Acta Neurochirurgica
https://doi.org/10.1007/s00701-021-04919-8

REVIEW ARTICLE - BRAIN TUMORS

Prevalence of incidental meningiomas and gliomas on MRI: a meta-analysis and meta-regression analysis

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Received: 26 April 2021 / Accepted: 14 June 2021

Abstract

Background The chance of incidentally detecting brain tumors is increasing as the utilization of magnetic resonance imaging (MRI) becomes more prevalent. In this background, knowledge is accumulating in relation to the prediction of their clinical sequence. However, their prevalence—especially the prevalence of glioma—has not been adequately investigated according to age, sex, and region.

Method We systematically reviewed the articles according to the PRISMA statement and calculated the prevalence of meningiomas and diffuse gliomas in adults using a generalized linear mixed model. Specifically, the differences related to age, sex, and region were investigated.

Results The pooled prevalence of incidental meningiomas in MRI studies was 0.52% (95% confidence interval (CI) [0.34–0.78]) in 37,697 individuals from 36 studies. A meta-regression analysis showed that the prevalence was significantly higher in elderly individuals, women, and individuals outside Asia; this remained statistically significant in the multivariate meta-regression analysis. The prevalence reached to 3% at 90 years of age. In contrast, the prevalence of gliomas in 30,918 individuals from 18 studies was 0.064% (95%CI [0.040 – 0.104]). The meta-regression analysis did not show a significant relationship between the prevalence and age, male sex, or region. The prevalence of histologically confirmed glioma was 0.026% (95%CI [0.013–0.052]).

Conclusions Most of meningiomas, especially those in elderlies, remained asymptomatic, and their prevalence increased with age. However, the prevalence of incidental gliomas was much lower and did not increase with age. The number of gliomas that developed and the number that reached a symptomatic stage appeared to be balanced.

Keywords Asymptomatic · Glioma · Incidental · Meningiomas · MRI

Introduction

The chance of incidentally detecting brain tumors is increasing as the utilization of magnetic resonance imaging (MRI) becomes more prevalent in research and clinical practices. Among incidental tumors, meningiomas, pituitary adenomas, schwannomas, and gliomas were assessed by MRI [50]. The accumulated knowledge on the natural course of these incidental asymptomatic brain tumors is still not sufficient to predict the future growth of individual tumors. Although it is assumed that early detection and treatment can improve survival, this hypothesis has not been validated [37, 60, 65]. On the other hand, both risks associated with treatment and psychological stress trigger dilemmas in patients with incidental tumors under a wait-and-see strategy [26, 50].

Very few meta-analyses have analyzed the prevalence of incidental brain tumors other than pituitary adenomas [13, 43]. Morris et al. reported that the prevalence of different types of incidental brain tumors among 19,599 individuals was as follows: meningiomas, 0.29%; pituitary adenomas,0.15%; vestibular schwannomas, 0.03%; and gliomas, 0.05% [43]. Conversely, Ezza et al. reported that

This article is part of the Topical Collection on Brain Tumors

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Published online: 06 July 2021

the prevalence of pituitary adenoma on imaging studies is as high as 22.5% [13]. The difference was due to MRI protocols including thin section section-coronal and -sagittal plains. Other meta-analyses reported a rate of brain tumors as a whole and did not describe the prevalence of each type of tumor [15]. The reported prevalence varied according to the age of the population and the male–female ratio in each study. The prevalence may also change according to the region targeted in the search. Such subgroup analyses of incidental brain tumors have been insufficient, although more than 20 studies have reported the prevalence of incidental brain tumors on MRI [1, 3–5, 7, 9, 16, 18–21, 24, 28–31, 34, 36, 39, 42, 54, 56, 57, 59, 61, 63] since the review by Morris et al. [43].

Although majority of incidental meningiomas are known to be indolent, the selection of patients who are suitable for treatment is still controversial [49]. The elucidation of the prevalence and age distribution of incidental meningiomas is important for predicting the possibility of symptomatic growth of meningiomas. Asymptomatic incidental meningiomas were found in 1.3–2.3% of autopsy studies [48, 55]. These data may not be applicable to a modern population because the studies were performed more than 30 years previously based on the data that were mainly obtained more than 50 years previously. Actually, from 1985 to 2019, the age-adjusted incidence of meningioma in the US population increased more than three times, 2.5/100,000-year in 1985 [22] vs. 8.33 in 2019 [38]. The increased incidence might be explained by alterations in the population composition, exposure to risk factors, and the widespread use of imaging studies. However, the true frequency of asymptomatic meningioma in the same period has not been elucidated.

Recent studies discussed the strategy to treat gliomas that were found incidentally [41, 60]. Gliomas are one of the most frequently encountered brain tumors, but they are rarely diagnosed during the asymptomatic phase. It is not known how often incidental gliomas become symptomatic because the prevalence of asymptomatic gliomas has not been clarified. Previous reports about the prevalence of incidental gliomas contained very few patients, and the majority of the cases were not histologically proven [3]. Furthermore, previous systematic reviews included not only diffuse gliomas (diffuse astrocytic and oligodendroglial tumors) but also other types of gliomas such as pilocytic astrocytomas and gangliogliomas [43]. The recent WHO classification clearly distinguishes the latter because of the different molecular and clinical features [40].

In this meta-analysis, we selected asymptomatic meningiomas and gliomas as candidates for the comparison of clinical implications, because they have a comparable clinical incidence but a different prevalence on MRI, and they are associated with controversial management issues that clinicians often encounter. Pituitary adenomas and vestibular schwannomas were excluded from this study because the patients with these tumors were often symptomatic, with accompanying manifestation of which they were unaware.

We systematically reviewed the relevant literature and calculated the prevalence of meningiomas and diffuse gliomas. Specifically, the difference among age groups, sex, and study regions was investigated.

Methods

Literature search and data extraction

The present study followed the PRISMA statement. The search flow diagram is outlined in Supplementary file 1. We searched for relevant English articles using the keywords "magnetic resonance OR MRI", "brain", and "incidental OR asymptomatic" and published from 1990 to November 2020 in PubMed, Scoups, and Google Scholar; "meningioma", "glioma", "tumor", or "neoplasm" were combined key words. The search was performed on November 24, 2020. The exact search strategy has been described in Supplementary file 1. Although studies confined to familial tumor syndromes such as neurofibromatosis were excluded, studies in patient groups with comorbidities (such as trauma, heart diseases, or migraine) were included when such findings were incidentally identified. We incorporated studies that recruited $\geqq$ 100 participants with a mean age of $\geqq$ 20 years. Two of the authors searched the relevant literature independently, and final selection was determined by discussion.

Risk of bias

The majority of incorporated studies were descriptive cross-sectional studies that reported the number of cases in a particular population at a time point or during a period of time. We used the JBI critical appraisal checklist for studies reporting prevalence data, which was developed as a tool for conducting systematic reviews of prevalence, to evaluate the risk of bias (Supplementary file 2) [45]. The adequate sample size was calculated by putting precision (d) as a half of expected prevalence, which was 1% for meningiomas and 0.1% for gliomas [47]. The adequate sample size was calculated to be 1520 for meningiomas and 15,200 for gliomas.

We estimated the publication bias using a funnel plot. As the assessment in traditional funnel plot is known to be inappropriate for the proportional studies with rare events, the estimate was performed using the method described by Hunter et al. [23]

Extraction of incidence data

In each study, we collected the mean age, sex (male ratio = the number of men/total population), and the numbers of meningiomas and diffuse gliomas. Follow-up results and histological diagnoses were also recorded if available. Pilocytic astrocytomas, gangliogliomas, and ependymomas were excluded from diffuse gliomas. When only the median age was recorded, the median value was used instead of the mean (two studies). In two studies in which only the age range was described (60 to 64 years, and 17 to 82 range), we used 62 years and 49.5 years, respectively, as the mean age. We grouped the regions from which the studies originated as Asia (Japan, Taiwan, and China) and other regions because white and black Americans had a significantly higher incidence of benign meningiomas in comparison to Native Americans and Asian/Pacific Islanders [12]. The studies were divided into small (< 500 participants) or large and normal participants (normal volunteer or health check-up) or participants with specific comorbidities (symptoms or diseases not related to incidental findings [e.g., cardiac disease, diabetes, dysmenorrhea, or migraine]).

Statistical analysis

We used the R software program (v4.03) to perform the statistical analyses. A random-effects model was applied in the meta-analysis. We used the "metaprop" function in R to perform a single-arm meta-analysis to calculate prevalence. Because several studies reported a null incidence, we initially used Freeman-Tukey double arcsine transformation. The results of the meta-analysis based on the back-transformation of the Freeman-Tukey double arcsine transformation can be erroneously smaller than all individual study results, especially in cases that include diverse sample sizes [58]. For this reason, we used the generalized linear mixed model (GLMM) with maximum-likelihood method. A GLMM can directly calculate the prevalence without transformation and has advantages in meta-analyses that include null incidence. The confidence intervals for individual studies were calculated by the Clopper-Pearson method.

The reviewed studies were tested for heterogeneity (I^2 statistic), and meta-regression analyses were performed to identify factors related to heterogeneity. Two-sided P values of < 0.05 were considered to indicate statistical significance.

Ethical approval & informed consent.

This review did not involve direct studies on humans, and informed consent was not required.

Results

After removing duplicates, we retrieved 125 articles for full-text assessment to determine their eligibility (Supplementary Fig. 1). Articles with symptomatic tumors, without radiological diagnosis, CT studies, and overlapping data were excluded. Studies without an adequate MR sequence or whole-body MRI using a body coil were also excluded. As a result, we selected 35 articles and added 1 through cross-referencing. We analyzed the frequency of meningiomas in 36 studies [1, 3–5, 7, 9, 16, 18–21, 24, 25, 27–36, 39, 42, 44, 52, 54, 56, 57, 59, 61–64, 66] and of gliomas in 34 studies [1, 3–5, 9, 16, 18–21, 24, 25, 27–29, 31–36, 39, 42, 44, 52, 54, 56, 57, 59, 61–64, 66] (Table 1, Supplementary File 3).

Meningiomas

The prevalence of incidental meningiomas in MRI studies was 0.52% (95% confidence interval (CI) [0.34–0.78], $I^2 = 80.7\%$) in a total of 37,697 individuals (Table 2) (Fig. 1a). The funnel plot and regression test did not detect a publication bias (P = 0.69) (Supplementary file 4). A subgroup analysis revealed a significant difference between Asia (0.22%, 95%CI [0.10–0.51] and other regions (0.66%, 95%CI [0.43–1.02] (P = 0.022) (Fig. 1a). We found no difference between large and small studies (large 0.56% [0.32–0.98] vs. small 0.59% [0.35–1.0], P = 0.89) or studies in healthy participants and those with comorbidity (healthy 0.42% [0.24–0.75] vs. comorbidity 0.81% [0.48–1.4], P = 0.10).

The results of meta-regression analyses were concordant with the results of subgroup analyses (Table 3). The prevalence was affected by the mean age (P < 0.0001) (Fig. 1b), male ratio (P = 0.0046), and region (P = 0.017). The multivariable meta-regression analysis showed statistically significant differences in mean age (P = 0.0004), male ratio (P = 0.012), and region (P = 0.043) (Table 3).

Gliomas

The prevalence of incidental gliomas in MRI studies was 0.071% (95%CI [0.045–0.110], $I^2 = 0\%$) in a total of 34,763 individuals (Fig. 2a). A funnel plot, however, showed moderate asymmetry with a significant regression test (P = 0.006) (Fig. 2b). As shown in the funnel plot, some of the small-sized studies (< 500 participants) had a relatively high prevalence. Considering the publication bias due to the small-study effect, we excluded these small-sized studies from the subsequent analyses. Consequently, the prevalence in 30,918 individuals in 18 studies is calculated to be 0.064% (95%CI [0.040–0.104]) in Table 2. A funnel plot of the large-sized

Table 1 Summary of analyzed articles

Author, year [reference]	Participants	Total number	Mean age	Male ratio	Menin	Glm	Other mass lesions	Treatment	Study type	Region
Alturkustani 2020 [1]	Adult migraine	275	M38,	0.418	4	1	Subep 1, Pit 2	Resect except for 1	C	Middle East
Boss 2016 [3]	≥45 years, in the Netherlands	5800	m64.9 SD10.9	0.449	143	6	Ggoma 1 Subep 1	Glm, 5 wait and see, 1 rad; Menin, 8 resect, 7 rad	H	Euro
Boutet 2017 [4]	PROOF study, volunteers. ≥ 65 years	503	m75.3 SD0.9	0.414	10	1	Sch 1	Astro, biopsied; Menin, observe	H	Euro
Brugulat-Serrat 2017 [5]	Normal first-degree descendants of Alzheimer patients	575	m56.0 (45–75)	0.395	10	0	clb mass 1, Pit2, Subep1	NA	C	Euro
Cerhan 2019 [7]	Mayo clinic study of aging	2402	m75	0.526	52	NA	NA	NA	H	USA
Cieszanowski 2014 [9]	Asymptomatic persons with special private health insurance, ≥ 18 years	666	m46.4 (20–77)	0.698	3	1	NA	Glm resect, 1; Menin resect	H	Euro
Glasmacher 2019 [16]	Patients attending early-onset cognitive disorder clinic	514	M60.5	0.501	2	1	Pit 1, Sch 1 DNET 1,	Glm, observ., Menin observ	C	Euro
Haberg 2016 [18]	50–66 years, HUNT study	1006	m58.5	0.473	10	1	Pit 3, Sch 1	1 mixed Glm resect; Menin, 2 resect	H	Euro
Hartwigsen 2010 [19]	Young healthy volunteers in brain research imaging studies	206	m25.68 SD5.72	0.568	0	0	NA	NA	H	Euro
Hedderich 2020 [20]	Prematurely born adults. Bavarian Longitudinal Study and control	206	m26.8 SD0.7	0.573	1	0	3 suspicious FLAIR high mass lesion	NA	C	Euro
Hegenscheid 2013 [21]	The German population-based study of health in Pomerania	2500	m53 (21–88)	0.492	9	2	Met 1, Pit 9, Sch 1	NA	H	Euro
Ikeda 2002 [24]	Brain check-up	2312	m53.5 /SD11	0.689	3	2	Pit 3, Sch 1, lymphoma 1	2 Glm, resect (GBM, Astro); Menin 1 surg	H	Asia
Illes 2004 [25]	Normal adult control	151	m47.1 (18–90)	0.543	0	0	NA	NA	H	USA
Katzman 1999 [27]	Volunteers participated various NIH research as control	1000	m30.6 (3–83)	0.546	0	2	Pilo 1	Glm 1 resect (oligo) 1 observ.;	H	USA
Keuss 2019 [28]	The 1946 British birth cohort	471	m70.2 SD0.7	0.512	3	0	Subep 1	Menin, observ	H	Euro
Konc 2018 [29]	Australian twin study > 65 years	400	m70.4	0.35	6	1	Undefined cystic mass 1, Subep 1	NA	H	Australia

Table 1 (continued)

Author, year [reference]	Participants	Total number	Mean age	Male ratio	Menin	Glm	Other mass lesions	Treatment	Study type	Region
Krampla 2004 [24]	Residents in Vienna, age 75 years	532	m75	0.402	9	NA	NA	Menin, 1 surgery, 8 observ., minimal growth in 1	H	Euro
Kumar 2008 [31]	Australian capital territory and Queanbeyan	478	range (60–64)	0.527	3	0	Pit 4	3 Menin observ	H	Australia
Laible 2012 [32]	Asymptomatic persons in routine health screening	138	m54 SD7.55	0.855	1	0	NA	NA	H	Euro
Lee W-J 2008 [32]	Self-referred body-imaging center	2164	m51.8	0.57	14	0	Pit 1, Sch 1	NA	H	Asia
Li S 2018 [34]	Taizhou longitudinal study, age 55–65 years	562	m59.25 SD2.72	0.461	5	0	NA	NA	H	Asia
Li W 2010 [35]	The memory and aging study (age 70–89)	542	m78.4	0.452	7	1	Pit 2	NA	H	Australia
Li WC 2015 [36]	Primary dysmenorrhea and control	330	m23.8 SD2.5	0	0	0	clb mass 1	NA	C	Asia
Lo 2008 [39]	Asymptomatic medical doctors	132	m56 (38–82)	0.841	0	0	NA	NA	H	Asia
Menzler 2010 [42]	Healthy volunteers	100	m29	0.42	0	1	NA	NA	H	Euro
Mullaly 2018 [44]	Neurologically normal adults with headache	100	m31.5 (18–56)	0.14	1	0	NA	Menin, resect (atypical)	C	USA
Onizuka 2001 [52]	Brain check-up	4000	m56 (24–85)	0.497	6	1	Pit 3, Epid 1	Glm, resect; Menin, 4 surgery, 2 observ	H	Asia
Papanikolau 2010 [54]	Patients with audio-vestibular symptoms	200	Range (17–82)	0.505	1	2	NA	NA	C	Euro
Reneman 2012 [56]	Control participants in studies on the effects of the drug ecstasy	203	m21.9 SD3.2	0.453	0	0	NA	NA	H	Euro
Sandeman 2013 [57]	Lothian Birth cohort 1936	700	m72.5 SD1.5	0.526	5	0	clb tumor 1, Pit 2	Observ	H	Euro
Serag 2020 [59]	Candidates referred for MRI of the orbito-paranasal or temporal bones	753	m49.8 SD18.68	0.517	19	1	Pit 9, Met 1, Sch 2	Menin, observ.; Glm, observ	C	Middle East
Trufyn 2014 [61]	Multiple sclerosis patients and control	166	m45.7	0.247	2	0	NA	NA	C	Canada
Tsushima 2005 [62]	Healthy adults with brain check-up	1113	m52.6 SD8.5	0.683	1	0	Pit 3, Epid 1	Observ	H	Asia
Vázquez-Justes 2020 [63]	Diabetes type 2 patients age 40–75	289	m57	0.509	2	0	temporal lobe T2 high nodule, Pit 1	Menin, observ	C	Euro

Table 1 (continued)

Author, year [reference]	Participants	Total number	Mean age	Male ratio	Menin	Glm	Other mass lesions	Treatment	Study type	Region
Weber 2009 [64]	All applicants for military flying duties	2536	m 20.5 (17–35)	1	0	1	Pilo, CPA1, 4th ventricle mass 1	Observ	H	Euro
Yue 1997 [66]	Cardiovascular disease ≥ 65 years	3672	m75.1	0.417	19	0	Pit 6	4 Menin, resect,	C	USA

Glm glioma, *Menin*, meningioma, Study type: *C*, participants with comorbidity or specific disease; *H*, healthy volunteer or asymptomatic patients in health check-up; *Astro*, astrocytoma; *CPA*, cerebellopontine angle tumor; *clb*, cerebellar; *Epid*, epidermoid; *Ggoma*, ganglioglioma; *Met*, metastasis; *Pilo*, pilocytic astrocytoma; *Pit*, pituitary adenoma; *Sch*, schwannoma; *Subep*, subependymoma; *M*, median; *m*, mean; *SD*, standard deviation; *rad*, radiotherapy; *Euro*, Europe; *NA*, not available; *observ.*, observation; *resect*, resection

studies showed slight asymmetry, which did not show statistical significance in a regression test (P = 0.41).

In the meta-regression analysis, we detected no significant differences in the mean age (P = 0.79) (Fig. 2c), male ratio (P = 0.73), regions (P = 0.10), participants (P = 0.48), or study size (P = 0.48) (Table 3).

In addition, we calculated the prevalence of histologically proven gliomas. The prevalence was 0.026% (95%CI [0.013–0.052], $I^2 = 0\%$) in 30,918 participants. The following tumors were histologically confirmed: astrocytoma, n = 3; oligodendroglioma, n = 1; mixed glioma, n = 1; low-grade gliomas, n = 1; high-grade glioma (a pontine tumor diagnosed from clinical course), n = 1; and glioblastoma (a patient with mild cognitive dysfunction who might have been symptomatic), n = 1. On the other hand, we noticed that several authors described suspicious mass lesions that showed hyperintensity on FLAIR without a diagnosis [18, 20, 63]. These lesions are not included in this analysis; however, they are included in Table 1.

Sensitivity analysis

The leave-one-out method (excluding each study one-by-one from the analysis) did not substantially change the pooled prevalence of meningiomas, which ranged from 0.49 to 0.59% (I^2 85.4–90.4%). The most influential study was a study in young men [64]. Although this study contained no meningioma cases, despite the large study population (n = 2536), we did not exclude the study because of the results of the meta-regression analyses.

In gliomas, the leave-one-out method showed that the change in pooled prevalence ranged from 0.06 to 0.073% with no change of I^2.

Discussion

In this study, we showed the prevalence of incidental meningiomas and gliomas on MRI. Meningioma was found in 0.52% of the studied populations. In contrast, the prevalence of glioma was much lower (0.064%). Each of the included studies targeted different populations with regard to age, sex, and region. Thus, we were able to analyze factors related to prevalence by a meta-regression analysis without individual data. In meningiomas, the prevalence changed with age, male ratio, and region, whereas the prevalence of glioma was not likely to be influenced by these factors.

Meningiomas

Previous studies reported that incidental meningiomas were found more frequently in elderly individuals and women. However, those reports rarely showed the exact age and sex

Table 2 Summary of study population

	Meningiomas	Diffuse gliomas
Analyzed studies	36 studies N = 37,697	18 studies N = 30,918
Prevalence	0.52% 95%CI [0.34–0.78]	0.064% 95%CI [0.040–0.104]
Gender	Male 20,126 Female 17,571	Male 16,917 Female 14,001
Mean age	56.97 years	56.30 years
Region	Asia 7 (Japan 3, China 3, Taiwan 1), Other 29 (USA 6, Europe 18, Australia 3, Middle East 2)	Asia 5 (Japan 3, China 1, Taiwan 1), Other 13 (USA 2, Europe 10, Middle East 1)
Participants	Healthy, 25 studies With comorbidity, 11 studies	Healthy, 14 studies With comorbidity, 4 studies

CI confidence interval

distribution because the majority of the studies lacked data of the whole cohort, with the exception of autopsy studies. The prevalence of meningioma in this study (0.52%) was higher in comparison to that in the meta-analysis by Morris (0.29%) [43] because the latter included studies in pediatric populations. We showed that age was strongly associated with prevalence (Fig. 2c), with the prevalence in the population of > 90 years of age approaching 3%. Although the rate is slightly lower in comparison to the value reported in an autopsy study (4.6% in individuals of ≥ 80 years of age) [48], some of the cases involving small meningiomas that were found on autopsy might have been missed on MRI. Despite the increase in the number of cases of clinically diagnosed meningiomas, the frequency of asymptomatic meningiomas in each age group is not likely to increase in comparison to the era of autopsy studies, which were based on the data obtained between 1950 and 1983 [48]. Consequently, recent increase in the incidence of meningiomas is likely due to the increase in the number of radiologically diagnosed tumors.

A report based on the SEER database showed that the incidence of meningiomas was lowest in Native Americans and relatively low in Asians and Pacific islanders [12]. This may be due to an identification bias, because the Central Brain Tumor Registry of the United States (CBTRUS) showed that > 50% of meningiomas were radiologically diagnosed [53]; Native American and Asian people may be less likely to undergo MRI; thus, incidental meningiomas may be less frequently diagnosed. Because there were no studies in Native Americans, we investigated the difference between Asian (actually obtained from East Asia) and non-Asian regions and found a difference in the prevalence of incidental meningiomas on MRI.

Gliomas

Diffuse gliomas (astrocytomas, oligodendrogliomas, and their malignant forms) were included in this study. The prevalence of diffuse glioma was 0.064%, when lesions that the authors diagnosed as glioma were included. However, the prevalence of histologically confirmed gliomas was 0.023% (including one clinically diagnosed tumor). Håberg cautioned that most cases in which glioma initially suspected were found to be false positives [18]. In their 13 cases in which low-grade glioma was initially suspected, one was found to be astrocytoma after resection; after additional imaging studies, the other 12 lesions were gliosis (n = 6), cyst (n = 2) and benign unspecific lesions (n = 4). Thus, lesions that were defined as glioma without histological confirmation might not actually be glioma. On the contrary, suspicious mass lesions that showed hyperintensity on FLAIR without histological confirmation [18, 20, 63] might have been gliomas. Thus, the prevalence of diffuse glioma was at least 0.023% and probably 0.054%.

Although various age groups, male ratios, and regions were included in this study, the heterogeneity of the pooled estimate of glioma prevalence was very low. We found no significant differences in age, sex, or region. Although epidemiological studies showed high incidence rates in males [53], clinical studies on incidental glioma showed a female preponderance [17]. Incidental gliomas in females might have slower growth or be less likely to be symptomatic in comparison to those in males.

Comparison with epidemiological studies

Epidemiological studies reported the incidence rate and prevalence of meningioma. The age adjusted incidence rate was reported to be 4.5–5.6/100,000 person-years [6, 8, 11, 14]), while that of CBTRUS in a middle-age or older

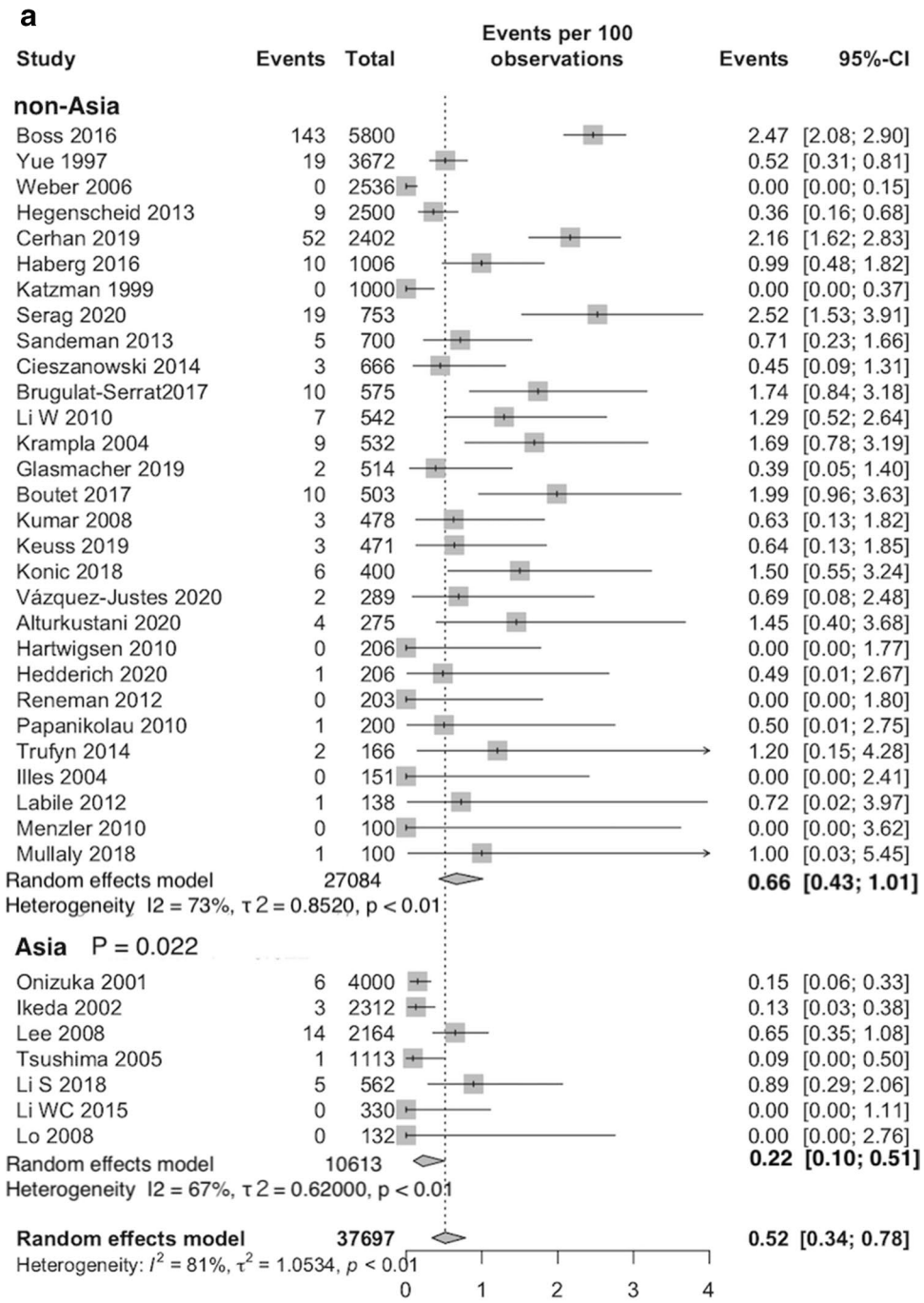


Fig. 1 The results of the meta-analysis of studies on meningioma. **a** A forest plot of the prevalence of incidental meningiomas on MRI. Studies from Asia showed a lower prevalence in comparison to those from other region (P = 0.022). **b** The mean age and prevalence of incidental meningiomas on MRI. A meta-regression analysis revealed a significant association between the mean age and prevalence. ($y = \exp(0.051 \times -8.1)/(1+\exp(0.051 \times -8.1))$, $P < 0.0001$). The size of the balloon represents the size of each study. Gray balloon, study in Asia

population was reported to be much higher (17.8/100,000 person-years) [53]. This is because > 50% of the population with CBTRUS had radiologically diagnosed meningiomas. Annually, 5–12 patients were treated per 100,000 population among middle-age and older individuals in a UK study. That study reported that the incidence rate and prevalence of meningiomas increased with age [6] (Fig. 3a). On the other hand, incidental meningiomas were found on MRI in > 1% of patients of ≥ 70 years of age and reached 3% in patients of > 90 years of age (Fig. 3a). It is assumed that many meningiomas develop even in old age and that most remain asymptomatic with a slow growth rate.

In epidemiological studies, the estimated age-adjusted incidence rates of glioma were 4.5 to 6.1 per 100,000 persons-years [2, 10, 51]. Although the incidence rate is comparable to that of meningiomas, the prevalence of incidental gliomas on MRI was much lower in comparison to the prevalence of meningioma (Fig. 3b). This was partly because incidental glioblastomas were very rarely detected on MRI because glioblastoma is a rapidly growing tumor that has a

Fig. 1 (continued)

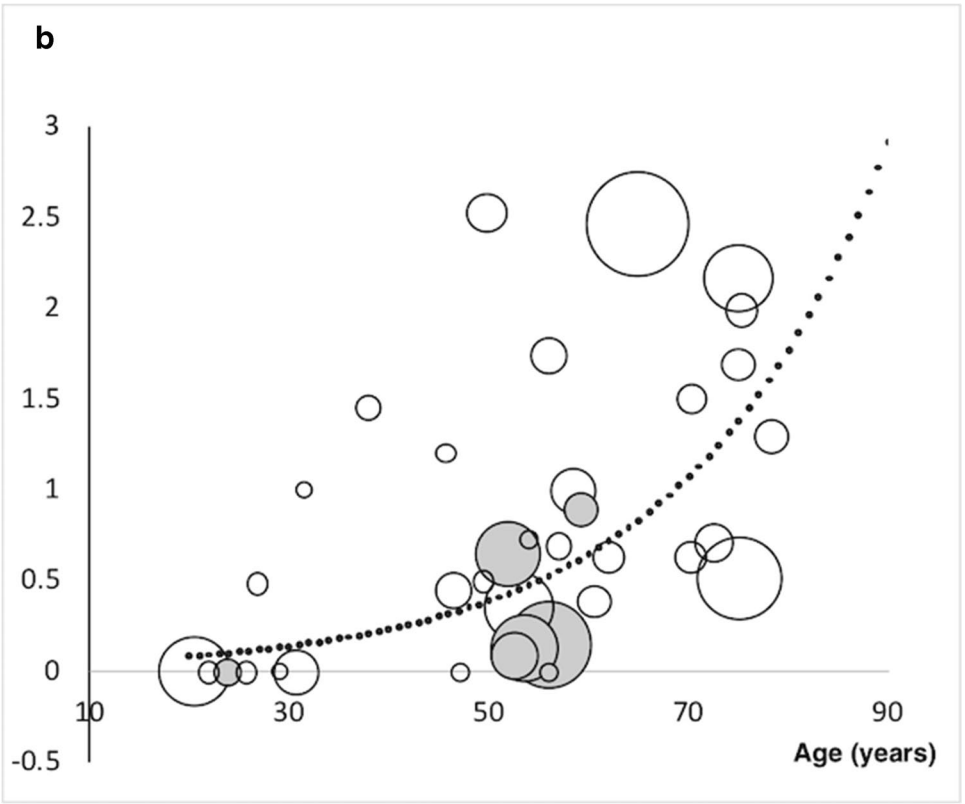


Table 3 Results of the meta-regression and multivariate meta-regression analyses

Meta-regression	Estimate	p
Meningiomas		
Mean age	0.051 [0.026–0.075]	< 0.0001
Male ratio	− 3.24 [− 5.48 to − 1.00]	0.0046
Region	1.15 [0.205–2.09]	0.02
Study size	− 0.339 [− 1.200.525]	0.44
Participants	− 0.462 [− 1.32–0.399]	0.29
Multivariate meta-regression		
Mean age	0.039 [0.017–0.060]	0.0004
Male rate	− 2.80 [− 4.95 to − 0.626]	0.012
Region	0.80 [0.026–1.57]	0.043
Diffuse gliomas*		
Mean age	− 0.0041 [− 0.034 to − 0.026]	0.79
Male ratio	− 0.523 [− 3.54–2.50]	0.73
Region	1.02 [− 0.208–2.24]	0.10
Participants	0.670 [− 0.791–2.13]	0.37

Estimate = logit transformed value; *CI*, confidence interval; *the results was calculated in large-size studies (N ≥ 500); [], 95% confidence interval

small chance of being detected in the incidental phase. We have to be cautious about such a "length–time bias". The prevalence of tumors with rapid growth is estimated to be lower than the true value, because, in screening studies that take several years to recruit participants, patients with malignant tumors would not be recruited before the manifestation of symptoms.

The most prominent difference between the prevalence of incidental meningiomas and gliomas on MRI was the distribution in age groups. The prevalence of incidental meningiomas increased markedly with age, while that of glioma did not. If a part of incidental tumors remains asymptomatic, their prevalence on MRI is expected to increase with age when new development is constant. In gliomas, development and symptomatic growth appear to balance out, and most of incidental gliomas become symptomatic with a latent period; another interpretation is that—while part of gliomas remain asymptomatic—the asymptomatic phase of gliomas becomes much shorter with age due to their more rapid malignant change.

Limitations

The present study was associated with some limitations. One critical limitation of this study is the lack of histological confirmation in the majority of cases. Although a dura-based mass with typical radiological features rarely has a histology other than meningiomas [46], it is difficult to diagnose glioma with a conventional MRI sequence. For this reason, we analyzed the incidence of histologically proven gliomas.

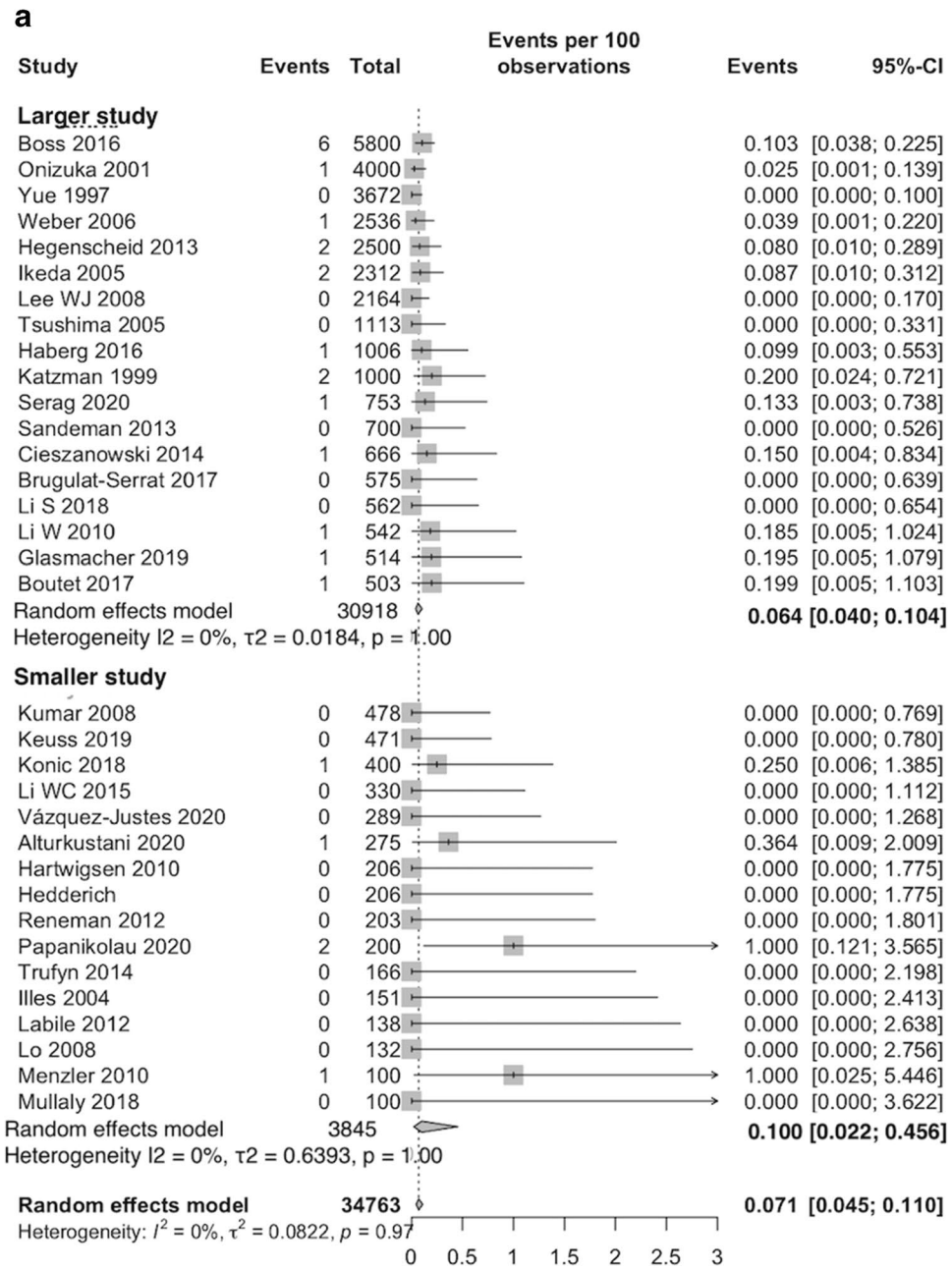
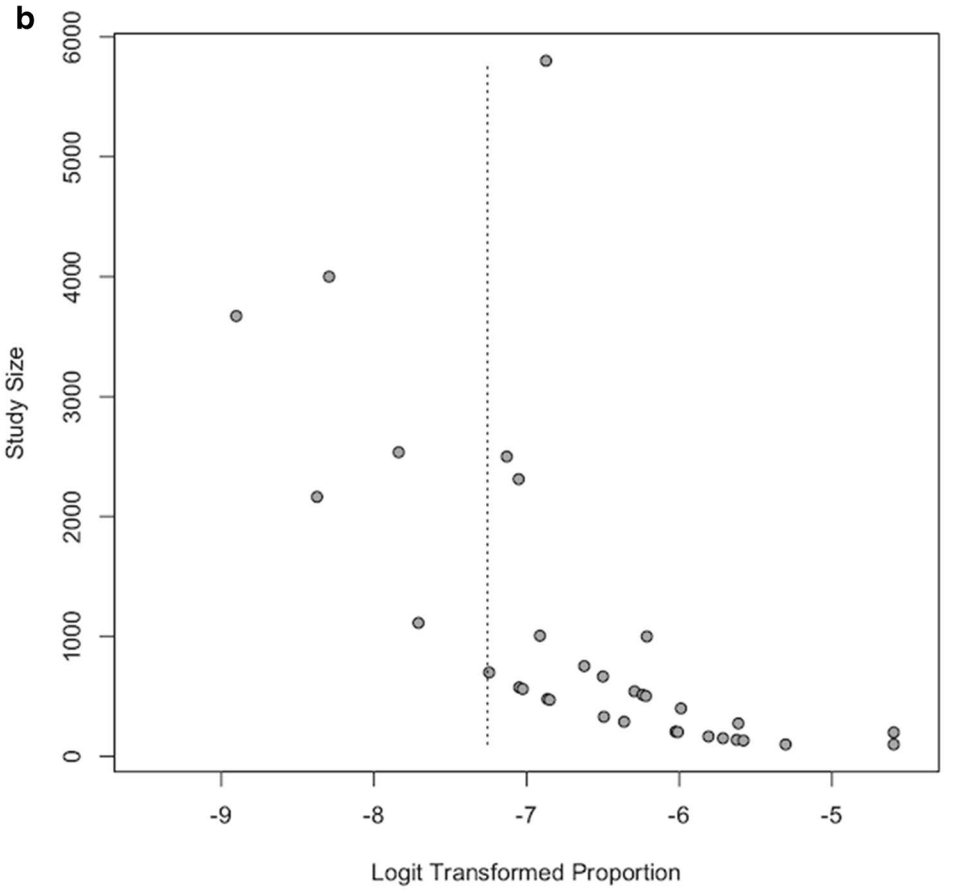


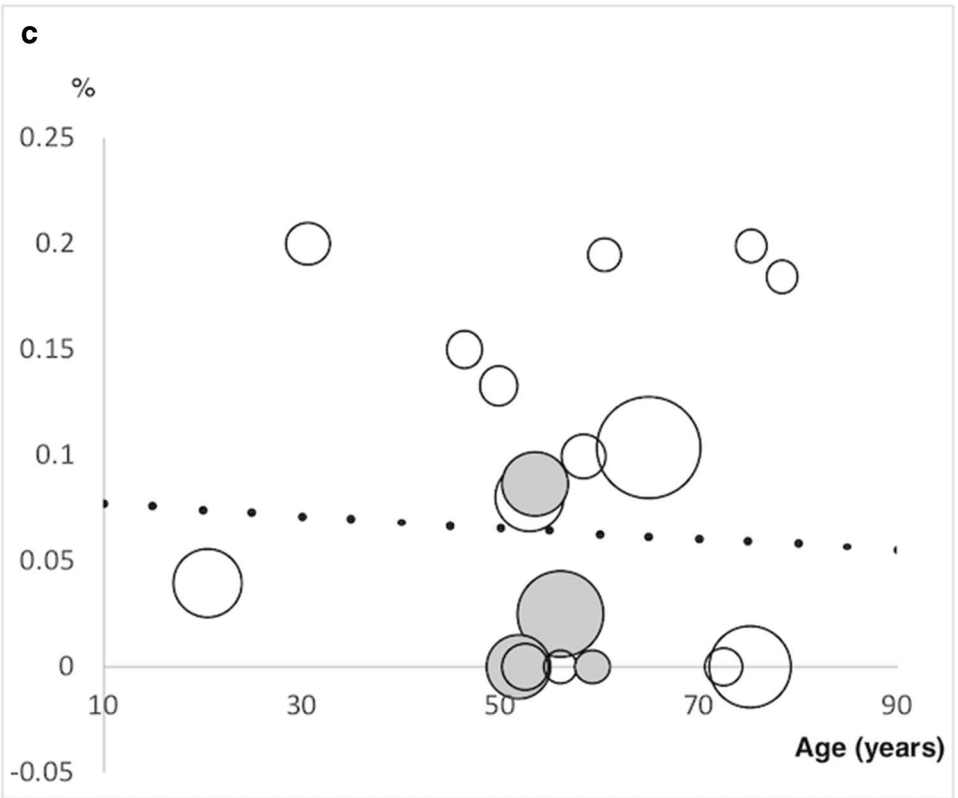
Fig. 2 The results of the meta-analysis of studies on glioma. **a** A forest plot showing the prevalence of incidental gliomas on MRI. Smaller studies (S, < 500) often had a larger prevalence although the difference was not statistically significant (P = 0.59). **b A** funnel plot showing moderate asymmetry (P = 0.006). **c** The mean age and prevalence of incidental gliomas on MRI. A meta-regression analysis revealed a non-significant relationship between the mean age and prevalence. (y = exp (− 0.004 × − 7.1)/(1 + exp (− 0.004 × − 7.1)), P = 0.79). The size of the balloon represents the size of each study. Gray balloon, study in Asia

Another problem is the study size. We calculated that the adequate study size was 1250 for meningioma and 12,500 for glioma. A minority of the studies on meningioma and none of the studies on gliomas reached an adequate size. Although the synthesized population reached > 30,000, the small studies on gliomas tended to report a higher prevalence. Because the prevalence of gliomas is very low, small studies with positive findings might be relatively easily published. In contrast, smaller studies are more likely suppressed from publication if their results are not impressive. Consequently, the pooled prevalence might be skewed to be higher. Although we excluded studies on glioma with < 500 participants, this might have been insufficient. While a previous meta-analysis included low-volume studies with even less than 100 cases [43], such a small-study effect should be cautiously considered when the calculated incidence is very low.

One possible problem is that the majority of population-based studies had a recruitment period of one to several years. Participants with a rapidly growing incidental tumor who wait months for MRI may become symptomatic. Such a length–time bias is not related

Fig. 2 (continued)





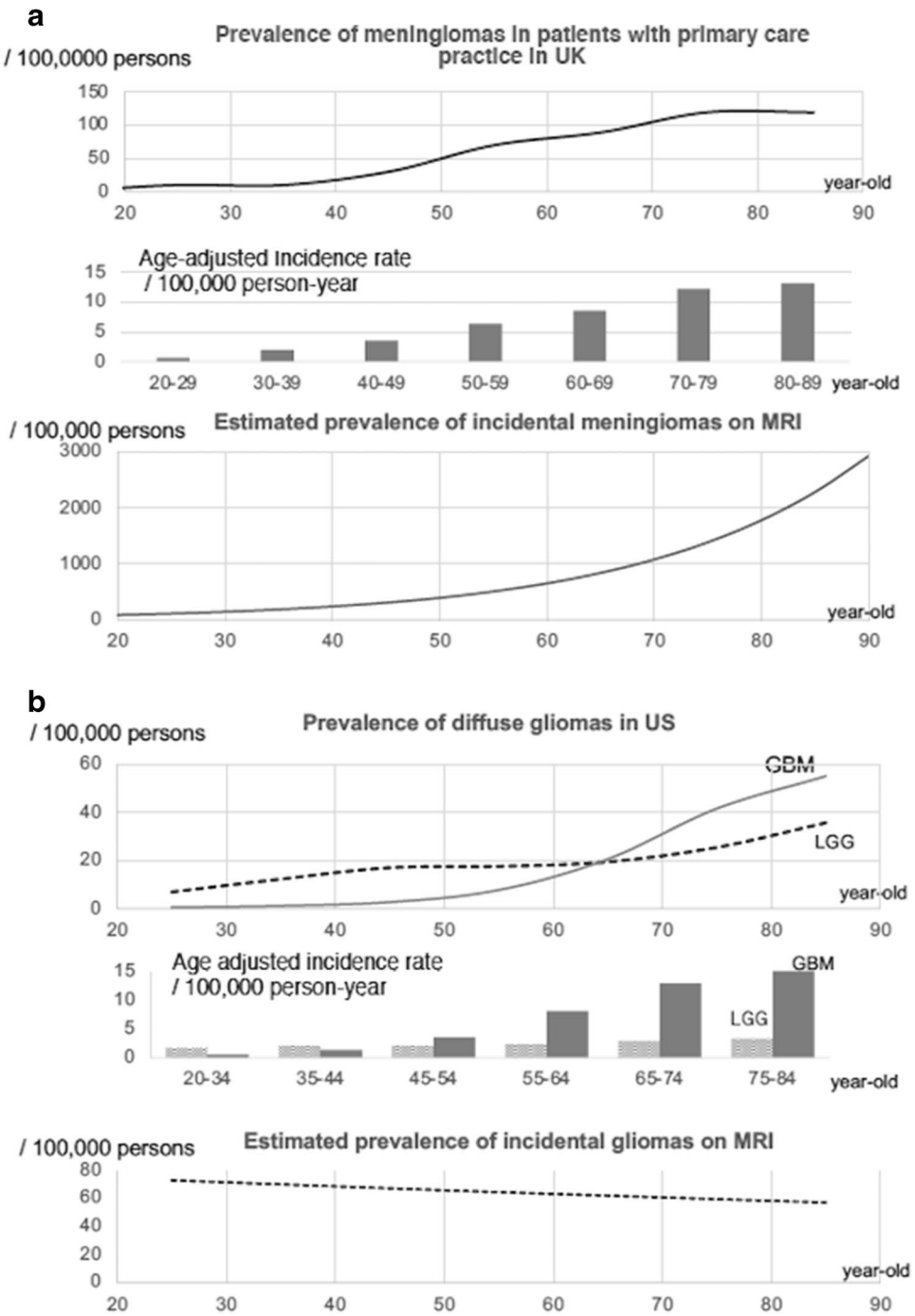


Fig. 3 Comparison between the prevalence of incidental tumors on MRI and epidemiological studies. **a** The prevalence of incidental meningioma and the age-adjusted incidence rate in an epidemiological study in UK [6]. **b** The prevalence of incidental gliomas and the age-adjusted incidence rate in an epidemiological study in the USA [52]

to the prevalence of meningiomas, which generally show slow growth; however, it is related to some gliomas, which may grow rapidly with possible malignant transformation.

Conclusions

We performed a meta-analysis to investigate the prevalence of incidental brain tumors on MRI using GLMM. The pooled prevalence of incidental meningiomas was 0.52% (95% CI [0.34–0.78]). A meta-regression analysis showed that the prevalence was significantly higher in the elderly, females, and in non-Asian areas; the findings remained

significant in the multivariate analysis. The prevalence increased markedly with age and reached to approximately 3% at > 90 years of age. In contrast, the prevalence of diffuse gliomas was low (0.064%), while the reported incidence rates of clinically diagnosed meningioma and diffuse glioma were comparable. The prevalence of incidental gliomas was not related to age, male sex, or region.

Most of meningioma, especially those in the elderly, remained asymptomatic, and their incidence increased with age. In contrast, the prevalence of incidental gliomas was much lower and did not increase with age. The number of gliomas that developed and the number that grew to a symptomatic stage appeared to be balanced.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00701-021-04919-8.

Acknowledgements We would like to thank Mr. Brian Quinn (Japan Medical Communication) for editing a draft of this manuscript.

Declarations

Conflict of interest The authors declare no competing interests.

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