The falling rates of hospital admission, case fatality, and population-based mortality for subarachnoid hemorrhage in England, 1999–2010

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OBJECTIVE In this study, the authors examined trends in population-based hospital admission rates, patient-level case fatality rates (CFRs), and population-based mortality rates for nontraumatic (spontaneous) subarachnoid hemorrhage (SAH) in England.

METHODS Population-based admission and mortality data (59,599 people admitted to a hospital with SAH, 1999–2010; 37,836 people whose death certificates mentioned SAH, 1995–2010) were analyzed.

RESULTS Hospital admission rates for SAH per million population declined by 18.3%, from 100.4 (95% CI 97.6–103.1) in 1999 to 82.0 (95% CI 79.7–84.4) in 2010. CFRs at less than 30 days per 100 patients decreased by 18.2%, from 29.7 (95% CI 28.5–31.0) in 1999 to 24.3 (95% CI 23.2–25.5) in 2010. Population-based mortality rates per million population, where SAH was recorded as underlying cause of death on the death certificate, declined by 39.8%, from 41.2 (95% CI 39.5–43.0) in 1999 to 24.8 (95% CI 23.6–26.1) in 2010.

CONCLUSIONS Population-based hospital admission rates, patient-level CFRs, and population-based mortality rates all declined between 1999 and 2010. Part of the decline in mortality rates for SAH is likely to be attributable to a decline in incidence. It is also, in part, attributable to increased survival after SAH. The available data do not allow us to compare the effects of different treatment methods for SAH on case fatality and mortality. During the period of study, mortality rates declined by almost 40%, and it is likely that there are a number of factors contributing to this substantial improvement in outcomes for SAH patients in England.

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NONTRAUMATIC (spontaneous) subarachnoid hemorrhage (SAH) affects about 9 people per 100,000 person-years in most of Western Europe and the United States.[1] Approximately 85% of these cases are due to rupture of an intracranial aneurysm. In patients who survive the initial rupture, and are suitable for active intervention, modern management is to secure the aneurysm responsible for the hemorrhage as promptly as reasonably possible, as the consequences of early aneurysm re-rupture are often catastrophic. The costs of treatment and care for dependent survivors represent a substantial burden to families, health care systems, and wider society. Accord-ingly, reductions in case fatality rates (CFRs) and dependency following treatment can have an important impact on all three.

Population-based mortality rates for SAH have declined in many developed countries, including the UK, over the past 4 decades.[3,4,8] Evidence from systematic reviews suggests that, during the same time period, population-based incidence rates for SAH have either remained stable,[7] or there have been modest declines, with wide variation in rates between countries.[1] There is conflicting evidence on trends in hospital admission rates for SAH, with evidence from the US suggesting rates have remained stable,[17] and

data from the UK pointing to a decline in hospital admission rates.[19] There is also some evidence to show declines in CFRs for SAH both in the UK and the US.[13,16]

Over the last 2 decades, there have been significant changes in the management of SAH in the UK, the US, and worldwide. In England, prior to 1992, neurosurgical clip ligation was the only option available to secure a ruptured aneurysm. In the US, the Guglielmi detachable coil (GDC) was first used to treat cerebral aneurysms in 1990, as part of an FDA investigational device exemption, and in the UK in 1992. Use of the GDC in Europe increased quite rapidly to treat high surgical risk aneurysms, such as those in the basilar location. In 1995, the GDC device was approved by the FDA for surgically high-risk intracranial aneurysms. Other improvements in the management of patients with SAH have occurred over the last 2 decades: improvements in neurointensive care, and in England, faster admission of patients to neurosurgical centers for aneurysm treatment. The introduction of computed tomography angiography (CTA) has expedited both the identification and treatment of patients with ruptured aneurysms. Operative neurosurgical care has also improved with the introduction of indocyanine green angiography and intraoperative ultrasound.

In 1994, the International Subarachnoid Aneurysm Trial (ISAT), a prospective randomized trial of endovascular coiling in the UK, commenced. It was funded by the UK Medical Research Council from 1997. Recruitment to the trial was halted by the Trial Steering Committee in 2002 following the release of unblinded data by the Data Monitoring Committee, which showed significant clinical benefit at 1 year in patients allocated to endovascular coiling compared with those allocated to craniotomy and neurosurgical clipping. The results of the trial were published in 2002 and 2005, and the findings of the trial informed and influenced routine clinical practice in the UK.[9,10]

In the present study, our objectives were to report on trends in population-based hospital admissions, patient-level case fatality, and population-based mortality rates for SAH. We then investigated whether the declines in case fatality and population-based mortality might, in part, be attributable to changes of practice in respect of neurosurgical clipping and coil embolization.

Methods
Data Sources

Data on all hospital admissions in all National Health Service (NHS) hospitals in England (1999–2011) were obtained from the Hospital Episode Statistics (HES) database, supplied to us in files from the Health and Social Care Information Centre (HSCIC). The HSCIC has been unable to supply more recent data. All patients in England with SAH are admitted to an NHS district hospital and treated in an NHS neurosurgical unit. In mid-2011, the census-based population estimate for England was 53.11 million.[15] Data on successive admissions for each person were linked into a time-sequenced file for each individual, and these were also linked to the person's mortality record (if death had occurred). Mortality data for England (1995–2011) were obtained from death registration data supplied

by the English Office for National Statistics. The earliest year in which the HES database can be reliably linked is 1999, and the earliest data available to us in which all certified causes of death are on each death certificate are for the year 1995. As some deaths that occur in each year are not registered until the following year, we examined data including those for 2011 registrations, but we confined our analyses of mortality to data for deaths that occurred in 2010 (to avoid end-year incompleteness of registrations). Our analyses of admission and CFRs were confined to admissions up to and including 2010 (to permit 365-day "follow up" into 2011 for those admitted in 2010).

Admission and mortality records were selected using codes 430 in the ninth revision and I60 in the tenth revision of the *International Classification of Diseases*.[20] Procedures were selected from admissions records using code L33.2 for clipping of aneurysm of cerebral artery, and codes O01.1–O02.9 for coil embolization of an aneurysm, in the fourth revision of the Office of Population Census and Surveys *Classification of Surgical Operations and Procedures*.[14] Coding for coil embolization of an aneurysm, a newer procedure, was not available for the full period of study. Codes for coil embolization were first introduced in the HES database in 2006, although data for coiling are likely to be incomplete for that year. For this reason, we have limited our analyses on rates for coiling to 2007–2010. For any patient with more than one admission for SAH, the first admission was selected for analysis.

Statistical Analysis: Calculation of Rates

Age-specific and age-standardized rates were calculated for rates of hospital admission, operative procedures, person-based case fatality, and population-based mortality. Admission rates, procedure rates, and mortality rates were standardized using the direct method, 5-year age groups, and the age distribution of the European standard population. CFRs in each year were age standardized using 5-year age groups and the age distribution of the population of patients admitted to a hospital for SAH in England in the years 1999–2010 combined as the standard. Trends in age-standardized hospital admissions, procedure, case fatality, and mortality rates were modeled using joinpoint regression (Joinpoint Desktop Software available at https://surveillance.cancer.gov/joinpoint/download).[5,6,11]

Statistical Analysis: Joinpoint Analysis

Joinpoint regression is a statistical technique for estimating the location of a significant change in the slope of a trend line. When modeling a series of annual rates, the location of an estimated significant change in trend, or joinpoint, will be a particular year. The log-linear option was used to model annual age-standardized hospital admission, procedure, case fatality, and mortality rates. The default number of joinpoints was allowed for each model (the default value changes as the number of data points increases), and the overall significance level for permutation tests was set at $\alpha = 0.05$. A model of best fit was compared with more and/or less nonsignificant joinpoint models of the same series of rates.

Binary Logistic Regression

Binary logistic regression analyses were used to calculate the odds of < 30-day and < 365-day case fatality.

Results

In the study period, there were 59,599 people admitted to hospital with SAH and 37,836 people whose death certificates mentioned SAH (as either the underlying or contributory cause on the death certificate).

Trends in Hospital Admission Rates for SAH, 1999–2010

Table 1 shows the decline in age-specific admission rates for SAH. Between 1999 and 2010, age-specific admission rates declined in all age groups, except for those aged 70 and over. For all ages combined, age-standardized rates fell from 100.4 per million in 1999 to 82.0 per million in 2010, an 18.3% decline (Fig. 1A).

Joinpoint analyses showed that for all age groups combined (see Supplementary Table 1) admission rates declined significantly between 1999 and 2010, but without an estimated significant change in the scale of downward trend in specific years (i.e., there were no joinpoints on the trend line and, therefore, no significant acceleration or deceleration of the downward trend). Trend lines for the individual age groups < 40, 40–49, 50–59, and 60–69 years all showed significant declines during the period of study, with no significant change in the downward trend in any particular year. For those 70 years of age and older, the annual percentage change (0.3%) was not significant.

Trends in Case Fatality Rates Following Hospital Admission for SAH, 1999–2010

Table 2 shows the decline in age-standardized patient-level CFRs for SAH. Between 1999 and 2010, < 30-day CFRs declined by 18.2%, < 60-day by 19.3%, < 90-day by 18.8%, and < 365-day by 18.3%. CFRs at less than 30 days were 29.7% in 1999, 30.3% in 2005, and 24.3% in 2010. CFRs under 365 days were 35.6% in 1999, 36.9% in 2005, and 29.1% in 2010.

Trends in Mortality Rates, 1995–2010

We analyzed mortality based on underlying cause and all mentions on the death certificate. Supplementary Table 2 shows that declines in age-specific mortality rates were similar for underlying cause and for all mentions.

Between 1995 and 2010, the largest decline in mortality observed was for individuals under 40 years of age (57.6% [all mentions]); during the same period, for all ages combined, mortality rates declined by 41.0% (all mentions).

Joinpoint analyses of age-standardized mortality rates (Supplementary Table 3) show that, for those under 40 years, an estimated change of trend occurred in 2006 for SAH as the underlying cause of death, with a significant acceleration of the downward trend in rates between Period 1 (1995–2006) and Period 2 (2006–2010). Measured as all mentions, there were significant accelerations of the downward trend for those aged 40–49 and 50–59 years in 2003, aged 60–69 in 1999, aged 70 and over in 2000, and for all ages in 2002. The changes in trend at these times were followed by significant acceleration in the decline in mortality.

For all ages combined, measured as underlying cause of death (Fig. 1B), the annual percentage decline for the period 2003–2010 was −6.3 (95% CI −7.2 to −5.3), which was more than 3 times greater than that for the period 1995–2003 (−2.0 [95% CI −2.7 to −1.2]).

Trends in Procedure Rates for Neurosurgical Clipping, 1999–2010

Table 3 shows that age-standardized rates for neurosurgical clipping, all ages combined, dropped by 68.3%, from 19.9 per million (95% CI 18.6–21.1) to 6.3 per million (95% CI 5.7–7.0) across the study period. Joinpoint analyses of these rates show estimated changes in trend in 2001 and 2005 (Fig. 1C). There were significant declines in all 3 periods of the trend line, with the steepest decline between 2001 and 2005, with an annual percentage change of −18.9% (95% CI −22.7 to −15.0). This decline is more than twice the annual percentage decline in the period 1999–2001. The pattern of decline is broadly

TABLE 1. Age-specific admission rates for nontraumatic SAH per million population in England by year and age-group, males and females combined, 1999–2010

Yr	No. of SAH Per Million Population					
	All Ages	<40 Yrs	40–49 Yrs	50–59 Yrs	60–69 Yrs	≥70 Yrs
1999	107.7	26.7	145.3	220.2	247.5	214.2
2000	101.3	27.8	132.5	195.3	219.7	212.3
2001	102.7	27.9	142.7	195.4	206.6	219.0
2002	100.3	26.9	137.0	190.6	202.7	214.4
2003	100.8	25.2	139.5	197.1	213.0	204.1
2004	99.9	26.4	140.2	179.7	194.8	220.4
2005	94.5	25.0	129.8	180.4	182.1	198.8
2006	93.7	25.4	122.4	164.1	180.4	214.8
2007	95.5	23.7	120.8	172.1	184.1	225.4
2008	95.4	24.3	122.4	167.7	176.2	227.5
2009	95.8	21.8	119.5	174.6	177.2	233.6
2010	94.9	21.3	122.0	174.1	175.6	223.3
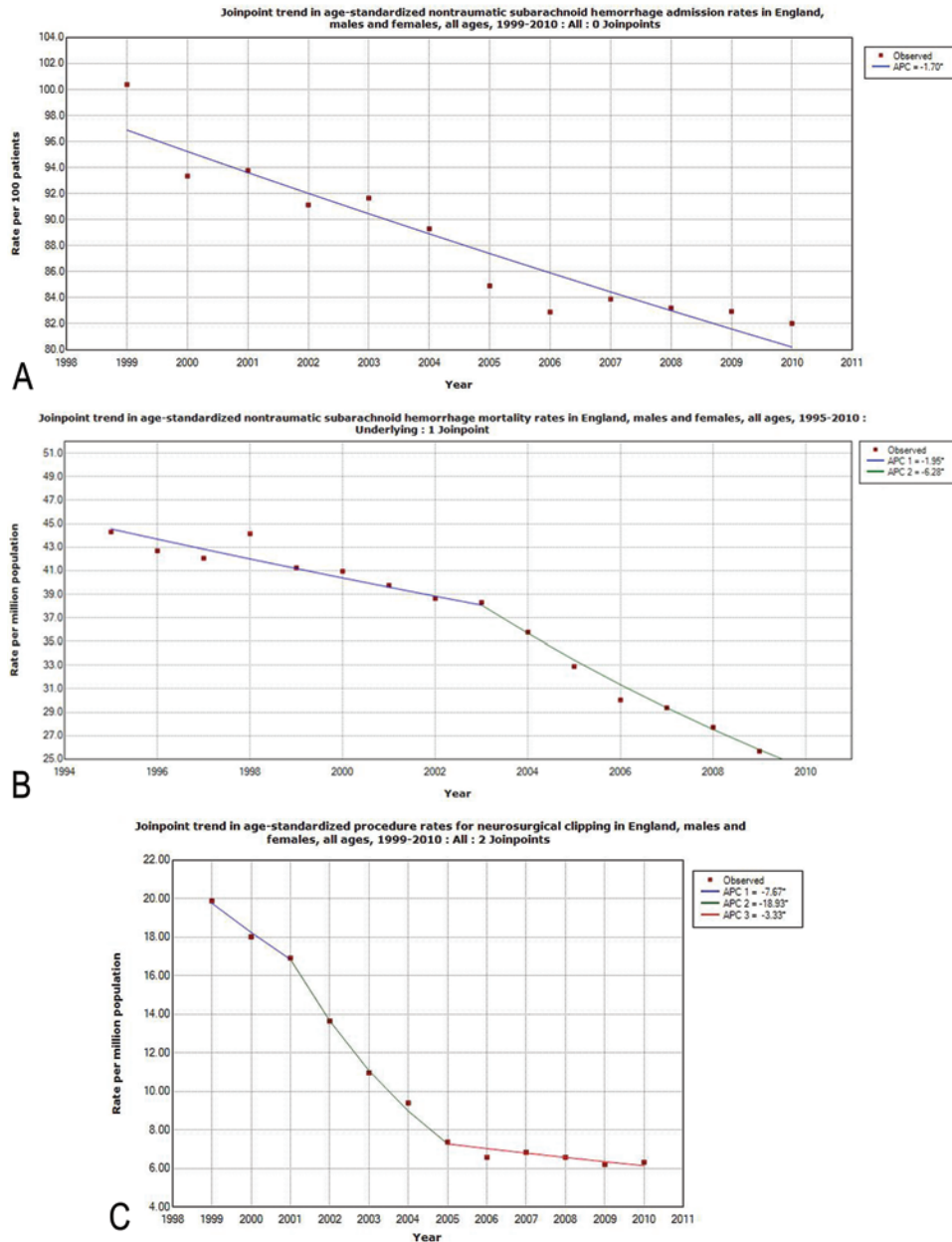
FIG. 1. Joinpoint trends for SAH admission, mortality, and neurosurgical clipping rates for males and females of all ages in England. **A:** Trend in age-standardized nontraumatic SAH admission rates from 1999 to 2010. All: 0 joinpoints. **B:** Trend in nontraumatic SAH mortality rates from 1995 to 2010. Underlying: 1 joinpoint. **C:** Trend in age-standardized procedure rates for neurosurgical clipping from 1999 to 2010. All: 2 joinpoints. APC = annual percentage change. Figure is available in color online only.

similar to that for all-ages mortality, measured as all mentions, where there was a significant downward change in trend in 2002, and where the percentage decline in Period 2 (2002–2010) was more than 3 times the rate of decline in Period 1 (1995–2002), see Supplementary Table 3.

Trends in Procedure Rates for Coil Embolization, 2007–2010

Data on coiling were not available for the full period of the study. Table 4 shows that age-standardized rates for coiling increased 14.3% between 2007 and 2010. The total number of coded procedures (clipping & coiling) in-

creased from 1392 in 2007 to 1537 in 2010, an increase of 10.4%.

Scatterplots

Supplementary Fig. 1A shows a scatterplot of age-standardized < 30-day CFRs and age-standardized procedure rates for neurosurgical clipping (1999–2010), and Supplementary Fig. 1B shows a scatterplot of age-standardized < 30-day CFRs and age-standardized procedure rates for coil embolization (2007–2010). The data do not meet the required assumptions of the Pearson's product-moment correlation coefficient nor the Spearman's rank correla-

TABLE 2. Age-standardized case fatality rates for nontraumatic SAH per 100 patients in England by time from hospital admission, males and females combined, 1999–2010*

Yr	No. of Admissions	Age-Standardized Case Fatality Rates (95% CI)			
		<30 Days	<60 Days	<90 Days	<365 Days
1999	5283	29.7 (28.5–31.0)	32.1 (30.9–33.3)	33.0 (31.8–34.2)	35.6 (34.4–36.9)
2000	4985	31.4 (30.1–32.7)	34.0 (32.7–35.3)	34.9 (33.6–36.2)	37.1 (35.8–38.4)
2001	5077	31.2 (29.9–32.4)	33.7 (32.4–34.9)	34.7 (33.4–35.9)	37.0 (35.8–38.3)
2002	4982	31.3 (30.1–32.6)	33.4 (32.2–34.7)	34.4 (33.1–35.6)	37.0 (35.7–38.2)
2003	5027	31.5 (30.3–32.8)	33.7 (32.4–34.9)	34.2 (32.9–35.4)	36.1 (34.8–37.4)
2004	5007	31.5 (30.3–32.8)	33.8 (32.5–35.0)	34.6 (33.3–35.8)	36.9 (35.6–38.2)
2005	4768	30.3 (29.0–31.5)	32.3 (31.0–33.5)	33.1 (31.9–34.4)	36.9 (35.6–38.2)
2006	4755	28.2 (27.0–29.5)	29.8 (28.6–31.1)	30.7 (29.5–31.9)	33.2 (32.0–34.5)
2007	4882	27.7 (26.5–29.0)	29.3 (28.1–30.5)	30.3 (29.0–31.5)	33.0 (31.7–34.2)
2008	4910	25.9 (24.8–27.1)	28.0 (26.8–29.2)	28.8 (27.6–30.0)	31.2 (29.9–32.4)
2009	4965	25.2 (24.0–26.3)	26.8 (25.7–28.0)	27.7 (26.5–28.9)	30.6 (29.4–31.8)
2010	4958	24.3 (23.2–25.5)	25.9 (24.8–27.1)	26.8 (25.6–28.0)	29.1 (27.9–30.3)

* The deaths within 60, 90, and 365 days include all those in each preceding time interval.

tion coefficient. We further examine the relationship between CFRs and procedure rates for coiling or clipping by conducting binary logistic regression analyses.

< 30-Day and < 365-Day Case Fatality, 2007–2010

Univariate analyses in Table 5 show that clipping (referent: coiling) and age were both significant predictors of < 30-day and < 365-day case fatality. Adjusted odds ratios in Table 5 show that the odds of case fatality < 30 days and < 365 days were significantly higher for patients treated with neurosurgical clipping compared with those treated with coil embolization. We were unable to adjust for case-mix in these analyses.

Relative Risk of Death, 2007–2010

The relative risk of death (RR) within 30 days of hospital admission was significantly higher for patients who underwent clipping, 1.31 (95% CI 1.09–1.59), compared

TABLE 3. Age-standardized procedure rates for neurosurgical clip ligation per million population in England, males and females combined, 1999–2010

Yr	No. of Procedures	Rate of Clip Ligation (95% CI)
1999	966	19.9 (18.6–21.1)
2000	887	18.0 (16.8–19.2)
2001	843	16.9 (15.8–18.1)
2002	684	13.7 (12.6–14.7)
2003	557	11.0 (10.0–11.9)
2004	484	9.4 (8.6–10.2)
2005	379	7.4 (6.6–8.1)
2006	345	6.6 (5.9–7.3)
2007	360	6.8 (6.1–7.6)
2008	349	6.6 (5.9–7.3)
2009	335	6.2 (5.5–6.9)
2010	340	6.3 (5.7–7.0)

with patients who underwent coil embolization. The RR within 365 days of hospital admission for those treated with clipping compared with those who underwent coiling was also significantly higher, at 1.34 (95% CI 1.14–1.57). We were unable to adjust for case-mix in these analyses.

Discussion
The Decline in Hospital Admission Rates

Between 1999 and 2010, age-standardized hospital admission rates for SAH per million population declined 18.3% in England. The reasons for this decline are unclear. A reduction in smoking rates, particularly in middle-aged females (the group most commonly affected by SAH), together with improved management of hypertension, are likely the most important factors contributing to the observed decline. It is unlikely to be due to an increase in the rate of patients dying from SAH before being admitted to hospital. This was not observed in two prospective population-based studies, the Oxford Community Stroke Project (1981–1986) and the Oxford Vascular Study (2002–2008), both based in Oxfordshire, England; in these two studies, only 3 of 65 patients died before reaching the hospital.[8] A significant decline in incidence rates for SAH was not observed in the interval between these two studies; however, the number of events was small (65), because these studies were based on small populations. On the other hand, a national study of admissions for SAH in England

TABLE 4. Age-standardized procedure rates for coil embolization per million population in England, males and females combined, 2007–2010

Yr	No. of Procedures	Rate of Coil Embolization (95% CI)
2007	1032	18.9 (17.7–20.0)
2008	1145	20.8 (19.6–22.0)
2009	1168	21.0 (19.8–22.2)
2010	1197	21.6 (20.3–22.8)

TABLE 5. Univariate and multivariate analyses of < 30-day and < 365-day case fatality, 2007–2010*

Analysis & Factor	Odds Ratio (95% CI)	
	<30 Days	<365 Days
Univariate analysis		
Male sex (referent female)	0.92 (0.75–1.12)	1.01 (0.85–1.20)
Age	1.02† (1.01–1.02)	1.03† (1.03–1.04)
Clipping (referent coiling)	1.32† (1.06–1.63)	1.34† (1.11–1.61)
Yr of admission	0.99 (0.91–1.08)	1.01 (0.94–1.09)
Multivariate analysis		
Clipping (referent coiling)	1.36 (1.10–1.68)†‡	1.44 (1.19–1.73)†‡

* These analyses exclude data for 104 patients who had codes for both clipping and coiling.
† Odds differ significantly from 1.
‡ Adjusted for age and sex.

showed that the number of admissions for SAH has declined over the past 13 years, from 7054 in 1998–1999 to 6166 in 2010–2011.[19]

Case Fatality Rates, Mortality Rates, and Changes in Clinical Practice

Between 1999 and 2010, age-standardized < 30-day CFRs per 100 patients decreased 18.2%, and age-standardized population-based mortality rates per million population where SAH was recorded as the underlying cause of death declined 39.8%. Our results support findings from a meta-analysis[13] and a systematic review[8] that both show that case fatality rates for SAH have declined. Our findings on mortality support those of previous studies, which indicate that population-based mortality for SAH has declined since the 1980s.[3,4,8]

There may be several reasons for beneficial trends in case fatality and population-based mortality rates in England. The urgent transfer of all SAH patients to neurosurgical care (most patients in England are admitted to a district general hospital without a neurosurgical service, and are transferred to the neurosurgical center after a diagnosis of SAH) is now standard care. In the past, there had been delays in the admission of some patients. A reduction of delays in transfer and aneurysm treatment is likely to have reduced the number of patients with early rebleeding, which, in turn, is likely to have reduced case fatality. It is also probable that more elderly patients and poor-grade patients, who may not have been deemed suitable for clipping, underwent coiling to secure the aneurysm.

Between 1999 and 2010, procedure rates for neurosurgical clipping in England declined by 68.3%. The pattern of decline was similar to that observed for mortality. Procedure rates for neurosurgical clipping showed an estimated acceleration in decline in 2001, and mortality rates measured as mentions accelerated downward in 2002, as did mortality rates as underlying cause in 2003. The decline in rates per year after each of these changes in trend in Period 2 was more than twice the annual percentage change before the change in trend in Period 1. Reliable year-on-year data on national rates of coiling are not available from the HES database for the full run of years covered by our

study. However, a study by the Royal College of Surgeons (RCS) in England showed that the decline in population-based mortality rates coincided with an increase in the use of coil embolization after the recognition of the clinical benefit of coiling shown in the ISAT.[18] A national study of SAH management in neurological and neuroscience centers in the UK by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) showed that in patients undergoing treatment for aneurysmal SAH, 84% had undergone coiling, 14% clipping, and 2% clipping after coiling had been attempted.[12] While codes for coil embolization of an aneurysm were not available for the full period of study, which is a shortcoming of the dataset, there is no evidence to suggest that patients who would have been suitable for treatment of an aneurysm after SAH, and who did not undergo clipping, were left untreated; given the findings of the RCS and NCEPOD studies, it is reasonable to assume that most of these patients underwent coiling.

We used the only available study design that allowed for the investigation of whole-population trends in admission and mortality rates for SAH. It is not a design best suited for comparing the outcomes of clipping versus those of coiling; this is best done, and has been done, in randomized controlled trials.[9,10]

Strengths and Limitations

The strengths of the study are that we used a very large, national (and therefore representative) record-linked dataset, allowing us to take account of multiple admissions for each patient and to identify deaths whenever and wherever they occurred. The data also included all certified causes of death, allowing us to compare trends for mortality where SAH is recorded as the underlying cause of death with trends where SAH is mentioned as a contributory cause.

One potential limitation is that there were changes in rules for the coding of underlying cause of death in England in 2001, which could have affected mortality trends for SAH, as has occurred for some other diseases.[2,3] In fact, for SAH, the analysis of mentions showed that these rates were very similar to those shown for underlying cause. Another limitation is that routinely collected hospital data can be subject to errors such as miscoding of the disease classification, but the coding of SAH is very straightforward, and, providing the clinical diagnosis is given in the patient's case notes, coding errors should be uncommon. Another limitation that cannot be remedied in historical anonymized datasets are possible errors and omissions in recording and coding the operative procedures of clipping and coiling.

Conclusions

In England, between 1999 and 2010, hospital admission rates for SAH declined 18.3%, < 30-day CFRs for SAH declined 18.2%, and population-based mortality rates for SAH declined 39.8%. Part of the decline in population-based mortality rates for SAH is likely to be attributable to a decline in incidence. It is also, in part, attributable to increased survival after SAH. The available data do not allow us to compare the effects of different treatment meth-

ods for SAH on case fatality and mortality. During the period of study, mortality rates declined by almost 40%, and it is likely that there are a number of factors contributing to this substantial improvement in outcomes for SAH patients in England.

Acknowledgments

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Disclosures

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Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Figures. http://thejns.org/doi/suppl/10.3171/2015.5.JNS142115.

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