



**Determinants of the decline in mortality from acute stroke
in England: linked national database study of 811 029
adults**

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Determinants of the decline in mortality from acute stroke in England: linked national database study of 811 029 adults

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Keywords stroke epidemiology, mortality reduction, record-linkage study, population-based study, case fatality, trends, survival, event rates

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Summary Box

What is already known on this topic	Stroke mortality rates have been declining in England, but little is understood about factors influencing this decline. Previous studies have shown that stroke incidence rates have fallen in England, but there are conflicting results for trends in short-term survival.
What this study adds	Using linked hospital episode and mortality data, which include the vast majority of all stroke events in England, we found that age-standardised stroke mortality rates halved between 2001 and 2010; and that this reduction was largely due to a reduction in case fatality rates, which decreased by 40%. The reduction in case fatality rates was observed in all age groups. There was an overall reduction in stroke event rates by 20%, but this concealed an increase in event rates in people aged under 55.

Abstract

Objective: To study trends in stroke mortality rates, event rates and case fatality rates, and to explain the extent to which the reduction in stroke mortality rates was influenced by changes in stroke event rates or case fatality rates.

Design: Population based study using person-linked routine hospital and mortality data

Setting: England

Participants: 811 029 people aged 20 and older who were admitted to hospital with acute stroke or who died from stroke.

Main outcome measures: Stroke mortality rates, stroke event rates (stroke admission or stroke death without admission), and case fatality rates.

Results: Between 2001 and 2010 stroke mortality rates decreased by 55%, stroke event rates by 20% and case fatality rates by 40%. Average annual change in mortality rates was -6.0% (95% confidence interval -6.2 to -5.8) in men and -7.0% (-7.2 to -6.7) in women, event rates -1.3% (-1.4 to -1.2) in men and -2.7% (-2.9 to -2.6) in women, and case fatality rates -4.7% (-4.9 to -4.5) in men and -4.5% (-4.7 to -4.3) in women. There was a decline in mortality and case fatality rates in all age-groups, but not in event rates: the latter decreased in older people but increased by 2% per year in people aged 35 to 54 years. Of the total decline in mortality rates, 78% in men and 66% in women was attributed to the decline in case-fatality rates and the remaining 22% and 34% to reduction in stroke event rates. The contribution of the two factors varied between age groups. While in people aged under 55 years all the reduction in mortality rates was due to the reduction in case fatality rates, in the oldest age group 85+ reduction in case fatality rates and event rates contributed nearly equally.

Conclusions: Declines in case fatality rates, probably driven by improvements in stroke care, contributed more than declines in event rates to the overall reduction in stroke mortality.

Mortality reduction in men and women under 55 was solely a result of decreases in CFR, while stroke event rates increased in the age group 35 to 54. The increase in stroke event rates in young adults is a concern. This suggests that stroke prevention needs to be strengthened to reduce the burden of stroke.

Introduction

Stroke mortality rates have been declining in almost every country in the world.[1] Reduction in mortality rates could result from decline in disease occurrence, decline in case fatality rates (CFRs), or both. From a public health perspective, declines in disease occurrence are preferable to declines in case fatality, since people who survive a stroke have high rates of disability and an increased risk of developing vascular dementia. A reduction in stroke event rates results from improvements in risk factors achieved through lifestyle modifications and drug treatments. Improved CFRs is almost certainly a reflection of improvements in acute stroke treatment and management, and somewhat, a prevention, which would moderate the severity of strokes in the population, leading to fewer severe strokes and more mild and moderate strokes.

Within existing evidence, it is not completely understood which of the two factors, declining event rates or CFRs, has a more important role in the observed reduction in mortality rates from stroke in England. A study of acute myocardial infarction published in the BMJ reported that decline in event rates contributed just over a half and improved survival at 30 days just under a half to the decline in mortality.[2] No studies analysed the factors that contributed to the decline in acute stroke mortality. Data from clinical trials or biobank studies alone cannot be used to answer this question, because they do not cover whole, representative populations, but large national epidemiologic data collected for the national statistics or datasets of routine medical records can.[3]

We aimed to quantify the contribution of changes in stroke event rates and CFRs to the reduction in stroke mortality using methodology developed by the WHO MONICA study [4, 5], as also used in the study of myocardial infarction.[2] We report on temporal changes in age-specific stroke mortality rates, event rates, and CFRs.

Methods

Data sources

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Data were obtained from two national datasets of routine medical data, Hospital Episode Statistics (HES) and death registration data. The HES data were supplied by Health and Social Care Information Centre. The Office for National Statistics (ONS) supplied the mortality data. The linkage of records between the datasets was based on encrypted personal identifiers, including the NHS number, date of birth and postcode, sent in their encrypted form by the data providers to the Unit of Health-Care Epidemiology, Oxford University, where the research was undertaken. The database covers the whole of England and contains information on every stroke in England that resulted in hospital admission to an NHS hospital or in death without hospitalisation. The majority of hospital care in England is funded by the NHS. Information on private patients, although a small minority of emergency admissions in England, managed in NHS hospitals is also included within HES. Thus, HES provides nearly complete coverage, with the exception of private hospitals, of all hospitalised stroke events in the country. Data on all deaths certified as stroke, including those that occurred out-of-hospital or in an emergency department, before a patient was admitted to a ward, were available from the national mortality data.

Study population and selection criteria

All residents of England aged 20 and older who were admitted to a hospital with stroke, or who died from stroke, between 1 January 2001 and 31 December 2010, were included in the analysis.

Population-based mortality, hereafter, for brevity, termed just mortality, for stroke was defined as a death with stroke as the certified underlying cause of death, and was expressed per 100 000 resident population of England.

The occurrence of stroke was defined as events, following the terminology used by the MONICA study. [5] Events were identified as a hospital admission for stroke, or as a death with stroke as the underlying cause without a corresponding hospital admission for stroke in the preceding 30 days. Event rates were expressed per 100 000 resident population of England.

Case fatality was defined as death from any cause within 30 days of occurrence of stroke, and expressed as a rate per 100 strokes.

We extracted data on stroke hospitalisations and deaths, and grouped them by sex in five-year age groups by calendar year. In our analyses we included multiple stroke events that occurred in each individual patient, if these events were more than 30 days apart.

Strokes were selected using the International Classification of Diseases (ICD) 10th revision codes I61-I64 as the primary diagnosis on hospital record or as the certified underlying cause of death. We restricted analysis to emergency admissions, and excluded all elective admissions. Only patients who spent more than a day in hospital were included in the analysis. The one-day criterion was used to exclude cases of suspected acute stroke, which likely were transient ischaemic attacks (TIA) or similar, in patients who were discharged home when the diagnosis was not confirmed. The length of stay criterion was not applied to patients who died in hospital with stroke recorded as the principal diagnosis: these cases were included.

Statistical analysis

Calculating mortality rate, event rate and case fatality rate

We calculated annual rates for stroke mortality, event and 30-day case fatality in men and women. The 95% confidence intervals for the rates were calculated assuming a Poisson distribution. Mortality rates were calculated by dividing the number of stroke deaths in a calendar year by mid-year populations, the population counts were obtained from the Office for National Statistics website. Our measure of stroke occurrence was a stroke event, as defined above. To calculate annual stroke event rates we divided the number of stroke events, both hospitalisations and deaths, by mid-year populations, and expressed per 100 000 people. Mortality and event rates, as population-based rates, were directly standardised to the European Standard Population (ESP) 2013 for men and women.[6, 7] CFRs were calculated by dividing the total number of deaths that occurred within 30 days after hospital admission for stroke and out-of-hospital deaths, by the total number of stroke events, and multiplied by 100. CFRs were directly age-standardised in 5 year age groups using the combined ten-year study population as the standard population, and expressed as percentages.

Analysis of trends in stroke mortality rates, event rates and CFRs

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The estimate of changes in rates was the average annual percentage change. For each rate - mortality rate, stroke event rate and CFR - a separate regression model was run for all ages and for specified age groups. Age-specific analysis was performed in the following six age groups 20 to 34 years, 35 to 54, 55 to 64, 65 to 74, 75 to 84, and 85 and older.

We used a Poisson regression model to calculate the average annual percentage change in mortality rates and event rates. In the analysis of changes in stroke mortality rates, the dependent variable was stroke deaths. In the analysis of changes in stroke event rates, the dependent variable was stroke events. In both analyses the calendar year of admission was an independent variable and, because we did Poisson regression analysis for rates, we used the corresponding age-specific mid-year population as the exposure variable.

We used two methods to calculate average annual changes in CFRs. Using the dataset, we calculated the annual changes in CFRs in a generalised linear model with binominal distribution, with death within 30 days after stroke as the dependent variable. We also calculated the annual change in CFR as a difference in annual change in mortality rates and stroke event rates using the WHO MONICA formula by subtracting the event rate from the mortality rate (see below). Both estimates are presented in Table 2.

Calculating the determinants of the decline in stroke mortality rates

We estimated the relative contribution of changes in event rates and CFR to changes in stroke mortality over years using an equation from the WHO MONICA study, which states that $\Delta M = \Delta C + \Delta E$, where ΔM is the annual percentage change in mortality rate, ΔC is the annual percentage change in CFR and ΔE is the annual percentage change in event rate.[4]

The equation is derived as follows: if M is the mortality rate, E is the event rate and C is the CFR, then at any moment in time $M = E \cdot C$, since the mortality rate is just the event rate multiplied by the CFR. To estimate the change in mortality rates by time (t), differentiation (d) is used, whereby it follows that $dM/dt = E \cdot dC/dt + C \cdot dE/dt$, or $M' = E \cdot C' + C \cdot E'$ where $M' = dM/dt$ and similar for E and C . The annual percentage change in rates is simply the annual change divided by the rate, so that $\Delta M = M'/M$, $\Delta E = E'/E$ and $\Delta C = C'/C$. From this $\Delta M = M'/M = (E \cdot C' + C \cdot E')/(E \cdot C) = C'/C + E'/E = \Delta C + \Delta E$.

Using this formula, we separated the contribution of percentage change in stroke event rates and CFRs to the percentage change in mortality rates. The relative contribution of each of the two parameters in the formula is calculated as the percentage of total mortality, which is set to 100%.

Results

The linked hospital episode and mortality dataset comprised data on 947 497 stroke events, including 337 085 stroke deaths, in 811 029 people. Of these events, 521 788 (55%) of strokes and 207 198 (61%) of stroke deaths occurred in women (Table 1). The mean age at the onset of stroke was 72 (Standard Deviation (SD) 13) years in men and 76 (SD 14) years in women. The mean age of those who died from stroke was 79 (SD 11) in men and 83 (SD 9) years in women.

Trends over time in mortality rates

The age-standardised mortality rates decreased by 55% during the study period; and a reduction was observed in all age groups. Age-standardised mortality rates decreased from 140 (95% CI 137–142) per 100 000 in 2001 to 74 (73–75) in 2010 in men and from 128 (126–130) to 72 (71–73) in women (Figure 1). The annual change in mortality rates was –6.0% (95%CI –5.8% to –6.2%) in men and –6.1% (–6.0% to –6.3%) in women. The largest reduction in mortality rates was in men and women aged 65 to 74, with an annual change of –8.1% (–7.7% to –8.6%) in men and –8.3% (–7.8% to –8.7%) in women. The lowest average annual reduction in mortality rates was in the youngest age group 20 to 34, –4.1% (–7.8 to –0.4) in men and –4.5% (–8.8 to 0.0) in women.

Trends over time in stroke event rates

Between 2001 and 2010 stroke event rates decreased from 345 (342–349) to 285 (282–287) per 100 000 in men, and from 280 (278–283) to 234 (232–236) in women (Figure 1), with an average annual reduction of –1.3% (–1.2% to –1.4%) per year in men and –2.1% (–2.0 to –2.2) in women. The reduction in stroke event rate was larger in older age groups, for example, in men and women aged 85 and older it was –3.4% (–3.1% to –3.6%) and –2.7% (–2.5% to –2.8%), respectively (Table 2). In contrast, among people aged 35 to 54 years old, stroke event rates increased by 2% per year. No statistically significant change was observed in men and women under 35 years old.

Trends over time in CFRs

CFRs at 30 days decreased from 42% in men and 44% in women in 2001 to 26% and 29% in 2010, respectively (Figure 2). Analysis of age-specific CFRs showed that rates increase with age. During the study period, a reduction in CFRs was observed in all age groups. In 2001 CFRs were 53% (51.1%–54.2%) in men and 57% (56.2%–58.2%) in women aged 85 and older, and decreased to 34% (33.1%–35.5%) in men and 38% (37.4%–39.1%) in women in 2010 (Table 2). Average annual changes in CFRs were calculated using the WHO MONICA formula and regression analysis. Each method produced similar results. On average annual reduction in CFRs was –4.7% in men and –4.0% in women calculated using the WHO MONICA formula, and –4.7% (–4.9% to –4.5%) in men and –4.4% (–4.5% to –4.2%) in women calculated in regression analysis. When trends were analysed by age group, the largest average annual reduction in CFRs was observed in men and women aged 35 to 54, at –6.0% and –7.5% per year, respectively.

Determinants of the reduction in mortality rates

The contribution to changes in mortality rates of changes in event rates and CFRs for men and women of all ages and in specific age groups is shown on Figure 3. Seventy eight percent of reduction in mortality from stroke in men was determined by a reduction in CFRs and 22% by a reduction in stroke event rates. In women, the equivalent percentage contributions were 66% and 34%, respectively. The contribution of these two factors varied between the age groups. In the two youngest age groups, 20 to 34 and 35 to 54, all the decline in stroke mortality was attributable to a reduction in CFRs. There was a gradual increase in the relative contribution of changes in stroke event rates to mortality reduction with increasing age, from 10% in men and 14% in women aged 55 to 64, to 43% in men and 48% in women aged 85 and older.

Discussion

Main findings

During the first decade of the 21st century stroke mortality rates in England halved, stroke event rates decreased by about 20% and CFRs by about 40%. Most of the decline in stroke mortality rates, 78% in men and 66% in women, resulted from a reduction in CFRs, and the remaining 22% and 34%, respectively, from a reduction in event rates. There were important variations

between the young and old: in people aged under 55 all the reduction in mortality from stroke was attributed to improved survival, and in people aged 85+ improved survival and reduction in event rates were equally important for mortality reduction. There was an increase in stroke event rates in people aged 35 to 54, on average at 2% per year, which is in contrast to the downward trend observed in other age groups. However, in this age group the increase in event rates did not translate into an increase in mortality rates, as it was offset by the reduction in CFRs.

Comparison with other studies on trends in mortality rates, event rates and CFRs

The findings on dramatic reduction in stroke mortality rates are consistent with other reports.[7-9] We found a reduction in stroke mortality rates in all ages and in specific age groups in men and women, the average annual reduction ranged from about 4% to about 8% depending on the age group, with the smallest reduction observed in people aged under 55.

Our findings on reduction in stroke event rates are comparable with studies reporting reduction in stroke incidence.[8-10] As reported in the literature, the observed trend can be attributed to improvements in hypertension control, use of statins, reduction in smoking, decreased salt consumption, as well as specific interventions for stroke prevention, such as the introduction of the transient ischaemic attack clinics across England.[11-15]

Reduction in age-standardised stroke event rates concealed the flat rates in people aged 20 to 34 and an increase of about 2% per year in the age groups 35 to 54. We found only one other study conducted in England reporting trends in age-specific incidence rates of stroke, which similar to us, found no improvement in stroke incidence in younger people, but a reduction in rates in people aged 55 and older.[10] These findings are consistent with increase in stroke morbidity in young people reported in other high income countries.[16, 17] It is possible that stroke rates are increasing as a result of increasing rates of obesity and diabetes in younger people.[18, 19] Some studies have suggested that increases in cocaine and other substance abuse might also contribute to the increasing rates of stroke in the young.[20-22]

Published studies of case fatality rates covered different time periods and populations, and produced conflicting findings. While some reported no changes in CFRs,[8] others found a reduction. [9, 23] We are first to reported on national trends in 30-day CFRs after stroke over a number of individual calendar years, as well as on changes in age-specific CFRs. Our findings

indicate that CFRs in England have gradually declined, with a relative reduction of 40% between 2001 and 2010.

Analysis of age-specific reduction in CFRs, demonstrated that the greatest improvement in survival after stroke was in people under 55 years old.

The factors that caused the reduction in CFRs, including age-specific rates, in England are not well investigated. According to a Cochrane review, stroke patients treated in a dedicated stroke unit have better outcomes, however, such treatment is not known to be more effective in particular age groups.[24] Thrombolysis, another novel intervention that has become available in hospitals in England during the study years, is more frequently used on younger stroke patients.[25, 26] The greater average annual reduction in age-specific CFRs in younger and middle aged patients with stroke observed in this study, which coincided with the introduction of thrombolysis, might have a cause and effect relationship; however, another study is needed to confirm this observation.

Explaining the factors behind the observed reduction in stroke mortality rates

Our findings are consistent with the original MONICA study, which collected data between 1982 and 1995, and reported that two-thirds of the decline in stroke mortality was attributable to a decline in CFR and one-third to a decline in event rates.[5] Findings of the two studies are similar, despite being conducted in different times and in different populations. The MONICA study, is now outdated, did not cover England, and did not include people older than 64 years.

A study from England applied the WHO MONICA equation and used the same datasets – national HES and ONS mortality – and covered the same time-period as in this study to explain the decline in mortality rates from myocardial infarction.[2] Stroke and myocardial infarction share many common risk factors. However, in contrast to these results on stroke, the study of myocardial infarction reported that more than a half of decline in mortality rates was due to reduction in event rates and less than a half from reduction in CFRs. Thus, distinctions in the findings of the two studies, covering the same period and country, might suggest that primary prevention of vascular events is more effective in reducing the rates of myocardial infarction, than stroke. Hospital care was more effective in improving short-term survival of stroke patients, than of patients with myocardial infarction.

The observed variations in age-specific trends in event rates between the young and older people, might reflect effective preventive strategies and policies, but ones with different levels of impact in different population subgroups. During the study years, prevention at the individual level was focused on reducing a 10-year risk of vascular disease.[27] The implication of this approach was that the middle aged and older people have been recognised as a high risk group, and, therefore, prescribed treatments to control their vascular risk factors. In contrast, younger people have fallen into an intermediate risk group and received no treatment, despite having higher life-long risks of cardiovascular events. In 2014, the updated British consensus recommendations for the prevention of vascular diseases were published, which shifted the focus of prevention from the short-term risk to changing the life-time risk.[28]

Strengths and limitations

This is the largest study of stroke morbidity and mortality in England to date, which includes all NHS-hospitalised patients and all deaths in the country, and covers a continuous period of ten calendar years. The findings of this study are applicable to the whole of England. However, epidemiological and medical care factors vary from place to place, and the challenge for local investigators, and investigators in other countries, is to determine how profiles of mortality, event and case fatality rates compare with these. The study is free from biases that may arise when analysing data collected by stroke registers, which are limited in terms of populations and time, or clinical trials in which participants are selected and therefore might not be representative of all stroke patients. The large size of study population enabled us to have the statistical power to undertake the age-specific analyses. There was no upper age limit, unlike that in the MONICA study, and trends in the old as well as young adults were reported. This study provides a summary of trends in stroke mortality rates, event rates and CFRs in the first decade of the 21st century, and could be used as a reference ‘benchmark’ for future studies.

For our analyses we relied on the quality of stroke diagnosis in routine hospital statistics and mortality statistics. Validation studies have consistently reported high validity of stroke codes in linked HES datasets, and confirmed above 90% accuracy when a narrow range of ICD codes for acute stroke is used.[29-31] For this study we combined all strokes coded I61 to I64, and did not perform analysis separately for haemorrhagic and ischaemic stroke. Additional analysis (findings not shown here) demonstrated that the reporting of stroke type in English routine hospital and

death records has been inconsistent through the study period.[32] Therefore, any findings of changes in trends in rates reported for stroke subtypes, as distinct from stroke overall, could be a result of changes in recording of stroke type rather than the true changes.

Changes in stroke event rates might be subject to improved sensitivity of stroke diagnostics, including better quality of brain imaging, and increasing population awareness of stroke signs. These might have caused an increase in hospital admission rates, in particular, increase in admissions for milder strokes; however, we found a decrease in stroke event rates.

In calculations of event rates, we only included people who were hospitalised with acute stroke, or those who died from stroke. Any silent infarcts or small strokes that did not result in a hospital admission or death were not captured by the study.

Information on stroke severity is not recorded in routine hospital statistics. Some of the decline in CFRs reported here could be a result of a shift in stroke severity and increase in hospital admissions with milder stroke or suspected strokes, rather than advances in acute stroke care. To avoid counting suspected strokes, we excluded all those patients who spent one day or less in hospital and were discharged alive. It is likely that hospitals would not keep patients without a serious condition, like stroke, for longer than 24 hours, regardless of any changes in hospital admission procedures occurring during the study period.

We could not extend our analysis to include data from more recent years, because NHS Digital, which now owns and distributes data that were in the custodianship of the ONS, stopped supplying the full date of death from April 2012 onwards. Without this information 30-day CFRs cannot be calculated, nor can any checks be made for any preceding hospital admissions in people who died from stroke.

Future research is needed to investigate on the contribution of changes in the prevalence of risk factors at the population level to the reduction in stroke events rates and CFRs. For example, further data are needed to determine how much of the reduction in stroke event rates was due to a reduction in hypertension, reduced consumption of salt, as well as impact of specific treatments and interventions on reducing CFRs, similar to research done for coronary heart disease.[33-35]

Conclusions

This paper is important for understanding the driving forces behind the observed reduction in stroke mortality rates. A dramatic decrease in stroke mortality rates in England in the first decade of the 21st century has been a result of improved survival of stroke patients more than a decrease in event rates. Seventy two percent of the reduction in mortality rates in men and 66% in women can be attributed to a reduction in CFRs, and the rest to declines in event rates. The contribution of the two factors varied across age groups: in young adults all the reduction in mortality was due to decreases in CFRs, whereas among patients aged 85 and older the reduction in CFRs and event rate contributed nearly equally. There was a reduction in CFRs during the study years in all age groups. Reduction in stroke event rates in middle aged and elderly people, which resulted in the overall decrease in event rates, concealed the unfavourable trends in men and women aged under 55. This indicates that, while prevention was effective in reducing stroke event rates in older people, it did not succeed in the young. Our findings highlight that that hospitals were instrumental in reducing the rates of stroke mortality through improvements in survival. However, to reduce the burden of stroke care on hospitals and decrease the dependence on emergency services, prevention of vascular events needs to be strengthened, which would lead to reduction in stroke mortality through reduction in stroke occurrence.

Table 1. Characteristics of acute stroke events and deaths by sex and time period, England:
number of strokes

Time period/ characteristics	2001-2010*		2001		2010	
	Men	Women	Men	Women	Men	Women
Stroke events						
Mean age in years (SD)	72 (13)	76 (14)	71 (13)	75 (14)	73 (13)	77 (14)
Age groups						
20 to 34 years	3040	2525	308	231	304	248
35 to 54 years	31300	19027	2770	1713	3597	2237
55 to 64 years	52409	28449	4898	2791	5640	3045
65 to 74 years	100942	74429	11088	8308	9900	7184
75 to 84 years	153201	189492	15833	20719	14513	16760
85+ years	84817	207866	8234	21758	9495	20944
Total number of stroke events	425709	521788	43131	55520	43449	50418
Crude event rate (95% CI) per 100 000**	229.6 (228.9- 230.2)	263.7 (263.0- 264.4)	241.6 (239.3- 243.9)	288.1 (285.7- 290.5)	224.0 (221.9- 226.2)	246.9 (244.7- 249.0)
Age-adjusted event rate (95% CI) per 100 000**	309.8 (308.8- 310.7)	254.1 (253.4- 254.8)	345.1 (341.7- 348.5)	280.2 (277.9- 282.5)	284.5 (281.8- 287.2)	233.7 (231.7- 235.8)
Stroke deaths						
Mean age (SD)	79 (11)	83 (9)	78(10)	83 (9)	79 (11)	84 (9)
Age groups						
20 to 34 years	314	222	37	22	26	12
35 to 54 years	4108	2515	436	293	363	201
55 to 64 years	8214	5008	964	582	680	422
65 to 74 years	22955	18308	3151	2578	1765	1353
75 to 84 years	53281	70758	6647	9109	3829	4867
85+ years	41015	110387	4669	13363	3818	9262
Total number of stroke deaths	129887	207198	15904	25947	10481	16117
Crude mortality rate (95% CI) per 100 000**	70.0 (69.7- 70.4)	104.7 (104.3- 105.2)	89.10 (87.7-90.5)	134.70 (133.0- 136.3)	54.0 (53.0- 55.1)	78.90 (77.7- 80.1)
Age- standardised mortality rate (95% CI) per 100 000**	103.1 (102.5- 103.6)	98.0 (97.6- 98.5)	139.60 (137.3- 141.9)	127.90 (126.3- 129.5)	73.90 (72.5-75.4)	71.70 (70.6- 72.8)

*Mean ages, total counts of stroke events and deaths in each sex and age group, as well as crude and age-standardised rates, were calculated for a combined 10-year period.

**Population denominators were obtained from the Office for National Statistics website.

Confidential: For Review Only

Figure 1. Trends in age-standardised stroke event rates and mortality rates in men and women between 2001 and 2010, England

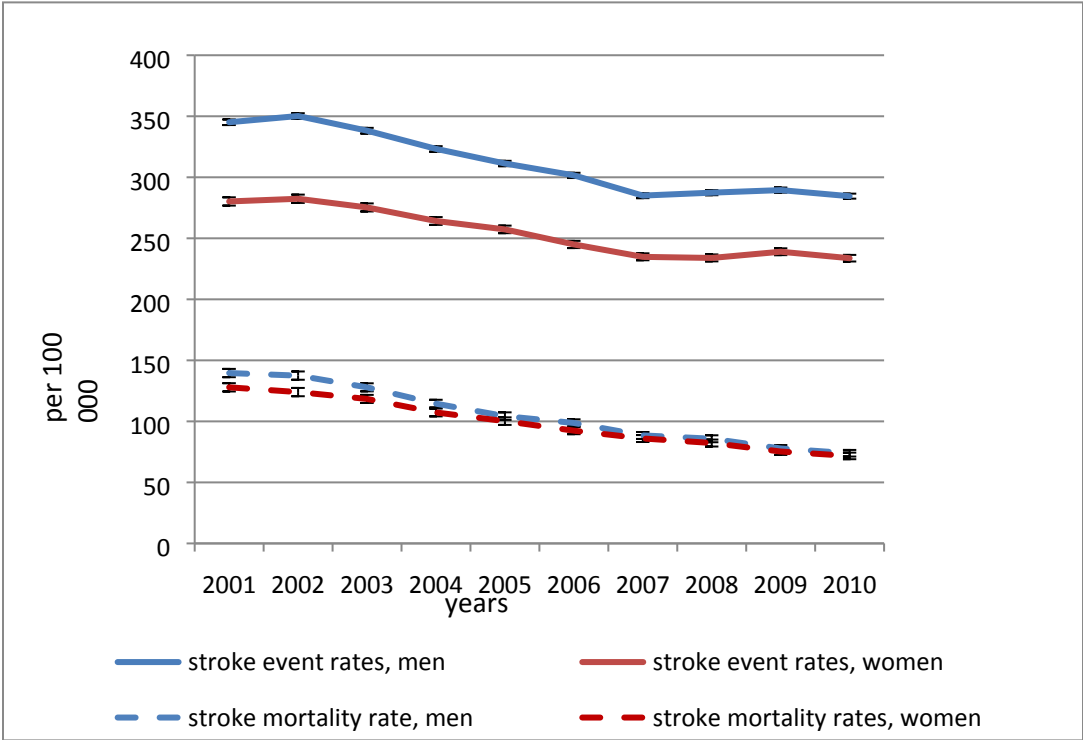


Figure 2. Trends in age-standardised 30-day case fatality rates from stroke in men and women, England

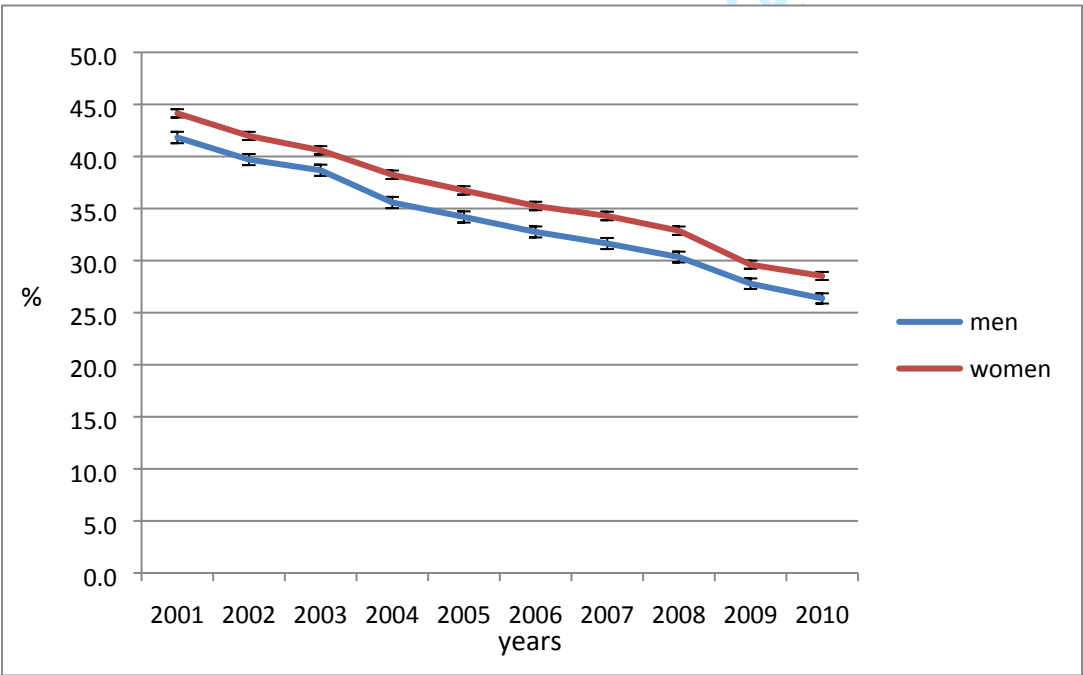


Table 2. Age-specific rates and average annual percentage change in stroke mortality, event and case fatality rates between 2001 and 2010 in men and women.

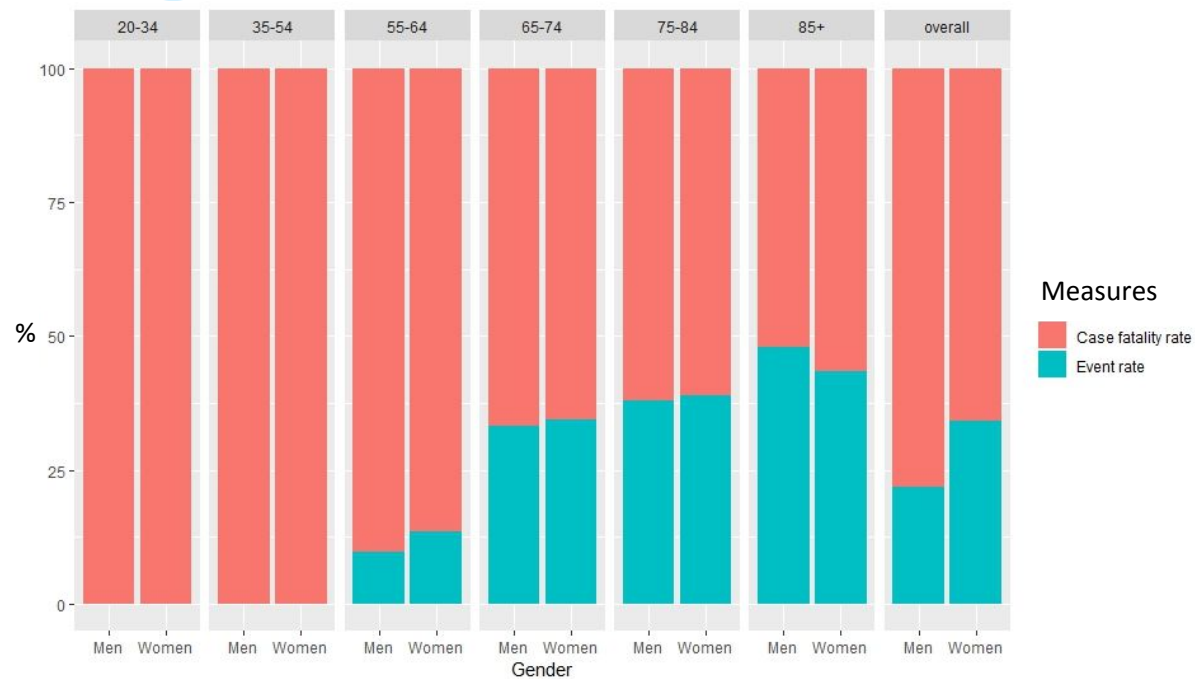
	Mortality rate (per 100 000)			Event rate (per 100 000)			Case fatality rate, %				Contribution to mortality decline, %	
	2001	2010	Annual % change (95% CI)	2001	2010	Annual % change (95% CI)	2001	2010	Estimated % change, Monica formula	Annual % change, from dataset (95% CI)	Event rate, %	Case fatality rate, %
Men												
20-34	0.73 (0.51-1.01)	0.49 (0.32-0.71)	-4.1 (-7.8, -0.4)	6.07 (5.4-6.8)	5.68 (5.06-6.35)	0.1 (-1.1, 1.4)	16.6 (12.3-21.8)	11.2 (7.7-15.6)	-4.3	-3.4 (-6.3, -0.5)	0	100
35-54	6.32 (5.74-6.94)	5.01 (4.51-5.55)	-3.8 (-4.8, -2.8)	40.1 (38.7-41.7)	49.7 (48.0-51.3)	2.2 (1.8, 2.6)	18.4 (16.8-20.1)	11.5 (10.4-12.6)	-6.0	-5.3 (-6.2, -4.5)	0	100
55-64	37.8 (35.1-39.8)	22.7 (21.0-24.5)	-6.1 (-6.8, -5.3)	189.87 (184.6-195.3)	188.3 (183.4-193.2)	-0.6 (-0.9, -0.3)	21.0 (19.7-22.3)	12.5 (11.6-13.5)	-5.5	-4.9 (-5.5, -4.2)	9.6	90.4
65-74	163.4 (157.8-169.3)	82.37 (78.6-86.3)	-8.1 (-8.6, -7.7)	575.1 (564.5-585.9)	462.0 (453.0-471.2)	-2.7 (-2.9, -2.5)	27.3 (26.3-28.3)	17.1 (16.3-18.0)	-5.4	-5.0 (-5.4, -4.6)	33.3	66.7
75-84	602.8 (588.9-617.5)	303.3 (293.8-313.0)	-7.7 (-8.0, -7.4)	1435.8 (1413.6-1458.4)	1149.5 (1130.9-1168.4)	-2.9 (-3.1, -2.8)	39.1 (38.1-40.1)	23.4 (22.6-24.2)	-4.8	-5.0 (-5.2, -4.7)	37.9	62.1
85+	1748.7 (1698.9-1799.6)	971.5 (940.9-1002.8)	-7.0 (-7.4, -6.7)	3083.9 (3017.6-3151.2)	2416.0 (2367.7-2465.1)	-3.4 (-3.6, -3.1)	52.5 (51.1-54.2)	34.3 (33.1-35.5)	-3.7	-4.3 (-4.5, -4.2)	47.8	52.2
All ages*	139.6 (137.3-141.9)	73.9 (72.5-75.4)	-6.0 (-6.2, -5.8)	345.1 (341.7-348.5)	284.5 (281.8-287.2)	-1.3 (-1.4, -1.2)	41.8 (41.3-42.4)	26.4 (25.9-26.9)	-4.7	-4.7 (-4.9, -4.5)	21.7	78.3
Women												
20-34	0.43 (0.27-0.66)	0.23 (0.12-0.41)	-4.5 (-8.8, 0.0)	4.54 (3.98-5.17)	4.82 (4.24-5.46)	0.7 (-0.7,2.1)	14.3 (9.8-20.1)	9.3 (5.9-13.9)	-5.2	-5.1 (-8.6, -1.5)	0	100
35-54	4.19 (3.72-	2.7 (2.37-	-5.3 (-6.6, -	24.5 (23.3-25.7)	30.4 (29.3-31.7)	2.1 (1.6, 2.6)	19.7 (17.7-	11.4 (10.1-	-7.5	-5.6 (-6.7, -4.5)	0	100

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	4.69)	3.14)	4.0)				22.0)	12.9)				
55-64	22.0 (20.2-23.8)	13.6 (12.3-14.9)	-5.7 (-6.6, -4.8)	105.4 (101.5-109.4)	97.8 (94.3-101.3)	-0.8 (-1.2, -0.4)	23.4 (21.6-25.3)	15.0 (13.7-16.4)	-4.9	-4.2 (-5.0, -3.4)	13.6	86.4
65-74	119.0 (113.5-122.6)	57.7 (54.7-60.9)	-8.3 (-8.7, -7.8)	380.2 (372.1-388.5)	306.5 (299.4-313.6)	-2.9 (-3.1, -2.6)	30.4 (29.2-31.6)	18.0 (17.0-19.0)	-5.4	-5.0 (-5.4, -4.6)	34.5	65.5
75-84	548.4 (537.2-559.8)	293.4 (285.2-301.7)	-7.0 (-7.2, -6.7)	1247.5 (1230.5-1264.6)	1010.3 (995.0-1025.7)	-2.7 (-2.9, -2.6)	40.9 (40.0-41.7)	25.9 (25.1-26.6)	-4.3	-4.5 (-4.7, -4.3)	39.0	61.0
85+	1931.4 (1898.7-1964.4)	1150.8 (1127.5-1174.5)	-6.2 (-6.4, -6.0)	3144.7 (3103.0-3186.7)	2602.4 (2567.3-2637.9)	-2.7 (-2.8, -2.5)	57.2 (56.2-58.2)	38.3 (37.4-39.1)	-3.5	-4.3 (-4.5, -4.2)	43.3	56.7
All ages*	127.9 (126.3-129.5)	71.7 (70.6-72.8)	-6.1 (-6.3, -6.0)	280.2 (277.9-282.5)	233.7 (231.7-235.8)	-2.1 (-2.2, -2.0)	44.1 (43.7-44.5)	28.5 (28.1-28.9)	-4.0	-4.4 (-4.5, -4.2)	34.1	65.9

* Mortality rates and stroke event rates for all ages were age-standardised to the ESP 2013 (see Method), and case fatality rates were standardised to the internal study population

Figure 3. Percentage contribution of changes in case fatality rates and event rates to the percentage reduction in stroke mortality by age group in men and women.



Footnotes

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Contributors: OS conceived the study and is the guarantor. OS, PS and MJG developed the study design. MJG developed and led the building of the linked dataset. OS undertook the data analysis and drafted the manuscript. All authors contributed to the interpretation of the data and revision of the manuscript. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. The Corresponding Author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Transparency declaration: The Corresponding Author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and there were no discrepancies from the study as planned.

Ethical approval: The building and analysis of the linked dataset were approved by Central and South Bristol research ethics committee (No 04/Q2006/176).

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Data sharing: Data from hospital episode statistics and the Office for National Statistics can be obtained from the NHS Digital at www.digital.nhs.uk.

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