risk in people who have had strokes.^{25 26}

Limitations of this study

Previous reports of trends in case-fatality of stroke have generally been from stroke registers. The strengths and limitations of data from primary care databases differ from those of stroke registers. This study had the strengths of a very large sample drawn from a large number of general practices throughout the UK. The study was not located in a single area and, by encompassing different contexts and levels of risk, should offer good external validity. Data recorded into the GPRD are subject to quality checks, and previous studies have provided evidence of the validity of recorded information on diagnoses and drug prescribing.^{18–20} A key advantage of utilising data from a primary care database is the opportunity to link data on stroke occurrence and mortality to clinical information concerning comorbidity and coprescribing.

A limitation of these clinical data is that the type of stroke was generally not well characterised with the majority of strokes being recorded using codes that do not distinguish haemorrhage from infarction. It is not possible to evaluate the contribution of changes in stroke type to changes in case-death. Lawlor *et al*³⁵ suggested that trends may have differed for haemorrhagic, compared with ischaemic stroke. Mortality

Table 3 Practice-level analysis showing number of general practices (row per cent) that prescribed drug class to different proportions of new patients with stroke in first year after stroke.

Year	Proportion of new patients with stroke at general practice prescribed drug class in first year after stroke								
	Antihypertensive drugs			Statins			Antiplatelet drugs		
	<33%	33–<66%	66–100%	<33%	33–<66%	66–100%	<33%	33–<66%	66–100%
1997	64 (27)	160 (69)	15 (6)	232 (97)	5 (2)	2 (1)	57 (24)	156 (65)	26 (11)
1998	58 (23)	169 (66)	30 (12)	243 (95)	11 (4)	3 (1)	39 (15)	170 (66)	48 (19)
1999	57 (21)	193 (70)	25 (9)	255 (93)	19 (7)	1 (0)	46 (17)	180 (65)	49 (18)
2000	46 (16)	189 (65)	58 (20)	240 (82)	46 (16)	7 (2)	34 (12)	192 (66)	67 (23)
2001	42 (13)	205 (64)	75 (23)	215 (67)	93 (29)	14 (4)	33 (10)	200 (62)	89 (28)
2002	25 (7)	196 (58)	119 (35)	134 (39)	175 (51)	31 (9)	21 (6)	190 (56)	129 (38)
2003	34 (9)	203 (56)	127 (35)	84 (23)	219 (60)	61 (17)	25 (7)	196 (54)	143 (39)
2004	24 (6)	204 (56)	142 (38)	52 (14)	216 (58)	102 (28)	30 (8)	193 (52)	147 (40)
2005	23 (6)	172 (46)	178 (48)	39 (10)	190 (51)	144 (39)	27 (7)	202 (54)	144 (39)

Table 4 Rate ratios (95% CI) for death within 1-year of stroke by period

	Adjusted for age group and sex (model 1)	Model 1 and deprivation quintile (model 2)	Model 2 and prevalent coronary heart disease and hypertension (model 3)	Model 3 and antihypertensive prescribing category (model 4)	Model 4 and statin and antiplatelet prescribing category
1997–1998	Reference	Reference	Reference	Reference	Reference
1999–2000	0.90 (0.85 to 0.95)	0.90 (0.85 to 0.95)	0.93 (0.88 to 0.99)	0.98 (0.92 to 1.04)	1.02 (0.96 to 1.09)
2001–2002	0.80 (0.75 to 0.85)	0.80 (0.75 to 0.85)	0.84 (0.79 to 0.89)	0.95 (0.89 to 1.01)	1.05 (0.99 to 1.12)
2003–2004	0.79 (0.74 to 0.84)	0.79 (0.74 to 0.84)	0.84 (0.79 to 0.89)	1.01 (0.95 to 1.08)	1.24 (1.15 to 1.34)
2005	0.73 (0.68 to 0.79)	0.74 (0.68 to 0.80)	0.79 (0.74 to 0.86)	1.03 (0.95 to 1.11)	1.29 (1.17 to 1.42)
p Value*	<0.001	<0.001	<0.001	0.461	<0.001

*Test for linear trend.

from haemorrhagic stroke may have declined in England and Wales throughout the 20th century, while mortality from ischaemic stroke may have increased up to the 1970s before declining.

Initial analyses for this study revealed changes over time in the use of medical codes for diagnosis of stroke. In particular, there was a substantial increase in the use of codes for 'stroke annual review' and 'stroke monitoring' in the period 2003–2005. When used as index codes for stroke, these were associated with a low 1-year case-fatality rate of approximately 5%.²² We therefore implemented a more stringent case definition for this study by utilising a restricted set of codes that led to selection of 82% of the initial sample. Exclusion of codes that might not be indicative of acute stroke events and which were associated with low case-death is likely to have had the effect of making the results of the present analyses more conservative than if all initial cases were used.²²

Many patients with stroke are initially admitted to hospital and, if they have not been seen by their family practitioner, may not have a stroke event recorded into their primary care record until a later date after discharge from hospital. Stroke diagnosis dates may therefore be recorded imprecisely, and there might be a consistent bias towards later recording of stroke onset in primary care and underestimation of case-fatality.

It is possible that this form of bias could contribute to apparently decreasing case-fatality if hospitalisation for stroke increased. However, as noted above, our estimates are very similar to those obtained by Carter *et al*³ in a population-based registry.

Longer survival following stroke presents greater opportunities for prescription of medicines to reduce vascular risk when compared with subjects who die soon after the stroke onset. Therefore, instead of estimating the association between antihypertensive prescribing and survival for each individual subject, we evaluated the proportion of subjects prescribed drug classes of interest at the practice at which subjects were registered. Confounding by indication may exist if patients who are considered unlikely to survive are not prescribed secondary prevention interventions. We also acknowledge the importance of unmeasured confounders, such as cigarette smoking, that may be contributing to secular trends. We also recognise the relevance of the 'inverse care law,' which suggests that individuals with the greatest needs may be least likely to receive treatment.³⁶ This leads to an interpretation that secondary prevention interventions will be more often prescribed to people with low mortality risk. However, the substantial changes in the prescribing patterns of family practices over time, and the limited impact of adjusting for deprivation quintile, argue against this interpretation.

What is already known on this topic

Reports from stroke registries have provided evidence of declining short-term case-fatality of stroke over a 20-year period during the 1980s and 1990s in a diverse range of settings including Auckland, New Zealand,³ Dijon, France²⁷ and rural Japan.²⁸ However, in a hospital-based study, Kleindorfer *et al*²⁹ did not find any decrease in 30-day case-fatality of stroke between 1993–1994 and 1999. The population-based OXVASC study in the UK also showed no change in 30-day case-fatality of stroke between 1981–1984 and 2002–2004.⁵ However, the OXVASC study was based on a local population whose profile differs from that of other parts of the UK, being less mobile and more highly educated. Studies of short-term case-fatality after stroke have focused on the prognostic importance of the acute management of stroke. Thus, Carter *et al*³ suggested that increased hospital utilisation, and use of neuroimaging to facilitate appropriate management, were important in contributing to the decline in 28-day case-fatality of stroke in Auckland, New Zealand. Saposnik *et al*³⁰ found that failure to use antithrombotic drugs in hospital, and lack of assessment by a stroke team, were important in determining both the short- and long-term prognosis. There are fewer data available on trends in 1-year case-fatality from stroke, but the present data are consistent with those from Auckland.³ Carter *et al*³ reported 1-year case-fatality for men of 31.9% in 1991/1992 and 25.6% in 2002–2003, while in women the equivalent figures were 35.9% in 1991/1992 and 31.1% in 2002–2003. The results for the stroke register on Auckland for 2002–2003 are very close to the estimates we obtained from UK primary care for the same year.

Systematic reviews have analysed evidence for the effectiveness of different therapies in the prevention of stroke, recurrent vascular events and all-cause mortality. Law and colleagues⁹ concluded that the effectiveness of antihypertensive therapy in reducing stroke and coronary heart disease, with a 41% reduction in stroke and 29% reduction in coronary heart disease, was similar in those with and without previous stroke. While the benefits of antihypertensive therapy are considered to be gained in both haemorrhagic and ischaemic stroke, treatment with either statins or antiplatelet drugs is more relevant to subjects with ischaemic stroke. Treatment with statins after stroke reduces the risk of recurrent stroke by approximately 16% and major cardiovascular events by about 20%.¹⁰ Antiplatelet therapy after stroke is associated with about 7% reduction in odds of death and 23% reduction in odds of recurrent ischaemic stroke.¹¹

What this study adds

This study demonstrates that there have been important increases in population coverage with therapies to reduce vascular risk over the period 1997–2005. A substantial proportion of patients with stroke were already prescribed antihypertensive and antiplatelet therapy in 1997, but this proportion continued to increase over the period. There was also a rapid increase in coverage with statins, rising from less than 10% in 1997 to between two-thirds and three-quarters of subjects in 2005.

We have previously noted wide variations between general practices in the prescribing of antihypertensive and lipid-lowering therapy.³¹ The present data from primary care identify the potential role of general practices' vascular risk-management strategies in influencing longer-term stroke outcomes. Our previous GPRD analyses showed that antihypertensive treatment after stroke was associated with lower mortality,³² consistent with findings from randomised controlled trials that antihypertensive therapy may reduce stroke recurrence³³ as well as reducing the risk of mortality and other vascular events.⁹ The present results demonstrate important increases in the utilisation of antihypertensive and antiplatelet therapy, as well as a very large increase in the proportion of patients with stroke who were prescribed statins. We show that gains in stroke survival appeared to result from an increase in the proportion of general practices that were high-prescribers of these drug classes to patients with recent strokes. After adjustment for prescribing category, there appeared to be a positive association of study year with case-fatality. The reason for this is unclear, and it would be unwise to conclude that case-fatality would have increased in the absence of changes in drug prescribing. Indeed, it is possible that an underlying secular trend in stroke severity might account for a reduction in stroke case-fatality that might be independent of the therapeutic interventions analysed here. This interpretation is supported by a study of stroke severity in Finland, which found that the severity of cerebral infarction and cerebral haemorrhage declined between 1972/1973 and 1989/1991.³⁴ We have analysed measures that are readily recorded and analysed from primary care records. We recognise that less easily measured exposures such as cigarette smoking may have contributed to secular trends, as may changes in the care of acute stroke in hospital settings as suggested by other authors.^{3 30}

We analysed anonymised data, and it was not possible to identify practice characteristics that were associated with either high or low prescribing. However, we noted that the deprivation quintile was not associated with a low prescribing rate. A number of influences may have contributed to changes in prescribing over time. These include the publication of important clinical trials and meta-analyses, the development and dissemination of national and local guidelines for stroke secondary prevention, and more recently the introduction of financial incentives that encourage general practices to adhere to recommended standards of practice.

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Contributors AMT and MCG designed the study. JC and MCG analysed the data. MCG wrote the first draft of the paper. All authors contributed to redrafting and approved the final version.

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Competing interest None.

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REFERENCES

1. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *The Lancet Neurology* 2009;**8**:345–54.
2. Goldacre MJ, Duncan M, Griffith M, et al. Mortality rates for stroke in England from 1979 to 2004: trends, diagnostic precision, and artifacts. *Stroke* 2008;**39**:2197–203.
3. Carter KN, Anderson CS, Hackett ML, et al. Improved survival after stroke: is admission to hospital the major explanation? Trend analyses of the Auckland Regional Community Stroke Studies. *Cerebrovasc Dis* 2007;**23**:162–8.
4. Feigin VL, Lawes CM, Bennett DA, et al. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol* 2003;**2**:43–53.
5. Rothwell PM, Coull AJ, Giles MF, et al. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *The Lancet* 2004;**363**:1925–33.
6. Sarti C, Tuomilehto J, Sivenius J, et al. Declining trends in incidence, case-fatality and mortality of stroke in three geographic areas of Finland during 1983–1989. Results from the FINMONICA stroke register. *J Clin Epidemiol* 1994;**47**:1259–69.
7. Stegmayr B, Asplund K. Exploring the declining case fatality in acute stroke. Population-based observations in the northern Sweden MONICA Project. *J Intern Med* 1996;**240**:143–9.
8. Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev* 2007;(4):CD000197.
9. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009;**338**:b1665.
10. Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. *The Lancet Neurology* 2009;**8**:453–63.
11. Sandercock PA, Counsell C, Gubitz GJ, et al. Antiplatelet therapy for acute ischaemic stroke. *Cochrane Database Syst Rev* 2008;(3):CD000029.
12. Coleman K, Austin BT, Brach C, et al. Evidence on the Chronic Care model in the new millennium. *Health Aff* 2009;**28**:75–85.
13. Shojania KG, Grimshaw JM. Evidence-based quality improvement: the state of the science. *Health Aff* 2005;**24**:138–50.
14. Charlton J, Latinovic R, Gulliford MC. Explaining the decline in early mortality in men and women with type 2 diabetes. Population-based cohort study. *Diabetes Care* 2008;**31**:1761–6.
15. Irwin P, Hoffman A, Lowe D, et al. Improving clinical practice in stroke through audit: results of three rounds of National Stroke Audit. *J Eval Clin Pract* 2005;**11**:306–14.
16. Raine R, Wong W, Ambler G, et al. Sociodemographic variations in the contribution of secondary drug prevention to stroke survival at middle and older ages: cohort study. *BMJ* 2009;**338**:b1279.
17. National statistics. *Key health statistics from general practice 1998*. Series MB6 No 2. London: National Statistics, 2000.
18. Lawson DH, Sherman V, Hollowell J. The General Practice Research Database. Scientific and Ethical Advisory Group. *QJM* 1998;**91**:445–52.
19. Lawrenson R, Todd JC, Leydon GM, et al. Validation of the diagnosis of venous thromboembolism in general practice database studies. *Br J Clin Pharmacol* 2000;**49**:591–6.
20. Jick H. Validation of information recorded on general practitioner based computerised data resource in the United Kingdom. *BMJ* 1991;**302**:766–8.
21. Hansell A, Hollowell J, Nichols T, et al. Use of the General Practice Research Database (GPRD) for respiratory epidemiology: a comparison with the 4th Morbidity Survey in General Practice (MSGP4). *Thorax* 1999;**54**:413–19.

22. **Gulliford MC**, Charlton J, Ashworth M, *et al*. Selection of medical diagnostic codes for analysis of electronic patient records. Application to stroke in a primary care database. *PLoS One* 2009;**4**:e7168.
23. **Doran T**, Fullwood C, Gravelle H, *et al*. Pay-for-performance programs in family practices in the United Kingdom. *N Engl J Med* 2006;**355**:375–84.
24. **Stata Corporation**. *Stata statistical software: release 10*. College Station, Texas: Stata Press, 2008.
25. **Doran T**, Fullwood C, Kontopantelis E, *et al*. Effect of financial incentives on inequalities in the delivery of primary clinical care in England: analysis of clinical activity indicators for the quality and outcomes framework. *Lancet* 2008;**372**:728–36.
26. **Intercollegiate Stroke Working Party**. *National clinical guidelines for stroke*. 3rd edn. London: Royal College of Physicians, 2008.
27. **Bejot Y**, Rouaud O, Durier J, *et al*. Decrease in the stroke case fatality rates in a French population-based twenty-year study. A comparison between men and women. *Cerebrovasc Dis* 2007;**24**:439–44.
28. **Morikawa Y**, Nakagawa H, Naruse Y, *et al*. Trends in stroke incidence and acute case fatality in a Japanese rural area: the Oyabe study. *Stroke* 2000;**31**:1583–7.
29. **Kleindorfer D**, Broderick J, Khoury J, *et al*. The unchanging incidence and case-fatality of stroke in the 1990s: a population-based study. *Stroke* 2006;**37**:2473–8.
30. **Saposnik G**, Hill MD, O'Donnell M, *et al*. Variables associated with 7-day, 30-day, and 1-year fatality after ischemic stroke. *Stroke* 2008;**39**:2318–24.
31. **Gulliford MC**, Charlton J, Latinovic R. Trends in anti-hypertensive and lipid lowering therapy in type 2 diabetes: clinical effectiveness or clinical discretion? *J Human Hypertension* 2005;**19**:111–17.
32. **Toschke AM**, Wolfe CD, Heuschmann PU, *et al*. Antihypertensive treatment after stroke and all-cause mortality—an Analysis of the General Practitioner Research Database (GPRD). *Cerebrovasc Dis* 2009;**28**:105–11.
33. **Rashid P**, Leonardi-Bee J, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. *Stroke* 2003;**34**:2741–8.
34. **Numminen H**, Kaste M, Aho K, *et al*. Decreased severity of brain infarct can in part explain the decreasing case fatality rate of stroke. *Stroke* 2000;**31**:651–5.
35. **Lawlor DA**, Smith GD, Leon DA, *et al*. Secular trends in mortality by stroke subtype in the 20th century: a retrospective analysis. *The Lancet* 2002;**360**:1818–23.
36. **Tudor HJ**. Commentary: three decades of the inverse care law. *BMJ* 2000;**320**:18–19.