Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis

Monique H M Vlak, Ale Algra, Raya Brandenburg, Gabriël J E Rinkel

Lancet Neurol 2011; 10: 626–36
Published Online June 3, 2011
DOI:10.1016/S1474-4422(11)70109-0

See Comment page 595

Utrecht Stroke Centre, Department of Neurology and Neurosurgery, Rudolf Magnus Institute of Neuroscience, University Medical Centre Utrecht, Utrecht, Netherlands (M H M Vlak MD, Prof A Algra MD, R Brandenburg BSc, Prof G J E Rinkel MD); **and Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, Netherlands** (Prof A Algra)

Correspondence to: Prof Ale Algra, Julius Centre for Health Sciences and Primary Care, mailbox STR 6.131, University Medical Centre Utrecht, PO Box 85500, 3584 CX Utrecht, Netherlands
a.algra@umcutrecht.nl

Background Unruptured intracranial aneurysms (UIAs) are increasingly detected and are an important health-care burden. We aimed to assess the prevalence of UIAs according to family history, comorbidity, sex, age, country, and time period.

Methods Through searches of PubMed, Embase, and Web of Science we updated our 1998 systematic review up to March, 2011. We calculated prevalences and prevalence ratios (PRs) with random-effects binomial meta-analysis. We assessed time trends with year of study as a continuous variable.

Findings We included 68 studies, which reported on 83 study populations and 1450 UIAs in 94 912 patients from 21 countries. The overall prevalence was estimated as 3·2% (95% CI 1·9–5·2) in a population without comorbidity, with a mean age of 50 years, and consisting of 50% men. Compared with populations without the comorbidity, PRs were 6·9 (95% CI 3·5–14) for autosomal dominant polycystic kidney disease (ADPKD), 3·4 (1·9–5·9) for a positive family history of intracranial aneurysm of subarachnoid haemorrhage, 3·6 (0·4–30) for brain tumour, 2·0 (0·9–4·6) for pituitary adenoma, and 1·7 (0·9–3·0) for atherosclerosis. The PR for women compared with men was 1·61 (1·02–2·54), with a ratio of 2·2 (1·3–3·6) in study populations with a mean age of more than 50 years. Compared with patients older than 80 years, we found no differences by age, except for patients younger than 30 years (0·01, 0·00–0·12). Compared with the USA, PRs were similar for other countries, including Japan (0·8, 0·4–1·7) and Finland (1·0, 0·4–2·4). There was no statistically significant time trend.

Interpretation The prevalence of UIAs is higher in patients with ADPKD or a positive family history of intracranial aneurysm of subarachnoid haemorrhage than in people without comorbidity. In Finland and Japan, the higher incidence of subarachnoid haemorrhage is not explained by a higher prevalence of UIAs, implicating higher risks of rupture.

Funding Julius Centre for Health Sciences and Primary Care and Department of Neurology and Neurosurgery, University Medical Centre, Utrecht.

Introduction

Rupture of an intracranial aneurysm causes subarachnoid haemorrhage. Because such haemorrhage mostly affects relatively young people (ie, younger than 65 years) and has a high case fatality and morbidity, it is an important subtype of stroke.[1] The proportion of years of potential life lost from subarachnoid haemorrhage is similar to that of ischaemic stroke and intracerebral haemorrhage,[2] and a recent calculation found a total economic burden of £510 million annually for subarachnoid haemorrhage in the UK.[3]

The incidence of subarachnoid haemorrhage is higher in Finland and Japan than in other regions, increases with age, and is higher in women.[4] These regional, sex, and age differences and the slight decline in the incidence of subarachnoid haemorrhage between 1950 and 2005[4] might result from differences in the prevalence of aneurysms, differences in the risk of rupture, or both.

In 1998, we published a systematic review on the prevalence of unruptured intracranial aneurysms (UIAs).[5] Since then, non-invasive techniques for imaging of intracranial vessels have become increasingly available and used, which has coincided with an increase in incidental detection of aneurysms[6] and the publication of many new studies on the prevalence of UIAs. We aimed to incorporate the new data into the existing pooled data to provide more accurate estimates on the prevalence of UIAs in healthy populations and in groups of people undergoing brain imaging for a specific reason. We also aimed to increase the knowledge of prevalence in sex, age, and comorbidity subgroups, and to study regional differences and time trends in the extended dataset.

See Online for webappendix

Methods

Search strategy and selection criteria

Our search methods were similar to those in our previous review.[5] We did a PubMed and Embase search to retrieve all studies on the prevalence of UIAs published before March, 2011. In brief, we used the keywords "aneurysm(s) AND (cerebral OR brain OR intracranial OR berry OR basilar OR saccular OR communicating) AND (unruptured OR incidental OR prevalence OR risk)" (see webappendix p 1). We also checked the Web of Science for articles citing our previous review and searched the personal database of one author (GJER) that has been prospectively built by daily searches of PubMed over the past 15 years with terms related to subarachnoid

haemorrhage and intracranial aneurysm. We searched the reference lists of all relevant publications for additional studies. We continued this method of cross-checking until we could not identify any further studies. Finally, all papers (or publications) used in our previous review were reassessed according to our present inclusion criteria.

We did not exclude any published work on the basis of language.[7] Our inclusion criteria were more strict than in our previous review: cross-sectional or case-control design (in which cases are defined as people with a specific comorbidity and controls as people without that comorbidity); presentation of data that included crude numbers on patients with UIAs and on the population at risk, or that allowed recalculation of these crude numbers; UIAs reported separately from ruptured intracranial aneurysms; and investigation of ten or more patients. In family studies, the procedure for selection of families had to be specified, and the indication for imaging or autopsy had to be given. In studies of healthy volunteers, if screening for aneurysms was the main reason for imaging, the motivation for participation had to be clear. Imaging studies had to use CT angiography, MRI, magnetic resonance angiography, or intra-arterial digital subtraction angiography (IA-DSA). In MRI studies, the text had to specify that there was a specific search for intracranial aneurysms. In IA-DSA studies, the number of investigated vessels had to include at least both internal carotid arteries; in case-control studies, case and control participants had to be comparable, without additional criteria for control participants. For cross-sectional studies in which more than 20% of the potential participants declined participation or did not undergo radiological examination, the reasons had to be specified.

MHMV did the literature search and screening of the titles for eligible studies. To assess further eligibility of the studies, MHMV and RB independently assessed the abstracts according to the predefined inclusion criteria. If an abstract was judged by both authors to meet the requirements, the full article was read. Any disagreement was resolved by a third reviewer (GJER or AA).

Data extraction

After our initial assessment for eligibility, MHMV and RB independently completed a data extraction form. Any disagreement about the data was resolved by a third reviewer (GJER or AA). If possible, we calculated the prevalence after exclusion of other types of intracranial aneurysm (eg, traumatic, mycotic, or fusiform), since these types of aneurysms have a different pathophysiology. For each study we extracted data on mid-year of study, study design (cross-sectional or case-control), size of study population, number of patients with UIAs, number of UIAs, site and size of UIAs, demographic data of the study population and patients with UIAs, type of investigation (autopsy or method of imaging), and reason for autopsy or imaging. If patients had UIAs that were additional to a ruptured aneurysm, these patients were excluded from our analysis.

We classified the studies as prospective or retrospective on the basis of how data were collected. We categorised imaging methods into IA-DSA, MRI, magnetic resonance angiography, and CT angiography. We classified IA-DSA studies as three vessel or four vessel (one or both vertebral and both carotid arteries) and two vessel (only both carotid arteries). We classified the site of the intracranial aneurysms as the internal carotid artery (including the posterior communicating artery), anterior cerebral arteries (including the anterior cerebral artery, anterior communicating artery, and pericallosal artery), middle cerebral artery, or posterior circulation (including the vertebral artery, basilar artery, cerebellar arteries, and posterior cerebral artery).

We categorised the sizes of intracranial aneurysms as less than 5 mm, 5–9 mm, or 10 mm or greater. Some of the studies we identified used other categories; to include more studies in our analyses on size, we classed 5 mm or less as less than 5 mm and 6–9 mm as 5–9 mm.

On the basis of our previous review, we subdivided the studies according to the reason for brain imaging or autopsy: screening (including healthy volunteers and healthy control groups), a positive family history of intracranial aneurysm or subarachnoid haemorrhage according to the paper being assessed, autosomal dominant polycystic kidney disease (ADPKD), atherosclerosis, pituitary adenoma, and other. We classed as screening any studies with cohorts of autopsied people and control series from case-control studies unless a different reason for autopsy or imaging was given. If there were two studies with the same reason for autopsy or imaging that did not fall into one of our predefined categories, we created a new category with that reason for investigation. If a study included more than one study population—eg, patients with ischaemic stroke and healthy controls—we classed them as two separate study populations; the patients with ischaemic stroke were included in the category of atherosclerosis and the healthy controls in the reference group without comorbidity.

Statistical analysis

We computed the crude prevalence for each study. We pooled the prevalences from multiple studies by means of a random-effects binomial meta-analysis, with the number of UIAs and the total number of included patients for each study population as variables.[8] Because of the heterogeneity in prevalence between studies, we used random-effects models to study possible causes of heterogeneity. When possible, we adjusted prevalences and prevalence ratios (PRs) for the presence of comorbidity, for percentage of men in the study population, and mean age of the study population.

We first assessed whether all methods of imaging were similar in their detection of UIAs. We therefore compared magnetic resonance angiography, MRI, or CT

	Country	Mid-year of study	Number of people included	Number of patients with aneurysm	Design or method*	Reported on:						
						Sex	% men	Mean age (years)	Age categories	Reason for investigation†	Aneurysm site	Aneurysm size
Cohen (1955)[9]	Norway	1952	539	9	P, A	No	No	No	No	E	No	No
Chason (1958)[10]	USA	..	2749	80	R, A	No	No	No	Yes	E	No	No
Housepian (1958)[11]	USA	1934	8660	11	R, A	No	No	No	No	E	No	No
Berry (1961)[12]	USA	1950	3804	39	R, A	No	No	No	No	E	No	No
Du Boulay (1965)[13]	UK	1954	51	0	R, I	Yes	53	No	No	I	No	No
McCormick A (1965)[14]	USA	..	7523	26	R, A	No	No	No	No	E	No	No
McCormick B (1965)[14]	USA	..	197	12	R, A	No	No	No	No	E	No	No
Yanagawa (1966)[15]	Japan	..	203	1	P, I	No	No	40	Yes	E	No	No
McCormick (1970)[16]	USA	..	1619	82	P, A	No	No	No	Yes	E	No	No
Romy (1973)[17]	France	1962	11 620	67	R, A	No	No	No	No	E	No	No
Stehbens (1975)[18]	Australia	1931	979	43	P, A	No	No	No	No	E	No	No
Jakubowski A (1978)[19]	UK	1973	150	10	R, I	Yes	56	48·1	No	I	Yes	Yes
Jakubowski B (1978)[19]	UK	1982	33	1	R, I	Yes	39	43·0	No	I	Yes	Yes
Wakabayashi (1983)[20]	Japan	1982	17	7	R, I	Yes	41	42	No	F	Yes	No
De la Monte (1985)[21]	USA	1971	12 911	39	R, A	No	No	No	No	E	No	No
Atkinson (1989)[22]	USA	1983	278	3	R, I	Yes	55	53·0	Yes	I	Yes	Yes
Inagawa (1990)[23]	USA	1969	10 259	84	R, A	No	No	No	Yes	E	Yes	Yes
Iwata (1991)[24]	Japan	1989	72	4	P, I	Yes	50	No	No	H	Yes	Yes
Ujiie A (1991)[25]	Japan	1989	616	16	R, I	Yes	51	40·1	No	H, I	No	No
Ujiie B (1991)[25]	Japan	1989	590	23	R, I	Yes	69	48·8	No	H, I	No	No
Schievink A (1992)[26]	USA	1969	72	3	R, A	No	No	No	No	E, F	No	No
Schievink B (1992)[26]	USA	1969	144	3	R, A	No	No	No	No	E, F	No	No
Chan (1993)[27]	China	1977	33	0	R, A	No	No	No	No	F	No	No
Huston A (1993)[28]	USA	1991	26	6	P, I	No	No	No	No	F	No	No
Huston B (1993)[28]	USA	1991	59	3	P, I	No	No	No	No	F	No	No
Sugai A (1994)[29]	Japan	1988	262	19	P, I	No	No	No	No	H, I	No	No
Sugai B (1994)[29]	Japan	1988	71	3	P, I	No	No	No	No	H, I	No	No
Leblanc (1995)[30]	Canada	..	41	1	P, I	Yes	32	41·2	No	G	No	No
Ronkainen (1995)[31]	Finland	1993	396	33	P, I	No	46	45·4	No	G	Yes	Yes
Griffiths (1996)[32]	UK	1993	100	9	P, I	No	52	62·0	No	H	Yes	Yes
Pappada (1996)[33]	Italy	..	389	10	R, I	Yes	75	67·0	No	H	Yes	Yes
Kann (1997)[34]	USA	..	209	10	R, I	No	No	No	No	H	Yes	Yes
Pant (1997)[35]	Japan	1985	465	23	R, I	Yes	36	41·0	No	I	Yes	Yes
Ronkainen A (1997)[36]	Finland	..	438	38	P, I	No	47	48·1	No	F, G	Yes	No
Ronkainen B (1997)[36]	Finland	..	22	2	P, I	No	No	No	No	F, G	Yes	No
Yue (1997)[37]	USA	..	3671	3	R, I	No	No	No	No	E	Yes	Yes
Cloft (1998)[38]	USA	1987	95	6	P, I	Yes	7	No	No	J	No	No
Iida (1998)[39]	Japan	1994	30	4	P, I	Yes	47	54·1	No	F	Yes	Yes
Kojima (1998)[40]	Japan	1994	380	40	P, I	Yes	40	54·8	No	G	Yes	Yes
Raaymakers (1998)[41]	Netherlands	1995	116	7	P, I	No	No	No	No	G	No	No
Ronkainen C (1998)[42]	Finland	1989	147	6	P, I	Yes	43	49·5	Yes	E, G	No	Yes
Ronkainen D (1998)[42]	Finland	1995	612	29	R, A	Yes	80	58·7	Yes	E, G	No	Yes
Brown A (1999)[43]	USA	1997	62	6	P, I	No	No	No	No	G	Yes	No
Brown B (1999)[43]	USA	1997	17	0	P, I	No	No	No	No	G	Yes	No
Cloft (1999)[44]	USA	1987	31	1	R, I	No	No	No	No	J	No	No
Conway (1999)[45]	USA	1965	25	1	R, A	Yes	68	39·0	No	J	Yes	Yes
Iwamoto (1999)[46]	Japan	1976	1192	27	R, A	Yes	55	No	Yes	J	No	No
MARS (1999)[47]	Netherlands	1996	626	25	P, I	Yes	48	No	No	G	Yes	No

(Continues on next page)

	Country	Mid-year of study	Number of people included	Number of patients with aneurysm	Design or method*	Reported on:						
						Sex	% men	Mean age (years)	Age categories	Reason for investigation†	Aneurysm site	Aneurysm size
(continued from previous page)												
Nakagawa A (1999)[48]	Japan	1994	244	34	R, I	Yes	65	50·9	No	G	Yes	Yes
Nakagawa B (1999)[48]	Japan	1994	99	12	R, I	No	56	No	No	G	Yes	Yes
Nagakawa C (1999)[48]	Japan	1994	481	33	R, I	No	No	No	No	J	No	No
Kappelle (2000)[49]	USA	1989	2885	90	R, I	Yes	70	No	No	H	Yes	Yes
Nakajima (2000)[50]	Japan	1995	15	3	R, I	Yes	27	57·9	Yes	F	Yes	Yes
Suyama (2000)[51]	Japan	1997	112	0	P, I	No	No	No	No	G	No	No
Yeung (2000)[52]	USA	1996	200	2	R, I	No	No	No	No	H	No	No
Conway (2001)[53]	USA	1948	25	0	R, A	No	60	30	No	J	No	No
Graf A (2002)[54]	Germany	..	32	3	P, I	No	47	46·8	No	F	No	No
Graf B (2002)[54]	Germany	..	11	3	P, I	No	55	42·5	No	F	No	No
Pittella (2002)[55]	Brazil	1988	237	2	R, A	No	62	No	No	J	No	No
Wang (2002)[56]	USA	..	96	4	P, I	Yes	36	39·0	No	G	Yes	No
Connolly (2003)[57]	USA	..	99	9	R, I	Yes	70	41·6	No	J	Yes	Yes
Nakatani A (2003)[58]	Japan	..	123	3	P, I	Yes	65	55·6	No	E	Yes	Yes
Nakatani B (2003)[58]	Japan	..	52	0	P, I	No	56	51·7	No	E	Yes	Yes
Weber (2004)[59]	Germany	2001	1813	0	P, I	Yes	98	20·5	No	E	No	No
Alphs (2005)[60]	USA	2002	589	5	P, I	Yes	100	60·1	No	J	No	No
Soljanlahti A (2005)[61]	Finland	..	39	1	P, I	No	No	30·0	No	E	No	No
Soljanlahti B (2005)[61]	Finland	..	25	0	P, I	No	No	30·6	No	E	No	No
Triantafyllidi (2005)[62]	Greece	..	10	1	P, I	No	No	51·0	No	H	Yes	No
Ballotta (2006)[63]	Italy	1995	474	11	P, I	No	No	No	No	H	Yes	Yes
Bourekas (2006)[64]	USA	..	78	8	R, I	Yes	51	47·8	No	I	No	Yes
Kumra (2006)[65]	USA	..	60	0	R, I	No	No	No	No	E	No	No
Uehara (2006)[66]	Japan	1994	84	6	R, I	Yes	69	61·1	No	H	No	No
Weber (2006)[67]	Germany	2002	2536	0	R, I	Yes	100	20·5	No	E	No	No
Vernooij (2007)[68]	Netherlands	2006	2000	35	P, I	Yes	48	63·3	No	E	No	Yes
Brown (2008)[69]	USA	..	303	58	P, I	Yes	40	51·0	No	G	Yes	No
Kumar (2008)[70]	Australia	..	478	1	P, I	No	53	No	No	E	No	No
Mostafazadeh (2008)[71]	Iran	2006	425	14	P, A	Yes	65	No	No	E	Yes	Yes
Oh (2008)[72]	South Korea	2007	258	17	P, I	Yes	62	66·1	No	H	Yes	Yes
Heman (2009)[73]	Netherlands	2005	194	8	R, I	Yes	68	70·0	No	H	Yes	Yes
Ishikawa A (2010)[74]	Japan	2007	7345	146	R, I	Yes	67	69·9	No	E	No	No
Ishikawa B (2010)[74]	Japan	2007	374	13	R, I	Yes	62	76·9	No	H	No	No
Kuzmik (2010)[75]	USA	2003	160	10	R, I	No	No	No	No	H	No	No
Xu (2011)[76]	China	2008	355	43	P, I	No	52	46·5	No	F	No	No

If several study populations are described in a paper, each study population has a different letter. Studies are listed according to publication date. Sex=sex-specific subgroup data available; studies reporting on number of included men and women, and on number of men and women with aneurysms. % men=studies reporting on proportion of men and women in the study population. Age=studies reporting on number of patients, and number of patients with aneurysms for different age categories. Mean age=mean age of the study population. *Design or method: R=retrospective, P=prospective, I=imaging, A=autopsy. †Reason for investigation: E=screening, F=autosomal dominant polycystic kidney disease, G=family, H=atherosclerosis, I=brain tumour, J=other.

***Table 1*: Overview of the 83 included study populations from 68 studies**

angiography with IA-DSA, and two-vessel IA-DSA with three or more vessel IA-DSA. If a method was inferior to the others we would exclude studies with this method from further analyses. Then we compared autopsy studies with imaging studies.

Before assessing the effect of the different types of comorbidity, we tested an assumption made in our previous systematic review, that patients with a brain tumour have no increased prevalence of UIAs and can therefore be included in the reference group. Thus, we compared studies of people who had no comorbidity with studies of patients who had a brain tumour (other than a pituitary adenoma) before doing further analyses. If a brain tumour was associated with an increased prevalence of UIAs we would assess this factor separately; if not, then we would include this group in the reference group. We

calculated PRs for presence of different comorbidities. We also calculated the prevalence for an average study population that was without comorbidity, consisted of 50% men, and had a mean age of 50 years. We calculated this prevalence as EXP (α+50β1+50β2), where α, β1, and β2 were the regression coefficients of the random-effects model for, respectively, the intercept, age, and sex.

For studies of people with a positive family history of subarachnoid haemorrhage or UIA, we did a subgroup analysis that compared studies of people who had two or more affected first-degree relatives with studies of patients who had only one affected first-degree relative. For ADPKD, we compared patients with APDKD who had a family history of subarachnoid haemorrhage or UIA with those who had no such family history.

We assessed sex differences in three ways. First, we calculated the PR for women with men as the reference. Second, we studied the influence of the percentage of men in a study population on the prevalence, because not all studies specified how many aneurysms were identified for each sex. The relation was expressed as the percentage change in the prevalence per increase in percentage of men. Third, we did a subgroup analysis to assesses the PR of women compared with men in study populations with a mean age of 50 years or younger and older than 50 years. We did this because a previous study showed that the incidence of subarachnoid haemorrhage was substantially higher in men than in women before the age of 50 years, but after 50 years the incidence was substantially higher in women.[4]

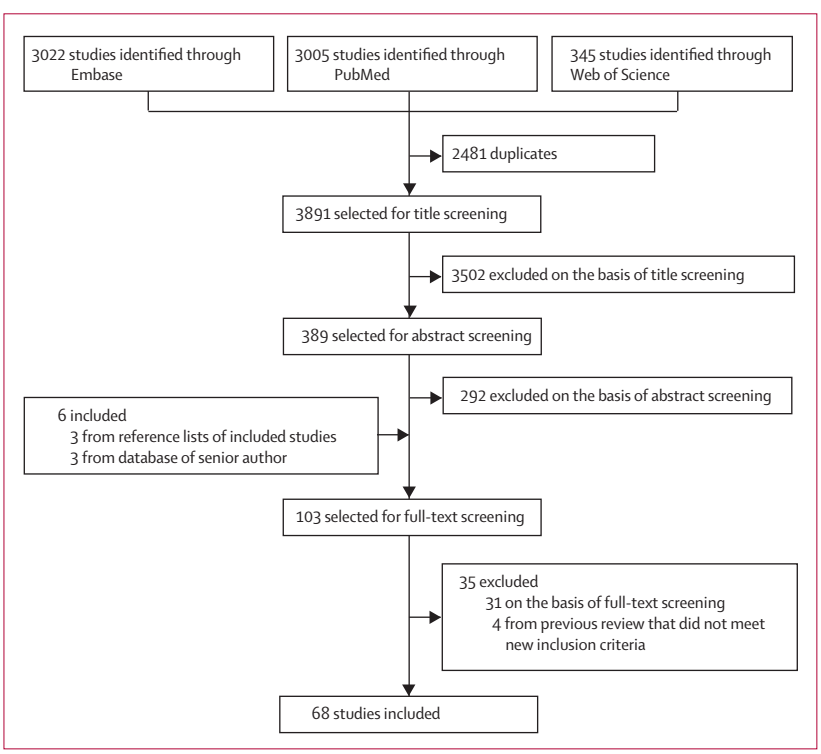

Figure 1: **Selection of included studies**

We assessed age differences in two ways. First, we compared groups of different decade bands with people older than 80 years as a reference. Second, we compared groups of different ages with the mean age of each study population and calculated PRs dichotomising at 30 years, 40 years, and 50 years.

For our analysis by country, there had to be at least two studies from a country for it to be assessed separately. Most studies came from the USA and therefore we used this country as reference. We assessed time trend with the mid-year of each study as an independent variable and expressed it as the percentage change of the crude prevalence rate per calendar year increase.

Role of the funding source

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

Results

68 studies met our predefined inclusion criteria (table 1 and figure 1),[9–76] 19 studies from our previous review[5] and 49 new studies. We included four case-control studies (of which one was an autopsy study),[26,58,61,74] 63 cross-sectional studies (16 autopsy studies),[9–25,27–41,43–57,59,60,62–73,75,76] and one combined cross-sectional and autopsy study.[42] Because our present inclusion criteria were stricter than in the 1998 version of our review, four studies included in our previous review did not fulfil our new inclusion criteria.[77–80] The 68 studies included 83 study populations, 94912 patients, and 1450 UIAs. The mean overall prevalence of UIAs of all included studies was 2·8% (95% CI 2·0–3·9). The prevalence varied from 0% to 41·8% between studies (figure 2).

With IA-DSA as the reference group,[13,19,20,22,24,25,29,32,34,38,44,49,52,64] we did not identify a significant difference in prevalence in studies with magnetic resonance angiography as the initial imaging method (PR 1·3, 95% CI 0·6–2·5),[15,28,31,36,39–43,47,48,50,51,54,56–58,61,62,66,69,70,74,76] but prevalence was lower in studies with MRI as the initial imaging method (0·04, 0·01–0·13).[37,59,60,65,67,68] The prevalence in studies with MRI as the initial method remained significantly lower after adjustment for sex and age (0·10, 0·01–0·35). The prevalence was also significantly lower in studies with MRI as the initial imaging method[37,60,68] if studies with magnetic resonance angiography as the initial imaging method were taken as the reference (0·03, 0·01–0·10).[15,28,40,41,47,48,50,51,54,56–58,61,62,66,69,70,74,76] No studies were done with CT angiography alone. The prevalences were not significantly lower in IA-DSA studies with both carotid arteries studied (0·9, 0·5–1·7)[13,19,32,49] compared with three-vessel or four-vessel IA-DSA studies.[24,25,29,44,64] We excluded studies primarily done with MRI from all further analyses because they had a significantly lower prevalence; the overall prevalence was then 3·5% (95% CI 2·7–4·7) instead of 2·8%.

The prevalence of UIAs was higher in imaging studies than in autopsy studies (PR 3·5, 95% CI 2·1–6·1; 62 studies including 77 study populations).[9–36,38–58,61–64,66,69,70–75] After adjustment for sex, age, and comorbidity, this difference disappeared (1·1, 0·3–3·6; 29 studies including 35 study populations).[19,20,22,25,30–33,35,36,39,40,42,45,48,50,53,54,56–58,62,64,66,69,72–74,76]

We did not identify a statistically significant difference in prevalence for patients with a brain tumour compared with people without comorbidity when adjusted for age and sex (PR 3·6, 95% CI 0·4–30).[19,22,25,42,58,64,74] Therefore, we included studies on patients with brain tumours in the reference group of studies on people without comorbidity. For the studies with data on sex and age, the crude prevalence of UIAs in the reference group was 2·9% (95% CI 1·9–4·5; 26 studies including 31 study populations). We estimated that the prevalence would be 3·2% (1·9–5·2) for a study population that consisted of 50% men and had a mean age of 50 years. Compared with patients who did not have the relevant comorbidity or risk factor, sex-adjusted and age-adjusted PRs were significantly higher for patients with ADPKD[20,39,50,54] or a family history of subarachnoid haemorrhage or UIA,[30,31,36,40,42,48,56,69] but not for patients with atherosclerosis[25,32,33,62,66,72,73] or a pituitary adenoma (table 2).[19,35]

The PR for patients with ADPKD and a family history of subarachnoid haemorrhage or UIA was 2·0 (95% CI 0·5–7·4) compared with patients with ADPKD but no family history of subarachnoid haemorrhage or UIA.[20,26–28,36,39,50,54,76] The PR was 2·2 (1·5–3·3) for patients who had a positive family history of subarachnoid haemorrhage or UIA with at least two affected first-degree relatives compared with those with only one affected first-degree relative.[30,31,36,41,47,48]

29 studies, including 34 study populations, reported on prevalences in men and women separately.[13,19,20,22,24,25,30,33,35,38–40,42,45–50,56–58,64,66,69,71–74] We identified a higher prevalence of UIAs in women (6·0%, 95% CI 4·5–8·0) than men (PR 1·57, 95% CI 1·04–2·37), which remained significant after adjustment for age and comorbidity (1·61, 1·02–2·54; 22 studies including 26 study populations).[19,20,22,25,30,33,35,39,40,42,45,48,50,56–58,64,66,69,72–74]

We also assessed the relation between the proportion of men in a study population and prevalence of UIAs (38 studies including 44 study populations) and identified a 2·1% relative decrease (95% CI 0·3–3·9) for each percentage point increase in percentage of men,[13,19,20,22,24,25,30–33,35,36,38,39,40,42,45–50,53–58,62,64,66,69,70–74,76] which remained statistically significant after adjustment for age (2·7% decrease, 95% CI 0·7–4·7; 29 studies including 35 study populations).[19,20,22,25,30–33,35,36,39,40,42,45,48,50,53,54,56–58,62,64,66,69,72–74,76] The PR for women compared with men was 1·1 (95% CI 0·6–1·8) for study populations with a mean age of 50 years or younger (10 studies including 12 study populations),[19,20,25,30,35,42,45,56,57,64] but 2·2 (1·3–3·6) for study populations with a mean age greater than 50 years (13 studies including 15 study populations).[22,33,39,40,42,48,50,58,66,69,72–74]

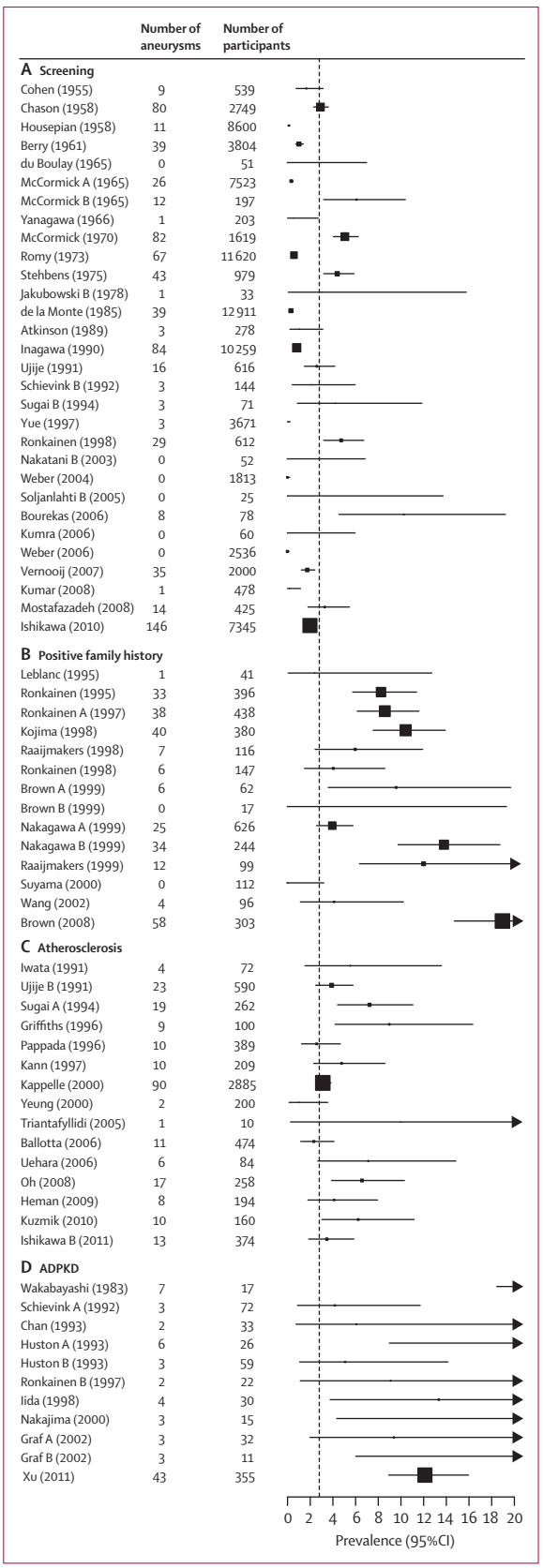

Figure 2: **Prevalences of unruptured intracranial aneurysms**
Prevalences of unruptured intracranial aneurysms in study populations without comorbidity (A), with a positive family history (B), with atherosclerosis (C), and with polycystic kidney disease (D). If several study populations are described in a paper, each study population has a different letter, as also indicated in table 1. The dotted line is the overall prevalence of the 83 study populations. 13 study populations that did not fall into one of the four categories are not depicted. Sizes of the point estimates are proportional to the weight of the studies. ADPKD=autosomal dominant polycystic kidney disease.

	Crude (57 studies, 69 study populations, 1353 UIA)	Age adjusted (28 studies, 33 study populations, 601 UIA)		Sex adjusted (34 studies, 39 study populations, 648 UIA)		Age and sex adjusted (26 studies, 31 study populations, 600 UIA)	
	PR	PR	Adjusted PR	PR	Adjusted PR	PR	Adjusted PR
ADPKD	8·8 (4·3–18·0)	8·1 (4·0–16·0)	8·3 (4·2–16·0)	9·4 (4·7–19·0)	8·9 (4·1–19·0)	6·2 (2·9–13·0)	6·9 (3·5–14·0)
Atherosclerosis	3·1 (1·7–5·5)	1·9 (1·1–3·6)	1·5 (0·7–3·1)	2·2 (1·2–3·7)	2·2 (1·3–3·8)	1·5 (0·7–3·0)	1·7 (0·9–3·0)
Family history*	4·8 (2·6–8·8)	3·9 (2·3–6·8)	4·0 (2·3–6·9)	4·0 (2·3–6·8)	3·7 (1·8–7·5)	2·9 (1·4–6·1)	3·4 (1·9–5·9)
Pituitary adenoma	4·1 (1·1–15·0)	2·7 (1·1–6·6)	2·6 (1·1–6·0)	2·7 (1·1–6·6)	2·6 (1·0–6·7)	1·9 (0·8–4·7)	2·0 (0·9–4·6)

Data are prevalence ratio (PR) or adjusted PR with 95% CI. The prevalence from studies of people without comorbidity or of patients with a brain tumour was used as the reference (brain tumour includes brain metastases). The calculated prevalence in a study population of people without comorbidity consisting of 50% men and with a mean age of 50 years is 3·2%, based on the model with 31 study populations. UIA=unruptured intracranial aneurysm. ADPKD=autosomal dominant polycystic kidney disease. *One or more affected relatives.

***Table 2*: Prevalence ratios per reason for investigation, adjusted for sex and age**

	Crude (55 studies, 70 study populations, 1306 UIA)	Age adjusted (28 studies, 35 study populations, 596 UIA)		Sex adjusted (33 studies, 39 study populations, 747 UIA)		Age and sex adjusted (26 studies, 32 study populations, 594 UIA)	
	PR	PR	Adjusted PR	PR	Adjusted PR	PR	Adjusted PR
Finland	1·8 (0·7–5·0)	0·9 (0·4–2·4)	0·8 (0·3–2·3)	1·2 (0·4–3·0)	0·8 (0·6–2·9)	1·1 (0·5–3·0)	1·0 (0·4–2·4)
Germany	6·4 (1·1–38·0)	3·0 (0·3–15·0)	3·0 (0·6–15·0)	3·1 (0·7–13·0)	3·1 (0·8–12·0)	2·9 (0·3–13·0)	2·5 (0·7–9·4)
Italy	0·9 (0·2–4·3)	0·4 (0·3–2·7)	0·3 (0·0–2·0)	0·5 (0·1–2·3)	0·9 (0·2–3·6)	0·4 (0·4–2·3)	0·6 (0·1–2·9)
Netherlands	1·7 (0·4–6·4)	0·7 (0·6–4·4)	0·4 (0·0–3·3)	0·7 (0·2–2·4)	0·9 (0·3–2·5)	0·7 (0·6–3·8)	0·7 (0·1–3·7)
UK	1·5 (0·4–5·4)	1·1 (0·1–3·9)	0·9 (0·3–3·5)	0·9 (0·3–2·4)	0·9 (0·4–2·3)	1·1 (0·1–3·6)	0·9 (0·3–2·5)
Japan	1·8 (1·0–3·6)	1·0 (0·4–2·2)	0·8 (0·3–2·0)	1·0 (0·5–2·0)	1·0 (0·6–1·9)	1·0 (0·5–2·3)	0·8 (0·4–1·7)
China	1·9 (0·3–12·0)	2·3 (1·0–13·0)	2·3 (0·4–13·0)	2·5 (0·5–11·0)	2·6 (0·7–9·5)	2·3 (1·0–11·0)	2·1 (0·6–7·5)

Data are prevalence ratio (PR) or adjusted PR with 95% CI. The prevalence in the USA was used as the reference. UIA=unruptured intracranial aneurysm.

***Table 3*: Prevalence ratios per country adjusted for sex and age**

Eight studies, including nine study populations, provided data on prevalence of UIAs in one or more decade age-groups.[10,15,16,22,23,42,46,50] We adjusted for sex and comorbidity in these eight studies. Compared with patients aged 80 years or older (prevalence 3·0%, 95% CI 1·1–8·1),[10,16,23,46,50] prevalence was lower in patients younger than 30 years (PR 0·01, 95% CI 0·00–0·12),[10,16,22,23,46] but not in patients aged 30–39 years (0·4, CI 0·1–1·6),[10,16,23,42,46,50] 40–49 years (0·4, 0·1–1·3),[10,15,16,23,42,46,50] 50–59 years (0·4, 0·1–1·3),[10,16,23,42,46,50] 60–69 years (1·0, 0·3–3·3),[10,16,23,42,46,50] and 70–79 years (0·6, 0·2–2·1).[10,16,23,46,50]

31 studies, describing 38 study populations, provided information on mean age of the individuals involved. Prevalences were not significantly different between patients with a mean age of less than 40 years (prevalence 2·1%, 95% CI 0·6–7·0) compared with those aged 40 years or older (PR 3·0, 95% CI 0·9–10·2). After adjustment for sex and comorbidity (35 studies including 29 study populations), we identified a PR of 2·8 (95% CI 0·1–10·0) for patients aged 40 years or older compared with patients younger than 40 years and a PR of 1·0 (0·6–1·7) for patients aged 50 years or older compared with patients younger than 50 years.[19,20,22,25,30–33,35,36,39,40,42,45,48,50,53,54,56–58,62,64,66,69,72–74,76] There were no studies left after adjustment for sex and comorbidity with a mean age of less than 30 years, so we could not a make a comparison with 30 years or older.

Table 3 lists PR for all countries compared with the USA, adjusted for sex and age. With the USA as a reference,[22,45,53,56,57,64,69] we identified similar prevalences in Japan,[20,25,35,39,40,48,50,58,66,74] China,[76] and several European countries including Finland,[31,36,42] Germany,[54] Italy,[33] the Netherlands,[73] and the UK.[19,32]

46 studies, including 56 different study populations, provided information on mean year of data acquisition (range 1931–2008).[9,11–13,17–29,31,32,35,38–53,55,57,63,66,71–76] Our regression analysis identified a 3·4% (95% CI 1·8–5·0) annual increase in prevalence. However, when we adjusted for sex, age, and comorbidity, the increase in UIAs over time was no longer significant (1·0%, –2·3 to 4·3; 20 studies including 24 study populations, range 1948–2008).[19,20,22,25,31,32,35,39,40,42,45,48,50,53,57,66,72–74,76]

We collected data on intracranial aneurysm size from three autopsy studies[23,42,45] and 20 imaging studies.[19,20,22,24,31–36,39,48–50,56–58,63,72,73] 368 intracranial aneurysms were assessed for size (table 4). Most aneurysms (241; 66%) were smaller than 5 mm. After correction for age, the number of aneurysms larger than 5 mm decreased by 4·9% (95% CI –8·3 to –1·5; 13 studies including 14 study populations) with each percentage point increase in percentage of men. This pattern remained significant after adjustment for comorbidity (5·7% decrease, –9·3 to –2·1). We did not identify a significant change in the prevalence of aneurysms larger than 10 mm (1·2% decrease, –6·9 to 10, with each percentage

point increase in percentage of men). Compared with all other countries, the proportion of aneurysms of 5 mm or larger was not higher in Japan (PR 1·9, 95% CI 0·6–6·4) or Finland (0·5, 0·1–2·0).

We extracted data on site of UIAs from three autopsy studies[23,45,71] and 26 imaging studies.[19,20,22,24,31–36,39,40,43,46–50,56–58,62,63,69,72–74] 864 intracranial aneurysms were assessed for site (table 4). The most common sites were the internal carotid artery (including posterior communicating artery) and the medial cerebral artery. In imaging studies, the internal carotid artery was the largest category, but in autopsy studies the medial cerebral artery was the most common site. The prevalence of aneurysms in the posterior circulation did not depend on the proportion of men (1·6% decrease with each percentage point increase in percentage of men; 95% CI –6·9 to 3·9). Compared with all other countries, the proportion of posterior circulation aneurysms was not higher in Japan (PR 1·2, 95% CI 0·4–3·5) and Finland (2·0, 0·4–8·8).

	Total number of aneurysms (%)
Size of intracranial aneurysm	368 (100%)
<5 mm	241 (66%)
5–9 mm	101 (27%)
≥10 mm	26 (7%)
Site of intracranial aneurysm	864 (100%)
Anterior cerebral artery and branches	154 (18%)
Medial cerebral artery	303 (35%)
Internal carotid artery including posterior communicating artery	360 (42%)
Posterior communicating artery alone	85 (10%)
Vertebrobasilar arteries	47 (5%)

Table 4: **Proportions of aneurysms by size and site**

Discussion

In our analysis, the prevalence of UIAs was influenced by the presence of polycystic disease, a positive family history, age, and sex, but not by region. The prevalence was significantly higher in patients aged 30 years or older compared with those who were younger than 30 years. Women had a higher prevalence of UIAs than men, mainly attributable to an excess in women older than 50 years. Patients with ADPKD and patients with a positive family history of intracranial aneurysm or subarachnoid haemorrhage both had a higher prevalence. We did not identify a higher prevalence in Finland and Japan. We identified a non-significant increase in the prevalence of UIAs per study year.

We calculated that in a population of people without comorbidity, consisting of 50% men and with a mean age of 50 years, the prevalence of UIAs is 3·2%. This is higher than the overall prevalence for people without comorbidity of 2·3% we identified in our previous review.[5] This difference can be explained by our correction for age and sex, inclusion of more recent studies with higher quality imaging techniques, and inclusion of fewer retrospective autopsy studies (which uncorrected for age and sex have a lower prevalence[5]). By contrast with our previous analysis, we did not identify a statistically significant increased prevalence in patients with atherosclerosis or a pituitary adenoma. Our present findings are probably more accurate, because we included three times as many studies as before and, more importantly, we were able to adjust PRs for sex and age.

Smoking and hypertension are major risk factors for subarachnoid haemorrhage, and patients who have survived a subarachnoid haemorrhage are at increased risk of cardiovascular diseases.[81] We identified a higher prevalence in study populations with atherosclerosis, but this increase in prevalence was not significant. Owing to a lack of data we could not separately assess the prevalence of UIAs in smokers and patients with hypertension. Patients who smoke and have high blood pressure were probably included in the reference group, which might explain the absence of a clear association between atherosclerosis and prevalence of aneurysms. This also means that the prevalence for people who do not smoke, do not have a high blood pressure, and do not have other risk factors might be lower than 3·2%. The absence of data on smoking and hypertension is a limitation of our present analyses.

A previous review[4] showed an overall higher incidence of subarachnoid haemorrhage in women than men, mainly caused by a higher incidence in women older than 55 years. Our data suggest that the number of aneurysms larger than 5 mm is higher in study populations with more women, which might partly explain the higher incidence of subarachnoid haemorrhage in women, because larger aneurysms have a higher risk of rupture.[82] We think that the higher incidence in older women might in part also be explained by the age-dependent prevalence of UIAs in women, since we identified a higher prevalence in women compared with men in study populations older than 50 years, but not 50 years or younger, although the women-to-men PRs did not differ significantly between the two age-groups. Together with the increased risk of rupture of aneurysms in older patients,[82] a higher prevalence might explain why the difference in incidence of subarachnoid haemorrhage between men and women increases with age. Other investigators[83] have postulated that decreases in oestrogen concentrations and oestrogen-receptor density contribute to an increased risk of intracranial aneurysm pathogenesis and an increased risk of aneurysm rupture in women during and after menopause. This hypothesis is supported by the fact that hormone-replacement therapy has been shown to be a protective factor for subarachnoid haemorrhage.[84] Whether the risk of rupture is also higher in postmenopausal women still needs to be assessed.

We did not identify higher prevalences of UIAs in Finland and Japan. However, the incidence of

subarachnoid haemorrhage is higher in these countries, suggesting a higher risk of rupture.[82] Investigators have also shown that UIAs larger than 5 mm or posterior circulation aneurysms have a higher risk of rupture.[82] We did not identify a higher proportion of aneurysms larger than 5 mm or posterior circulation aneurysms in Finnish and Japanese study populations compared with other study populations. Thus, the higher risk of rupture cannot be explained simply by higher proportions of larger or posterior circulation aneurysms in Finland and Japan. The reasons for higher risk of aneurysm rupture in these countries remain unknown.

The incidence of subarachnoid haemorrhage has declined slightly between 1950 and 2005.[4] In our analysis we did not identify a decrease in the prevalence of UIAs. Therefore, the decrease in incidence is probably the result of an overall decreased risk of aneurysm rupture, related to factors such as changes in smoking habits or an increased use of preventive treatment.

The large number of studies, the large number of included patients, the use of strict inclusion criteria, and the adjustment for sex, age, and reason for investigation all add to the reliability of our data. Accurate estimates are of great importance, because they are used in cost-effectiveness analyses to develop screening strategies. Our subgroup analysis by age, sex, family history and comorbidity, country, and time period were based on smaller numbers of studies and should be interpreted with caution, especially in those subgroups where point estimates had wide CIs. Nevertheless, most of our confidence limits were narrow, even after adjustment for sex, age, and comorbidity. A limitation of our study is that the prevalence might be influenced by our search strategy; theoretically, negative studies on incidental findings might be less likely to use "aneurysm" as a keyword than studies on intracranial aneurysms. This might have caused an under-representation of studies that did not show a relation between a presumed risk factor and prevalence of UIAs.

Our finding that older women might have a higher prevalence is possibly an important clue for how aneurysms are formed and future well designed studies should focus on the role of oestrogen in the pathogenesis of UIAs. Our findings also show that the prevalence of UIAs in Japan and Finland is not higher; nor do they have a higher prevalence of aneurysms larger than 5 mm or posterior circulation aneurysm to explain the higher incidence of subarachnoid haemorrhage. Research on subarachnoid haemorrhage in Finnish and Japanese populations should therefore be aimed at finding risk factors for rupture of intracranial aneurysms.

Contributors

MHMV, AA, and GJER were responsible for study design, data analysis, and data interpretation. MHMV and RB collected data. MHMV drafted the report, tables, and figures. All authors critically revised the manuscript.

Conflicts of interest

We declare that we have no conflicts of interest.

References

1 Nieuwkamp DJ, Setz LE, Algra A, Linn FH, de Rooij NK, Rinkel GJ. Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis. *Lancet Neurol* 2009; **8:** 635–42.

2 Johnston SC, Selvin S, Gress DR. The burden, trends, and demographics of mortality from subarachnoid hemorrhage. *Neurology* 1998; **50:** 1413–18.

3 Rivero-Arias O, Gray A, Wolstenholme J. Burden of disease and costs of aneurysmal subarachnoid haemorrhage (aSAH) in the United Kingdom. *Cost Eff Resour Alloc* 2010; **8:** 6.

4 de Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. *J Neurol Neurosurg Psychiatry* 2007; **78:** 1365–72.

5 Rinkel GJ, Djibuti M, Algra A, van Gijn J. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. *Stroke* 1998; **29:** 251–56.

6 Gabriel RA, Kim H, Sidney S, et al. Ten-year detection rate of brain arteriovenous malformations in a large, multiethnic, defined population. *Stroke* 2010; **41:** 21–26.

7 Moher D, Fortin P, Jadad AR, et al. Completeness of reporting of trials published in languages other than English: implications for conduct and reporting of systematic reviews. *Lancet* 1996; **347:** 363–66.

8 Hamza TH, van Houwelingen HC, Stijnen T. The binomial distribution of meta-analysis was preferred to model within-study variability. *J Clin Epidemiol* 2008; **61:** 41–51.

9 Cohen MM. Cerebrovascular accidents; a study of two hundred one cases. *AMA Arch Pathol* 1955; **60:** 296–307.

10 Chason JL, Hindeman WM. Berry aneurysms of the circle of Willis; results of a planned autopsy study. *Neurology* 1958; **8:** 41–44.

11 Housepian EM, Pool JL. A systematic analysis of intracranial aneurysms from the autopsy file of the Presbyterian Hospital, 1914 to 1956. *J Neuropathol Exp Neurol* 1958; **17:** 409–23.

12 Berry RG, Alpers BJ, White JC. The site, structure and frequency of intracranial aneurysms, angiomas and arteriovenous abnormalities. *Res Publ Assoc Res Nerv Ment Dis* 1966; **41:** 40–72.

13 Du Boulay GH. Some observations on the natural history of intracranial aneurysms. *Br J Radiol* 1965; **38:** 721–57.

14 McCormick WF, Nofzinger JD. Saccular intracranial aneurysms: an autopsy study. *J Neurosurg* 1965; **22:** 155–59.

15 Yanagawa Y, Hirata F, Gotoh M, Fujita K, Makiyama T, Ishikawa J. Experience of brain checkup by MRI. *Japan J Neurosurg* 1996; **5:** 336–40.

16 McCormick WF, Costa-Rua GJ. The size of intracranial saccular aneurysms. An autopsy study. *J Neurosurg* 1970; **33:** 422–27.

17 Romy M, Werner A, Wildi E. Occurrence of intracranial arterial aneurysms and their rupture, from a series of routine autopsies. *Neurochirurgie* 1973; **19:** 611–26.

18 Stehbens WE. Aneurysms and anatomical variation of cerebral arteries. *Arch Pathol* 1963; **75:** 45–64.

19 Jakubowski J, Kendall B. Coincidental aneurysms with tumours of pituitary origin. *J Neurol Neurosurg Psychiatry* 1978; **41:** 972–79.

20 Wakabayashi T, Fujita S, Ohbora Y, Suyama T, Tamaki N, Matsumoto S. Polycystic kidney disease and intracranial aneurysms. Early angiographic diagnosis and early operation for the unruptured aneurysm. *J Neurosurg* 1983; **58:** 488–91.

21 de la Monte SM, Moore GW, Monk MA, Hutchins GM. Risk factors for the development and rupture of intracranial berry aneurysms. *Am J Med* 1985; **78:** 957–64.

22 Atkinson JL, Sundt TM Jr, Houser OW, Whisnant JP. Angiographic frequency of anterior circulation intracranial aneurysms. *J Neurosurg* 1989; **70:** 551–55.

23 Inagawa T, Hirano A. Autopsy study of unruptured incidental intracranial aneurysms. *Surg Neurol* 1990; **34:** 361–65.

24 Iwata K, Misu N, Terada K, Kawai S, Momose M, Nakagawa H. Screening for unruptured asymptomatic intracranial aneurysms in patients undergoing coronary angiography. *J Neurosurg* 1991; **75:** 52–55.

25 Ujiie H, Sato K, Onda H, et al. Clinical analysis of incidentally discovered unruptured aneurysms. *Stroke* 1993; **24:** 1850–56.

26 Schievink WI, Torres VE, Piepgras DG, Wiebers DO. Saccular intracranial aneurysms in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 1992; **3:** 88–95.

27 Chan KW. Adult polycystic kidney disease in Hong Kong Chinese: an autopsy study. *Pathology* 1993; **25:** 229–32.

28 Huston J III, Torres VE, Sulivan PP, Offord KP, Wiebers DO. Value of magnetic resonance angiography for the detection of intracranial aneurysms in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 1993; **3:** 1871–77.

29 Sugai Y, Hamamoto Y, Ookubo T, So K. Angiographical frequency of unruptured incidental intracranial aneurysms. *No Shinkei Geka* 1994; **22:** 429–32 (in Japanese).

30 Leblanc R, Melanson D, Tampieri D, Guttmann RD. Familial cerebral aneurysms: a study of 13 families. *Neurosurgery* 1995; **37:** 633–38.

31 Ronkainen A, Puranen MI, Hernesniemi JA, et al. Intracranial aneurysms: MR angiographic screening in 400 asymptomatic individuals with increased familial risk. *Radiology* 1995; **195:** 35–40.

32 Griffiths PD, Worthy S, Gholkar A. Incidental intracranial vascular pathology in patients investigated for carotid stenosis. *Neuroradiology* 1996; **38:** 25–30.

33 Pappada G, Fiori L, Marina R, Vaiani S, Gaini SM. Management of symptomatic carotid stenoses with coincidental intracranial aneurysms. *Acta Neurochir (Wien)* 1996; **138:** 1386–90.

34 Kann BR, Matsumoto T, Kerstein MD. Safety of carotid endarterectomy associated with small intracranial aneurysms. *South Med J* 1997; **90:** 1213–16.

35 Pant B, Arita K, Kurisu K, Tominaga A, Eguchi K, Uozumi T. Incidence of intracranial aneurysm associated with pituitary adenoma. *Neurosurg Rev* 1997; **20:** 13–17.

36 Ronkainen A, Hernesniemi J, Puranen M, et al. Familial intracranial aneurysms. *Lancet* 1997; **349:** 380–84.

37 Yue NC, Longstreth WT Jr, Elster AD, Jungreis CA, O'Leary DH, Poirier VC. Clinically serious abnormalities found incidentally at MR imaging of the brain: data from the Cardiovascular Health Study. *Radiology* 1997; **202:** 41–46.

38 Cloft HJ, Kallmes DF, Kallmes MH, Goldstein JH, Jensen ME, Dion JE. Prevalence of cerebral aneurysms in patients with fibromuscular dysplasia: a reassessment. *J Neurosurg* 1998; **88:** 436–40.

39 Iida H, Naito T, Hondo H, Demachi H, Aoki S. Intracranial aneurysms in autosomal dominant polycystic kidney disease detected by MR angiography: screening and treatment. *Nippon Jinzo Gakkai Shi* 1998; **40:** 42–47.

40 Kojima M, Nagasawa S, Lee YE, Takeichi Y, Tsuda E, Mabuchi N. Asymptomatic familial cerebral aneurysms. *Neurosurgery* 1998; **43:** 776–81.

41 Raaymakers TW, Rinkel GJ, Ramos LM. Initial and follow-up screening for aneurysms in families with familial subarachnoid hemorrhage. *Neurology* 1998; **51:** 1125–30.

42 Ronkainen A, Miettinen H, Karkola K, et al. Risk of harboring an unruptured intracranial aneurysm. *Stroke* 1998; **29:** 359–62.

43 Brown BM, Soldevilla F. MR angiography and surgery for unruptured familial intracranial aneurysms in persons with a family history of cerebral aneurysms. *AJR Am J Roentgenol* 1999; **173:** 133–38.

44 Cloft HJ, Razack N, Kallmes DF. Prevalence of cerebral aneurysms in patients with persistent primitive trigeminal artery. *J Neurosurg* 1999; **90:** 865–67.

45 Conway JE, Hutchins GM, Tamargo RJ. Marfan syndrome is not associated with intracranial aneurysms. *Stroke* 1999; **30:** 1632–36.

46 Iwamoto H, Kiyohara Y, Fujishima M, et al. Prevalence of intracranial saccular aneurysms in a Japanese community based on a consecutive autopsy series during a 30-year observation period. The Hisayama study. *Stroke* 1999; **30:** 1390–95.

47 The Magnetic Resonance Angiography in Relatives of Patients with Subarachnoid Hemorrhage Study Group. Risks and benefits of screening for intracranial aneurysms in first-degree relatives of patients with sporadic subarachnoid hemorrhage. *N Engl J Med* 1999; **341:** 1344–50.

48 Nakagawa T, Hashi K, Kurokawa Y, Yamamura A. Family history of subarachnoid hemorrhage and the incidence of asymptomatic, unruptured cerebral aneurysms. *J Neurosurg* 1999; **91:** 391–95.

49 Kappelle LJ, Eliasziw M, Fox AJ, Barnett HJ. Small, unruptured intracranial aneurysms and management of symptomatic carotid artery stenosis. *Neurology* 2000; **55:** 307–09.

50 Nakajima F, Shibahara N, Arai M, Gohji K, Ueda H, Katsuoka Y. Intracranial aneurysms and autosomal dominant polycystic kidney disease: followup study by magnetic resonance angiography. *J Urol* 2000; **164:** 311–13.

51 Suyama K, Minagawa T, Onizuka M, Mizota S, Miyazaki H. Brain check-up and treatment for asymptomatic unruptured cerebral aneurysms. *J Stroke Cerebrovasc Dis* 2000; **9** (suppl 2): 281–82.

52 Yeung BK, Danielpour M, Matsumura JS, Ailawadi G, Batjer H, Yao JS. Incidental asymptomatic cerebral aneurysms in patients with extracranial cerebrovascular disease: is this a case against carotid endarterectomy without arteriography? *Cardiovasc Surg* 2000; **8:** 513–18.

53 Conway JE, Hutchins GM, Tamargo RJ. Lack of evidence for an association between neurofibromatosis type I and intracranial aneurysms: autopsy study and review of the literature. *Stroke* 2001; **32:** 2481–85.

54 Graf S, Schischma A, Eberhardt KE, Istel R, Stiasny B, Schulze BD. Intracranial aneurysms and dolichoectasia in autosomal dominant polycystic kidney disease. *Nephrol Dial Transplant* 2002; **17:** 819–23.

55 Pittella JE, Duarte JE. Prevalence and pattern of distribution of cerebrovascular diseases in 242 hospitalized elderly patients, in a general hospital, autopsied in Belo Horizonte, Minas Gerais, Brazil, from 1976 to 1997. *Arq Neuropsiquiatr* 2002; **60:** 47–55.

56 Wang MC, Rubinstein D, Kindt GW, Breeze RE. Prevalence of intracranial aneurysms in first-degree relatives of patients with aneurysms. *Neurosurg Focus* 2002; **13:** e2.

57 Connolly HM, Huston J III, Brown RD Jr, Warnes CA, Ammash NM, Tajik AJ. Intracranial aneurysms in patients with coarctation of the aorta: a prospective magnetic resonance angiographic study of 100 patients. *Mayo Clin Proc* 2003; **78:** 1491–99.

58 Nakatani T, Naganuma T, Uchida J, et al. Unruptured intracranial aneurysms in haemodialysis patients. *Nephrology* 2003; **8:** 127–29.

59 Weber F, Knopf H. Cranial MRI screening in healthy young men. *Stroke* 2003; **34:** e99.

60 Alphs HH, Schwartz BS, Stewart WF, Yousem DM. Findings on brain MRI from research studies of occupational exposure to known neurotoxicants. *AJR Am J Roentgenol* 2006; **187:** 1043–47.

61 Soljanlahti S, Autti T, Lauerma K, et al. Familial hypercholesterolemia patients treated with statins at no increased risk for intracranial vascular lesions despite increased cholesterol burden and extracranial atherosclerosis. *Stroke* 2005; **36:** 1572–74.

62 Triantafyllidi H, Rizos I, Arvaniti C, Stefanadis C. Incidental aneurysms of aorta and basilar artery in patients with coronary artery ectasia. A magnetic resonance angiography study. *Acta Cardiol* 2005; **60:** 619–23.

63 Ballotta E, Da GG, Manara R, Baracchini C. Extracranial severe carotid stenosis and incidental intracranial aneurysms. *Ann Vasc Surg* 2006; **20:** 5–8.

64 Bourekas EC, Newton HB, Figg GM, Slone HW. Prevalence and rupture rate of cerebral aneurysms discovered during intra-arterial chemotherapy of brain tumors. *AJNR Am J Neuroradiol* 2006; **27:** 297–99.

65 Kumra S, Ashtari M, Anderson B, Cervellione KL, Kan L. Ethical and practical considerations in the management of incidental findings in pediatric MRI studies. *J Am Acad Child Adolesc Psychiatry* 2006; **45:** 1000–06.

66 Uehara T, Tabuchi M, Mori E. High frequency of unruptured intracranial aneurysms in female patients with ischaemic heart disease. *J Neurol Neurosurg Psychiatry* 1998; **64:** 536–38.

67 Weber F, Knopf H. Incidental findings in magnetic resonance imaging of the brains of healthy young men. *J Neurol Sci* 2006; **240:** 81–84.

68 Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. *N Engl J Med* 2007; **357:** 1821–28.

69 Brown RD Jr, Huston J, Hornung R, et al. Screening for brain aneurysm in the Familial Intracranial Aneurysm study: frequency and predictors of lesion detection. *J Neurosurg* 2008; **108:** 1132–38.

70 Kumar R, Sachdev PS, Price JL, Rosenman S, Christensen H. Incidental brain MRI abnormalities in 60- to 64-year-old community-dwelling individuals: data from the Personality and Total Health Through Life study. *Acta Neuropsychiatr* 2008; **20:** 87–90.

71 Mostafazadeh B, Farzaneh SE, Afsharian ST, Seraji FN, Salmasian H. The incidence of berry aneurysm in the Iranian population: an autopsy study. *Turk Neurosurg* 2008; **18:** 228–31.

72 Oh YS, Lee SJ, Shon YM, Yang DW, Kim BS, Cho AH. Incidental unruptured intracranial aneurysms in patients with acute ischemic stroke. *Cerebrovasc Dis* 2008; **26:** 650–53.

73 Heman LM, Jongen LM, van der Worp HB, Rinkel GJ, Hendrikse J. Incidental intracranial aneurysms in patients with internal carotid artery stenosis: a CT angiography study and a metaanalysis. *Stroke* 2009; **40:** 1341–46.

74 Ishikawa Y, Hirayama T, Nakamura Y, Ikeda K. Incidental cerebral aneurysms in acute stroke patients: comparison of asymptomatic healthy controls. *J Neurol Sci* 2010; **298:** 42–45.

75 Kuzmik GA, Feldman M, Tranquilli M, Rizzo JA, Johnson M, Elefteriades JA. Concurrent intracranial and thoracic aortic aneurysms. *Am J Cardiol* 2010; **105:** 417–20.

76 Xu HW, Yu SQ, Mei CL, Li MH. Screening for intracranial aneurysm in 355 patients with autosomal-dominant polycystic kidney disease. *Stroke* 2011; **42:** 204–06.

77 Wakai S, Fukushima T, Furihata T, Sano K. Association of cerebral aneurysm with pituitary adenoma. *Surg Neurol* 1979; **12:** 503–07.

78 Ruggieri PM, Poulos N, Masaryk TJ, et al. Occult intracranial aneurysms in polycystic kidney disease: screening with MR angiography. *Radiology* 1994; **191:** 33–39.

79 Chapman AB, Rubinstein D, Hughes R, et al. Intracranial aneurysms in autosomal dominant polycystic kidney disease. *N Engl J Med* 1992; **327:** 916–20.

80 Nagashima M, Nemoto M, Hadeishi H, Suzuki A, Yasui N. Unruptured aneurysms associated with ischaemic cerebrovascular diseases. Surgical indication. *Acta Neurochir (Wien)* 1993; **124:** 71–78.

81 Nieuwkamp DJ, Algra A, Blomqvist P, et al. Excess mortality and cardiovascular events in patients surviving subarachnoid hemorrhage: a nationwide study in Sweden. *Stroke* 2011; **42:** 902–07.

82 Wermer MJ, van der Schaaf I, Algra A, Rinkel GJ. Risk of rupture of unruptured intracranial aneurysms in relation to patient and aneurysm characteristics: an updated meta-analysis. *Stroke* 2007; **38:** 1404–10.

83 Harrod CG, Batjer HH, Bendok BR. Deficiencies in estrogen-mediated regulation of cerebrovascular homeostasis may contribute to an increased risk of cerebral aneurysm pathogenesis and rupture in menopausal and postmenopausal women. *Med Hypotheses* 2006; **66:** 736–56.

84 Feigin VL, Rinkel GJ, Lawes CM, et al. Risk factors for subarachnoid hemorrhage: an updated systematic review of epidemiological studies. *Stroke* 2005; **36:** 2773–80.