Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis

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Summary

Background Since the early 1980s, imaging techniques have enabled population-based studies of intracerebral haemorrhage. We aimed to assess the incidence, case fatality, and functional outcome of intracerebral haemorrhage in relation to age, sex, ethnic origin, and time period in studies published since 1980.

Methods From PubMed and Embase searches with predefined inclusion criteria, we identified population-based studies published between January, 1980, and November, 2008. We calculated incidence and case fatality. Incidences for multiple studies were pooled in a random-effects binomial meta-analysis. Time trends of case fatality were assessed with weighted linear-regression analysis.

Findings 36 eligible studies described 44 time periods (mid-year range 1983–2006). These studies included 8145 patients with intracerebral haemorrhage. Incidence did not decrease between 1980 and 2008. Overall incidence was 24·6 per 100 000 person-years (95% CI 19·7–30·7). Incidence was not significantly lower in women than in men (overall incidence ratio 0·85, 95% CI 0·61–1·18). Using the age group 45–54 years as reference, incidence ratios increased from 0·10 (95% CI 0·06–0·14) for people aged less than 45 years to 9·6 (6·6–13·9) for people older than 85 years. Median case fatality at 1 month was 40·4% (range 13·1–61·0) and did not decrease over time, and was lower in Japan (16·7%, 95% CI 15·0–18·5) than elsewhere (42·3%, 40·9–43·6). Six studies reported functional outcome, with independency rates of between 12% and 39%. Incidence of intracerebral haemorrhage per 100 000 person-years was 24·2 (95% CI 20·9–28·0) in white people, 22·9 (14·8–35·6) in black people, 19·6 (15·7–24·5) in Hispanic people, and 51·8 (38·8–69·3) in Asian people.

Interpretation Incidence of intracerebral haemorrhage increases with age and has not decreased between 1980 and 2006. Case fatality is lower in Japan than elsewhere, increases with age, and has not decreased over time. More data on functional outcome are needed.

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Introduction

Intracerebral haemorrhage is the second most common cause of stroke, and has a high case fatality.[1] Since 1980,[2] knowledge of the epidemiology of stroke has increased with the increasing availability of brain-imaging techniques.

Age-adjusted stroke incidence in high-income countries has decreased by 42% in the past four decades,[1] mostly owing to a reduction in incidence of ischaemic stroke. Whether incidence of intracerebral haemorrhage has also fallen is unclear. In Perth, Australia, the incidence of intracerebral haemorrhage decreased between 1989 and 2001.[3] Between 1981 and 2006, in Oxfordshire, UK, there was a decrease in incidence of intracerebral haemorrhage associated with premorbid hypertension in patients less than 75 years of age, whereas the incidence associated with antithrombotic medication and the incidence of non-hypertensive lobar bleed in patients over 75 years of age increased.[4] By contrast, incidence rates were stable between 1985 and 2004 in Dijon, France, and from 1983 to 1997 in Finland.[5,6]

Overall, stroke case fatality has not decreased substantially over the past four decades,[1] but crude case fatality of subarachnoid haemorrhage decreased by 17% between 1972 and 2002.[7] Whether the case fatality rate of intracerebral haemorrhage has changed has not been studied in detail. Although numerous population-based studies have reported intracerebral haemorrhage epidemiology,[1] few data are available from developing countries. Data on intracerebral haemorrhage incidence, case fatality, and functional outcome in age and sex subgroups are also scarce.

Although worldwide stroke epidemiology has been reviewed previously,[1] a more detailed analysis of intracerebral haemorrhage epidemiology is important for future research and management. We therefore did a meta-analysis on the incidence, case fatality, and functional outcome of intracerebral haemorrhage in relation to age, sex, ethnic origin, and time trends.

Methods

Search strategy and selection criteria

We searched PubMed and Embase for population-based studies of intracerebral haemorrhage epidemiology from

January, 1980, to November, 2008, with different combinations of the following key words: "h(a)emorrhagic stroke" or "intracranial" or "cerebral" or "intracerebral" or "intraparenchymal" and "h(a)emorrhage" or "h(a)ematoma" and "population (based)" or "region(al)" or "community (based)" or "stroke register/registry" and "incidence" or "fatality" or "mortality" or "trend" (see webappendix for syntaxes). Further studies were identified from the reference lists, related articles, and citation lists of each of the papers identified in the initial searches. This was repeated until no further studies were found.

See Online for webappendix

We included population-based and prospective studies with designs that allowed calculation of crude incidence, case fatality, or functional outcome for first intracerebral haemorrhage. If the data provided in a study were not restricted to first ever occurrences of intracerebral haemorrhage or if data on first ever occurrences could not be extracted and analysed separately, the study was excluded.

Because clinical scoring systems do not reliably differentiate haemorrhagic stroke from ischaemic stroke (sensitivity for intracerebral haemorrhage <0·5)[8,9] we included only studies in which less than 20% of intracerebral haemorrhage cases were not confirmed with imaging or autopsy (so-called undefined strokes). We excluded studies that were hospital based, studies based only on international classification of diseases (ICD) codes, and retrospective studies because they are inadequate indicators of stroke incidence in a population.[2,10] If other types of intracranial haemorrhage (eg, subarachnoid haemorrhage or subdural haematoma) could have been included in the intracerebral haemorrhage group and could not be identified, these studies were excluded. Papers published in English, French, German, and Spanish were included in the meta-analysis.

Data extraction

Two authors (CJJvA and MJAL) did the data search and quality assessment independently and completed a data extraction form. Any disagreements in the data were resolved by a third reviewer (CJMK).

We aimed to study only data on non-traumatic intracerebral haemorrhage. Thus, for each study we assessed whether stroke was defined according to WHO criteria. WHO criteria for stroke exclude intracerebral haemorrhage from malignancy, trauma, and extracerebral intracranial haemorrhage. Also, other criteria to exclude non-spontaneous and extracerebral haemorrhages were assessed. If data on the criteria used were not included in the publication we contacted the original investigators. If possible we recalculated incidence without other types of intracranial haemorrhage (eg, subarachnoid haemorrhage or subdural haematoma).

For each study included we analysed case-finding methods, proportion of ICH confirmed with imaging or autopsy, time from symptom onset to imaging, confirmation of diagnosis by study investigator, proportion of patients with undefined stroke, age limits, and demographic data of the study population and patients with intracerebral haemorrhage. Case-finding methods were categorised as excellent if all patients' data were obtained from regional hospitals, family doctors, or review of death certificates. For each time period we assessed the mid-calendar year, number of new cases of intracerebral haemorrhage, number of person-years, number of people with incident intracerebral haemorrhage who died within 1 month of diagnosis (and within 1 year if applicable), and outcome with either the modified Rankin scale (mRS) or Glasgow outcome scale (GOS), which are both validated disability scales.[11] Numbers of patients with intracerebral haemorrhage and person-years were also assessed in relation to age, sex, and ethnic subgroups. Populations were judged to be from Asia if they were from east or southeast Asia.

Statistical analysis

For each study we computed crude incidence per 100 000 person-years. Incidences for multiple studies were pooled by use of a random-effects binomial meta-analysis, with the number of intracerebral haemorrhages and the number of person-years for each study as variables (PROC NLMIXED, SAS Inc, Cary, NC, USA).[12] Random-effects models were used because of heterogeneity in incidence between studies. Incidence was calculated for age range, sex, and ethnic groups for studies that provided this information. To study sources of heterogeneity of incidence we did subgroup analyses and binomial meta-regression. We calculated the percentage of variance in incidence caused by age, sex, and ethnic origin by comparison of models with and without these characteristics.

Data on patients younger than 45 years of age were pooled. Because intracerebral haemorrhage is a rare condition before age 45 years,[13] we calculated age incidence ratios with the 45–54-year-old age group as the reference. For sex incidence ratios we used men as the reference, and for ethnic group incidence ratios we used the ethnic group with the largest number of events as the reference group.

Time trend was analysed at the mid-year of each study period and was expressed as the percentage change of the crude incidence rate per calendar year increase. We adjusted the relation between time period and intracerebral haemorrhage incidence for age, sex, and Asian versus non-Asian ethnic origin. The relation between intracerebral haemorrhage incidence and time period could not be adjusted for the demographics of the patients with intracerebral haemorrhage because these data were available for only three studies;[14–16] therefore, we used demographic data of the population in the region. The relations of age and sex with intracerebral haemorrhage incidence were analysed for studies that provided demographic data of all people at risk of intracerebral haemorrhage in the studied region, the

proportion of people older than 65 years, and the proportion of women in the study population.

Case fatality was calculated as percentage of patients with intracerebral haemorrhage who died within a 1 month or 1 year time period. For 1 month case fatality, we pooled case fatality data assessed at 28 days or 1 calendar month after intracerebral haemorrhage. The case fatality for the various time periods was expressed as the median with range. Case fatality by sex, age range, and ethnic group was calculated with data from those studies that provided this information.

We used weighted linear regression to assess the relation between the case fatality rate and the mid-year of the study. The inverse of the standard error of the case fatality for each study was used as weight. We reported the percentage change of case fatality per calendar year increase.

Data regarding functional outcome was measured with the mRS or the GOS. Patients who survived to the end of study follow-up were grouped into dependent (mRS score 3–5 or GOS score 2–4) or independent (mRS 0–2 or GOS 5) from others for daily activities.

We used SPSS 15.0 software (SPSS Inc, Chicago, IL, USA) for all statistical analyses, except for the random effects binomial regression, for which we used SAS 9.1 (SAS Institute Inc, Cary, NC, USA).

Role of the funding source

The sponsor had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

47 articles reported 36 studies[3,6,13–57] (figure 1). A total of 9151929 people from 21 countries were studied. 8145 of the 9151929 people had had an intracerebral haemorrhage and were observed for a total of 28034233 person-years. All 36 studies reported incidence, 26 case fatality, and six functional outcome. Two studies were cohort studies;[17,18] the other were stroke registers, of which seven studies reported intracerebral haemorrhage incidence in two[13,19–28] or three[3] non-overlapping time periods. Case-finding methods were excellent in 28 of 36 studies reporting incidence,[3,13,16,19–51] 22 of 26 reporting case fatality,[3,13,16,19–23,25–30,32,33,37–45,47–50,52,53] and four of six reporting functional outcome.[13,19,41,54]

Nine studies provided data on the time interval from symptom onset to imaging (range of median 0–7 days). Review of death certificates was not mentioned as a case-finding method in three studies.[38,44,55] 30 studies used the WHO definition of stroke; additional criteria for the definition of (primary) intracerebral haemorrhage were numerous (webappendix).

The 36 studies described 44 time periods (table 1).[3,6,13–52,55,56] Overall, intracerebral haemorrhage incidence was 24·6 per 100000 person-years (95% CI 19·7–30·7). However, the incidence of intracerebral haemorrhage varied from 1·8 to 129·6 person-years between studies (figure 2).[17,23] Two studies described only patients younger than 45 years,[13,56] and 11 studies reporting on 13 time periods also had age limitations.[6,16–19,20,24,33–35,44,48,50,52] The incidence of intracerebral haemorrhage in 29 time periods in studies without age limits[3,14,15,19,21–23,25–32,36–43,45–47,49,55] was 23·5 per 100000 person-years (20·1–27·6).

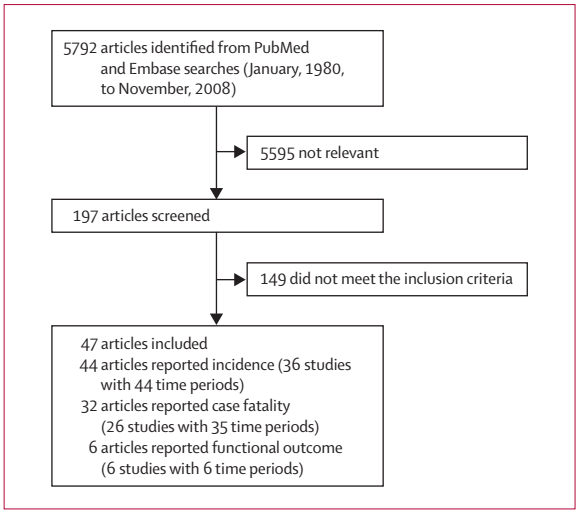

Figure 1: **Literature search**

Incidence could be calculated for men and women separately in 24 time periods (table 1).[3,6,14–19,21–25,27,32,34,36,38–41,43,44,46,48] The incidence of intracerebral haemorrhage was not significantly lower in women than in men (overall incidence ratio 0·85, 95% CI 0·61–1·18), with sex explaining 2·1% of the variance in intracerebral haemorrhage incidence. The difference between the sexes was greatest in the five Japanese studies, with an incidence ratio of 0·65 (0·50–0·86) compared with 0·92 (0·72–1·19) in the other regions (p=0·14).

18 studies provided data on incidence of intracerebral haemorrhage in one or more mid-decade age bands (table 2).[13,19,20,23,26,27,29,30,32–34,38–41,43,46–48,52,56] 12 studies showed a continuous increase of intracerebral haemorrhage incidence with age,[20,26,27,29,30,32,38,40,43,46–48,52] whereas in six studies there was a stabilisation or a decrease of incidence for people older than 85 years of age.[19,23,33,34,39,41] 94% of the variance in intracerebral haemorrhage incidence between age and study strata was explained by age.

After exclusion of the two studies that included only patients with intracerebral haemorrhage who were up to 45 years old,[13,56] we noted an annual decrease in crude incidence of intracerebral haemorrhage of 2·9% (95% CI 0·1–5·6).[3,6,14–50,51,52,55] Year of study explained 9·2% of the variance in intracerebral haemorrhage incidence. These results were similar after adjustment for sex[3,6,14,16–19,21,23,24,26–30,32,34,35,37–44,48,51] or age.[14,16,19–23,27,29,30,32,33,37,39,40,42–45,47–49,51,55]

We assessed the influence of studies with a limited age range on the observed time trend by doing a sensitivity analysis with the 29 time periods used in studies that had no age limit. This analysis did not show an annual

	Mid-year of study	Patients with intracerebral haemorrhage (n)	Person-years	Age limit (years)	Patients who had imaging (%)	Patients with undefined stroke (%)	Case-finding methods	Review study investigator	Incidence ratio women *vs* men (95% CI)
Oxford, UK[19]	1983	66	345 948	No	80·0%	4·6%	ABCEFGHJKMN‡	Yes	1·31 (0·80–2·12)
Florence, Italy[56]	1984	10	531 597	15–44	91·4%	4·3%	ACKMN	Yes	..
Oyabe, Japan[24]	1984	120	164 295	>25	..	10·7%	ABJLN‡	Yes	0·64 (0·44–0·92)
Dijon, France[23]	1987	87	678 560	No	88·0%	11·0%	ABDEHKN‡	Yes	0·89 (0·58–1·36)
Jyvaskyla, Finland[14]	1987	158	502 810	No	90·0%	7·5%	AHKN	Yes	0·96 (0·70–1·31)
Frederiksberg, Denmark[37]	1989	17	85 611	No	74·0%	15·0%	ABDHN‡	..	..
Okinawa, Japan[55]	1989	1412	3 667 194	No	98·4%	0·6%	ABDN	Yes	..
Oyabe, Japan[24]	1989	115	164 295	>25	..	2·3%	ABJLN‡	Yes	0·62 (0·43–0·89)
Perth, Australia[3]	1989	32	131 392	No	74·9%	14·3%	ABCDFHJMN‡	Yes	..
Valle d'Aosta, Italy[21]	1989	33	114 325	No	81·0%	17·7%	ABDEN‡	..	1·72 (0·85–3·49)
Belluno, Italy[40]	1992	93	211 389	No	89·5%	10·5%	ABFJN‡	Yes	1·20 (0·80–1·82)
Turku and Kuopio, Finland[6]	1993	506	1 933 660	25–74	86·0%	2·7%	AEHKN	Yes	0·86 (0·73–1·03)
Hisayama, Japan[18]	1994	41	31 644	>40	..	0·0%	BELM	Yes	0·54 (0·29–0·99)
Arcadia, Greece[48]	1994	77	161 548	>18	81·8%	18·2%	ABHJN‡	Yes	0·58 (0·37–0·93)
l'Aquila, Italy[20]	1994	114*	297 838	>18	89·0%	2·0%	ABCDFHN‡	Yes	..
Erlangen, Germany[39]	1995	48	202 900	No	95·5%	4·5%	ABCDJKN‡	Yes	1·58 (0·88–2·84)
Innherred, Norway[33]	1995	45	138 590	>15	87·5%	12·0%	ABDEHKN‡	Yes	..
Izumo city, Japan[15]	1995	350	678 832	No	100·0%	0·0%	AIN	..	0·75 (0·61–0·93)
Manhattan, USA[16,44]	1995	155	548 000	>20	99·0%	..	BDEFGJKLN‡	Yes	0·75 (0·55–1·03)
Perth, Australia[3]	1995	22	136 095	No	78·4%	9·4%	ABCDFHJMN‡	Yes	..
Malmö, Sweden[38]	1995	699	2 674 144	No	..	16·0%	ABIN‡	Yes	0·87 (0·75–1·01)
Dijon, France[28]	1996	37	429 264	No	96·0%	4·0%	ABDEHKN‡	Yes	..
l'Aquila, Italy[13]	1996	16*	874 375	0–44	100·0%	0·0%	ABCDFHN‡	Yes	..
Melbourne, Australia[26]	1996	40	133 816	No	..	8·7%	ABDFGKN‡	Yes	0·77 (0·41–1·43)
Vibo Valentina, Italy[32]	1996	62	179 186	No	95·9%	4·1%	ABDEJKN‡	Yes	0·92 (0·56–1·51)
Valle d'Aosta, Italy[22]	1997	36	118 723	No	97·4%	2·6%	ABDEN‡	..	0·70 (0·36–1·36)
Jichi Medical School, Japan[17]	1998	102	131 718	Yes†	..	0·2%	AEFHLM	Yes	0·63 (0·43–0·93)
China[50]	1998	2275	5 657 595	>25	92·0%	8·3%	ABHN‡	Yes	..
Martinique[45]	1998	83	360 000	No	92·8%	2·4%	ABEJKN‡	Yes	..
Melbourne, Australia[27]	1998	151	613 262	No	88·7%	10·8%	ABDFGKN‡	Yes	1·01 (0·73–1·39)
North Portugal[31]	1999	108	243 116	No	96·9%	4·4%	ABDFHIJKMN‡	Yes	..
Örebro, Sweden[29]	1999	44	123 503	No	84·0%	15·2%	ABDFHJKMN‡	Yes	..
Scotland, UK[47]	1999	50	212 704	No	91·9%	8·1%	ABEFKLN‡	Yes	..
Perth, Australia[3]	2000	19	143 417	No	89·1%	7·7%	ABCDFHJMN‡	Yes	..
South London, UK[36,46]	2000	395	2 701 909	No	89·8%	7·5%	ABEFJKN‡	Yes	0·87 (0·72–1·06)
Lund, Sweden[35]	2001	46	235 505	>15	..	6·0%	ABDEJKMN‡	Yes	..
Iquique, Chile[41]	2001	69	396 712	No	91·0%	7·9%	ABDFHJKN‡	Yes	0·62 (0·38–1·01)
Auckland, New Zealand[34]	2002	177	897 882	>15	91·0%	8·9%	ABDE‡	Yes	1·10 (0·82–1·48)
Barbados[30]	2002	42	239 068	No	96·0%	4·3%	ABCFHJMN‡	Yes	..
Puglia, Italy[42]	2002	24	77 474	No	93·7%	6·3%	ABDIJKN‡	..	..
Tartu, Estonia[49]	2002	57	202 244	No	90·0%	10·0%	ABJMN‡	Yes	..
Oxford, UK[25,51]	2003	34	273 318	No	96·0%	4·0%	ABCEFGHIJKMN‡	Yes	0·95 (0·48–1·86)
Matão, Brazil[43]	2004	11	75 053	No	100·0%	0·0%	ABFJN‡	Yes	0·57 (0·17–1·95)
Mumbai, India[52]	2006	67	313 722	>25	89·2%	1·6%	BDFHLN	Yes	..

A=death certificates. B=family doctors. C=rehabilitation. D=nursing homes. E=regular search. F=review of radiology requests or reports. G=media attention (campaign or newspaper). H=outpatient clinics, health centres. I=sudden deaths, very early death. J=emergency, ambulance, on call medical services. K=international classification of diseases codes. L=door-to-door, home visit, social services, phone calls. M=autopsy reports. N=all hospitals in the region. ..=not applicable. *Calculation of crude incidence of intracerebral haemorrhage after exclusion of cases with subdural haematoma. †Consisted of 12 communities, of which eight included only patients aged 40–69 years. ‡Case-finding methods categorised as excellent.

Table 1: **Characteristics of 36 studies reporting on intracerebral haemorrhage**

	Patients with intracerebral haemorrhage (n)	Person-years	Incidence per 100 000 person-years (95% CI)	Number of time periods	Incidence ratio (95% CI)
≤44 years[13,19,23,26,27,30,32,39–41,43,46–48,52,56]	119	5 958 646	1·9 (1·6–2·2)	16	0·10 (0·06–0·14)
45–54 years[19,23,26,27,30,32,33,39–41,43,46–48,52]	164	725 660	19·1 (13·4–27·4)	15	Reference
55–64 years[19,20,23,26,27,30,32,33,38–40,43,46–48,52]	305	865 173	36·5 (28·4–46·7)	16	1·8 (1·3–2·6)
65–74 years[19,23,26,27,29,30,32–34,38–41,43,46–48,52]	597	812 077	77·1 (65·0–91·5)	18	3·8 (2·7–5·4)
75–84 years[19,23,26,27,29,30,32–34,38–41,43,46–48,52]	665	531 845	136·9 (111·3–168·4)	18	6·8 (4·8–9·6)
≥85 years[19,23,26,27,29,30,32–34,38–41,46–48,52]	274	170 580	196·0 (148·3–259·1)	17	9·6 (6·6–13·9)

Because intracerebral haemorrhage is rare in people under age 45 years, the incidence ratios were calculated with the 45–54 years age group as the reference.

Table 2: **Incidence of intracerebral haemorrhage according to age**

decrease in intracerebral haemorrhage incidence (1·2%, 95% CI –1·7 to 4·0).[3,14,15,19,21–23,25–32,36–43,45–47,49,55] When we restricted the analysis to the 26 time periods of studies that had excellent case-finding methods and no age limit, we also found no substantial decrease of intracerebral haemorrhage incidence over time (0·3%, –2·7 to 3·3).[3,19,21–23,25–32,36–43,45–47,49]

Incidence was comparable for white people (24·2, 95% CI 20·9–28·0, reference group),[3,6,13,14,16,19–22,25–29,31–40,42–44,46–49,56] black people (22·9 14·8–35·6; incidence ratio 1·0, 95% CI 0·6–1·4),[16,30,44–46] Hispanic people (19·6, 15·7–24·5; incidence ratio 0·8, 0·5–1·3),[16,41,43,44] Indian people (21·4, 16·6–27·1; incidence ratio 1·1, 0·4–1·9),[52] and Maoris (22·2, 15·8–30·3; incidence ratio 0·9, 0·4–2·0),[34] but two times higher for east and southeast Asian people (51·8, 38·8–69·3; incidence ratio 2·1, 1·6–2·9,[15,17,18,24,34,50,55] figure 3). Ethnic origin explained 42% of the variance in incidence of intracerebral haemorrhage between studies.

Incidence of intracerebral haemorrhage for black people was higher in northern Manhattan (49·5, 95% CI 35·1–67·9)[16,44] than in Martinique (23·1, 18·4–28·6),[45] south London (14·9, 12·1–18·3),[46] and Barbados (17·6, 12·7–23·7),[30] with an incidence ratio of 2·7 (1·7–4·3) for Manhattan versus elsewhere. Hispanic people in Manhattan also had a higher incidence of intracerebral haemorrhage (24·0, 19·2–29·6)[16,44] than did those in Chile or Brazil (14·5, 11·4–18·3);[41,43] however, the number of studies with data on Hispanic people was too small to analyse regional differences in incidence of intracerebral haemorrhage in this group. The incidence of intracerebral haemorrhage in white people in Manhattan (22·6, 15·2–32·5)[16,44] was similar to that in white people in general (incidence ratio 0·9, 0·4–2·1). In Auckland, incidence of intracerebral haemorrhage in east and southeast Asian immigrants (20·7, 13·5–30·3) was similar to that in white people (18·6, 15·3–22·4) and Maori people (22·2, 15·8–30·3) living in that region (incidence ratio 1·1, 0·7–1·6),[34] and lower than in Asian people living in China[50] and Japan[15,17,18,24,55] (57·6, 46·0–72·0; incidence ratio 0·36, 0·18–0·71).

Because the incidence in Asian people was higher than in people of other ethnic origins (figure 3), we investigated the influence of these populations on the observed time trend. After adjustment for Asian versus non-Asian studies, the decrease of intracerebral haemorrhage incidence was no longer significant (adjusted annual decrease of incidence 1·1%, 95% CI –1·1 to 3·3). In addition, we found no pronounced annual decrease of intracerebral haemorrhage incidence after exclusion of the Chinese study and the six Japanese studies (1·2%, –1·2 to 3·6),[3,6,14,16,19–23,25–49,52] or within the Chinese[50] and Japanese[15,17,18,24,55] studies (0·5%, –5·3 to 6·0).

Median case fatality at 1 month was 40·4% (range 13·1–61·0) for 26 study populations in 35 time periods (table 3).[3,13–16,19–23,25–27,29,30,32,33,38–45,47–50,53,55,56] Ten studies reported case fatality after 1 year (median 54·7%, range 46·0–63·6).[3,19,20,26,27,32,39,43,48,54,57]

Five studies provided data on 1 month case fatality in men and women separately (table 4)[27,38,48,50,55] and five studies provided data in age groups.[19,29,38,48,55] In Melbourne, Australia case fatality was higher in women than in men,[27] whereas the other regions reported similar case fatalities for men and women. The pooled case fatality was higher in patients older than 75 years (28·1%, 95% CI 24·9–31·2) than in younger patients (17·8%, 15·9–19·7; difference 10·3%, 95% CI 6·6–14·0). Case fatality at 1 month (table 3) was lower in the two Japanese studies (16·7%, 15·0–18·5)[15,55] than in the other regions (42·3%, 40·9–43·6; difference 25·5%, 23·3–27·7).[3,13,14,16,19–23,25–27,29,30,32,33,38–45,47–50,53,56]

We noted no change in case fatality over time[3,13–16,19–27,29,30,32,33,38–45,47–50,53,55] (annual increase of 0·4% per year, 95% CI –0·5 to 1·4), with a similar result after adjustment for age (0·3%, –0·7 to 1·3). Sensitivity analysis excluding the Japanese studies produced similar results (annual decrease 0·6% per year, –1·3 to 0·2). Sensitivity analysis including only the 22 time periods of studies with excellent case-finding methods also did not show a time trend for case fatality (annual decrease 0·2% per year, –1·1 to 0·7).[3,13,16,19–23,25–30,32,33,37–45,47–50,52,53]

Six studies reported functional outcome at some point after intracerebral haemorrhage (table 3).[13–15,19,41,54] The proportion of patients leading an independent life after intracerebral haemorrhage varied from 12% at 12 months in Estonia[54] to 39% at last follow-up visit in young Italian adults (mean follow-up period 50 months, range

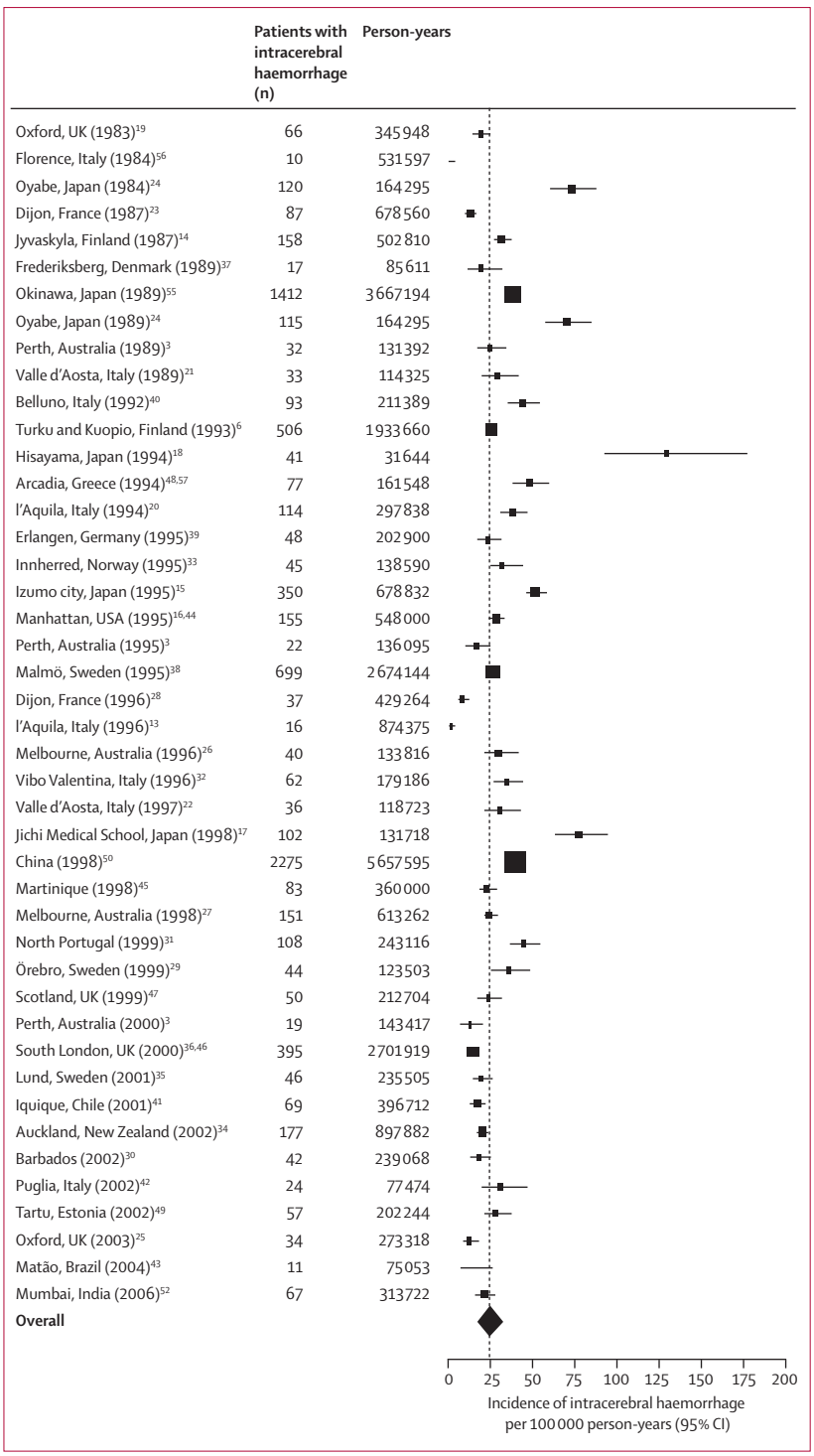

Figure 2: **Incidence of intracerebral haemorrhage in 44 study periods**
Size of the point estimates is proportional to the weight of the studies.

19–79 months).[13] Because the study design and the timing of the functional outcome assessment in these six studies were variable, we did not do a formal meta-analysis.

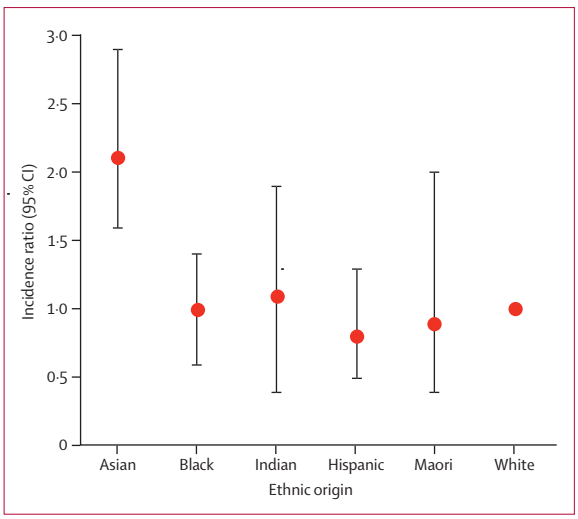

Figure 3: **Intracerebral haemorrhage incidence ratios in ethnic groups**
White ethnic origin was taken as reference because it was the ethnic group with the largest number of patients with intracerebral haemorrhage. Circles are means and bars are 95% CI.

Discussion

Overall, we did not find a substantial decrease in incidence of intracerebral haemorrhage between January, 1980, and November, 2008. We have reported overall higher incidence of intracerebral haemorrhage in men compared with women, especially in Japanese studies; a two times higher rate of intracerebral haemorrhage incidence in Asian people compared with other ethnic groups; and an increasing incidence of intracerebral haemorrhage with increasing age.

Case fatality at 1 month was low in Japanese studies compared with the other regions. Overall, case fatality was similar in men and women and increased with increasing age. We did not find a substantial time trend for 1 month case fatality.

The higher incidence of intracerebral haemorrhage in elderly patients has been attributed to high prevalences of amyloid angiopathy and hypertension, and to the use of antithrombotic drugs in this age group.[4] In a subset of studies we noted a stabilisation or decrease in intracerebral haemorrhage incidence in the oldest age groups. This is probably an anomaly because accurate community-based case finding in elderly patients is known to be difficult,[58] and stroke subtype is more likely to be categorised as undefined.[19]

Japanese men showed a higher incidence of intracerebral haemorrhage than Japanese women,[15,17,18,24] whereas in the other regions only small sex differences in intracerebral haemorrhage incidence were reported. Data from the Japanese Hisayama study[18,59] suggest that the effect of alcohol intake on incidence of intracerebral haemorrhage might be different in Japanese men and women, because the age-adjusted incidence of intracerebral haemorrhage increased more with higher daily alcohol intake in men than in women.

	Mid-year of study	Patients with intracerebral haemorrhage (n)	Age limit (years)	Case fatality at 1 month, % (95% CI)	Case fatality at 1 year, % (95% CI)	Patients living independently (%)
Oxford, UK[19]	1983	66	No	50·0% (37·4–62·6)	62·1% (49·3–73·8)	26 (at 12 months)
Florence, Italy[26]	1984	10	15–44	50·0% (18·7–81·3)	..	..
Dijon, France[23,53]	1987	87	No	42·6% (31·6–54·6)	..	..
Jyvaskyla, Finland[14]	1987	158	No	50·6% (42·8–58·4)	..	18*
Okinawa, Japan[55]	1989	1412	No	17·6% (15·6–19·6)	..	..
Perth, Australia[3]	1989	32	No	37·5% (21·1–56·3)	46·7% (29·1–65·3)	..
Valle d'Aosta, Italy[21]	1989	33	No	45·0% (28·1–63·7)	..	..
Belluno, Italy[40]	1992	93	No	34·4% (24·9–45·0)	..	..
Dijon, France[53]	1992	94	No	39·4% (29·4–50·0)	..	..
Arcadia, Greece[48,57]	1994	77	>18	46·8% (35·3–58·5)	53·2% (41·5–64·7)	..
l'Aquila, Italy[20]	1994	122	No	51·6% (46·1–64·4)	58·2% (49·4–66·9)	..
Erlangen, Germany[39]	1995	48	No	41·6% (27·6–56·8)	58·3% (43·2–72·4)	..
Innherred, Norway[33]	1995	45	>15	37·8% (23·8–53·5)	..	..
Izumo city, Japan[15]	1995	350	No	13·1% (9·6–16·7)	..	30†
Manhattan, USA[16,44]	1995	155	>20	35·0% (27·3–42·3)	..	..
Perth, Australia[3]	1995	22	No	45·4% (24·4–67·8)	..	..
Malmö, Sweden[38]	1995	699	No	23·3% (20·2–26·5)	..	..
l'Aquila, Italy[13]	1996	18	0–44	38·9% (17·3–64·3)	..	39‡
Melbourne, Australia[26]	1996	40	No	45·0% (29·3–61·5)	50·0% (33·8–66·2)	..
Vibo Valentina, Italy[32]	1996	62	No	40·3% (28·0–53·5)	56·5% (43·3–69·0)	..
Dijon, France[53]	1997	97	No	34·0% (24·7–44·3)	..	..
Valle d'Aosta, Italy[22]	1997	36	No	38·9% (23·1–56·5)	..	..
China[50]	1998	2275	>25	49·9% (47·3–51·4)	..	..
Martinique[45]	1998	83	No	37·3% (27·0–48·7)	..	..
Melbourne, Australia[27]	1998	151	No	40·4% (32·6–48·2)	49·7% (41·7–57·6)	..
Scotland, UK[47]	1999	50	No	46·0% (31·8–60·7)	..	..
Örebro, Sweden[29]	1999	44	No	20·5% (9·8–35·3)	..	..
Perth, Australia[3]	2000	19	No	47·4% (24·4–71·1)	..	..
Iquique, Chilie[41]	2001	69	No	28·9% (18·7–41·2)	..	33 (at 6 months)
Puglia, Italy[42]	2002	24	No	20·8% (7·1–42·2)	..	..
Barbados[30]	2002	42	No	61·0% (44·5–75·8)	..	..
Dijon, France[53]	2002	102	No	24·5% (16·2–32·9)	..	..
Tartu, Estonia[49,54]	2002	57	No	40·4% (27·6–54·2)	54·4% (40·7–67·6)	12 (at 12 months)
Oxford, UK[25]	2003	34	No	55·8% (37·9–72·8)	..	..
Matão, Brazil[43]	2004	11	No	45·4% (16·8–76·6)	63·6% (30·8–89·1)	..

CFR=case fatality rate. *Outcome at last follow-up visit, median follow-up 32 months (range 8–60). †Glasgow outcome score assessed at discharge. ‡Outcome at last follow-up visit, mean follow-up period 50 months (range 19–79).

Table 3: **Case fatality and functional outcome of intracerebral haemorrhage**

In northern Manhattan, the risk of deep intracerebral haemorrhage was two times higher in men than in women, whereas the prevalence of hypertension was similar.[15] Inadequate treatment of hypertension in men, involvement of another risk factor for deep intracerebral haemorrhage, or a higher susceptibility of men to the effects of hypertension might contribute to this difference.[16]

Incidence of intracerebral haemorrhage is high in Japan and China, whereas the rate in Asian migrants in New Zealand is not different from that in white people or Maori people.[34] An opposite relation between ethnic origin and environment was found for black Caribbean people living in south London, who have higher intracerebral haemorrhage incidence than do those living in Barbados. This difference can probably be explained by a difference in cardiovascular risk factors after migration.[60] We found that intracerebral haemorrhage incidence was two to three times higher in black people in Manhattan compared with those in other regions (Barbados, Martinique, and south London), whereas the incidence rate in white people in Manhattan was similar to the incidence rate in those elsewhere. These findings suggest environmental factors influence indcidence of intracerebral haemorrhage.

Studies on time trends in intracerebral haemorrhage incidence have shown regional differences. In line with

	Mid-year of study	Patients with intracerebral haemorrhage (n)	Case fatality					
			Men	Women	<65 years	65–74 years	75–84 years	>85 years
Oxford, UK[19]	1983	66	..	..	42·0 (20·3–66·5)	44·4 (21·5–69·2)	58·0 (36·6–77·9)	80·0 (28·4–99·5)
Okinawa, Japan[55]	1989	1412	18·8 (16·1–21·5)	16·2 (13·3–19·1)	17·3 (14·6–19·9)	14·5 (10·4–18·7)	18·8 (13·8–23·7)	24·8 (17·1–32·5)
Arcadia, Greece[48]*	1994	77	44·0 (30·0–58·7)	51·8 (32·0–71·3)	33·3 (14·6–57·0)	31·8 (13·9–54·9)	63·2 (38·4–83·7)	60·0 (32·3–83·7)
Malmö, Sweden[38]	1995	699	23·9 (19·4–28·3)	22·7 (18·2–27·1)	14·3 (8·9–19·6)	18·9 (13·4–24·5)	29·8 (24·0–35·5)	31·3 (22·4–41·4)
China[50]†	1998	2275	48·4 (45·7–51·1)	50·7 (47·5–53·9)	..	..	..	..
Melbourne, Australia[27]	1998	151	29·2 (19·0–41·1)	50·6 (39·1–62·1)	..	..	..	..
Örebro, Sweden[29]	1999	44	..	..	25·0 (3·2–65·1)	21·4 (4·7–50·8)	12·5 (1·6–38·3)	33·3 (4·3–77·7)
Overall	..	..	35·4 (33·6–37·1)	35·3 (33·2–37·4)	17·6 (15·3–20·0)	18·1 (14·8–21·4)	26·8 (23·1–30·5)	30·9 (25·1–36·7)

Data are % (95% CI). *Patients older than age 18 years. †Patients older than age 25 years.

Table 4: **Intracerebral haemorrhage case fatality at 1 month according to sex and age**

the results of our meta-analysis, the numbers of patients with intracerebral haemorrhage in all age groups did not decrease over time in Oxford and Dijon.[4,5,51] Interestingly, in Oxford, time trends differed according to age group and type of intracerebral haemorrhage.[4] A decrease in incidence of intracerebral haemorrhage was reported for Perth, Australia, which was most prominent in men.[3] No decline in incidence of intracerebral haemorrhage was found in Finland and France.[5,6] In Finland the intracerebral haemorrhage incidence in the 1980s might have been underestimated because only a small proportion of patients with stroke had CT scans at that time.[6] On the basis of our meta-analysis, the decrease in incidence of intracerebral haemorrhage is moderate at best and similar to that for subarachnoid haemorrhage[61] rather than that for ischaemic stroke.[1] Changes in incidence might be different for specific subtypes of intracerebral haemorrhage, but we could not assess changes in subgroup-specific incidence because these data were not available from the parent studies.

The overall intracerebral haemorrhage case fatality at 1 month of about 40% is much the same as that in a previous report.[1] Case fatality was similar between regions, except for the low case fatality of about 13%[15] and 18%[55] in the two Japanese studies. Japanese patients also have a high incidence and a low case fatality for subarachnoid haemorrhage.[7,61] The two Japanese studies reporting on case fatality did not meet our criteria for excellent quality because family doctors were not involved in case finding. Therefore, patients who died from intracerebral haemorrhage at an early stage were possibly missed, which might in part explain the low case fatality.[15,55] Also, differences in treatment strategies might explain the differences in case fatality after haemorrhagic stroke between Japan and the rest of the world. In theory, early referral to a stroke unit and surgical intervention for more patients might reduce intracerebral haemorrhage case fatality in Japan.[15] Six studies reported functional outcome after intracerebral haemorrhage,[13–15,19,41,49] one of which was from Japan.[15] Because these studies varied considerably in study design and time of assessment, no conclusions can be drawn from these data.

Several limitations of this meta-analysis should be mentioned. The definition of intracerebral haemorrhage varied or was not specified in detail in the studies. Also, population-based stroke epidemiology data were limited for countries outside Europe and North America. A recent review, including ischaemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage, reported a decrease of stroke incidence in high-income countries and an increase of stroke incidence in low-income countries.[1] Investigation of the influence of known prognostic factors (eg, use of antithrombotics or anticoagulants, intracerebral haemorrhage size, or presence of intraventricular extension) on case fatality would be interesting. Unfortunately, there were few data on prognostic factors in these population-based studies and therefore we could not assess the influence of prognostic factors.

Age, sex, and ethnic background influence incidence of intracerebral haemorrhage. Environmental factors are probably also involved. The change in environmental factors, such as hypertension control, has probably led to a decreasing incidence of intracerebral haemorrhage in some regions. Because case fatality has not decreased, the best way to reduce mortality from intracerebral haemorrhage seems to be further treatment of risk factors. More data on functional outcome after intracerebral haemorrhage are needed.

Contributors

CJJvA, GJER, and CJMK designed the study. CJJvA and MJAL did the data search and extracted data. CJJvA, IVDT, and AA did the statistical analyses. CJJvA and AA designed the tables and figures. All authors contributed to the writing of the Article.

Conflicts of interest

We have no conflicts of interest.

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