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Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis

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ABSTRACT

Objective To quantify the prevalence of incidental findings on magnetic resonance imaging (MRI) of the brain.

Design Systematic review and meta-analysis of observational studies.

Data sources Ovid Medline (1950 to May 2008), Embase (1980 to May 2008), and bibliographies of relevant articles.

Review methods Two reviewers sought and assessed studies of people without neurological symptoms who underwent MRI of the brain with or without intravenous contrast for research purposes or for occupational, clinical, or commercial screening.

Main outcome measures Overall disease specific and age specific prevalence of incidental brain findings, calculated by meta-analysis of pooled proportions using DerSimonian-Laird weights in a random effects model.

Results In 16 studies, 135 of 19 559 people had neoplastic incidental brain findings (prevalence 0.70%, 95% confidence interval 0.47% to 0.98%), and prevalence increased with age (χ2 for linear trend, P=0.003). In 15 studies, 375 of 15 559 people had non-neoplastic incidental brain findings (prevalence 2.0%, 1.1% to 3.1%, excluding white matter hyperintensities, silent infarcts, and microbleeds). The number of asymptomatic people needed to scan to detect any incidental brain finding was 37. The prevalence of incidental brain findings was higher in studies using high resolution MRI sequences than in those using standard resolution sequences (4.3% v 1.7%, P<0.001). The prevalence of neoplastic incidental brain findings increased with age.

Conclusions Incidental findings on brain MRI are common, prevalence increases with age, and detection is more likely using high resolution MRI sequences than standard resolution sequences. These findings deserve to be mentioned when obtaining informed consent for brain MRI in research and clinical practice but are not sufficient to justify screening healthy asymptomatic people.

INTRODUCTION

Apparently asymptomatic intracranial abnormalities of potential clinical significance, or incidental brain findings (box), are fast becoming problematic, with the increasing use of magnetic resonance imaging (MRI) of the brain by clinicians,1 researchers,2 and companies that carry out health “check-ups.”3

The detection of incidental findings is an unintended consequence of brain MRI in clinical situations where the prevalence of any relevant finding is likely to be low. Detection is potentially detrimental because the treatment can have harmful as well as beneficial consequences. Knowing the chance of discovering incidental brain findings would help clinicians inform patients of these risks, help researchers adequately inform healthy volunteers in imaging research, and adequately inform people who seek screening by brain MRI.

The overall prevalence of incidental brain findings including silent infarcts in a recent study of 2000 volunteers aged 46-97 years using high resolution MRI sequences, without injected contrast or angiographic sequences, was more than 10%.4 However, a systematic review and meta-analysis of the published literature has been recommended4 because it could provide
more precise estimates of the range of incidental findings on brain MRI and explore the influence of study design, patient characteristics, and imaging parameters on the detection of incidental brain findings.

METHODS
In May 2008 we searched Ovid Medline from 1950 and Embase from 1980 (http://gateway.ovid.com, see web extra appendix 1 for search strategy) for reports on the use of brain MRI in healthy people, volunteers, research controls, and people undergoing commercial, clinical, or occupational screening. We did not restrict the search by language or patients’ age. We supplemented the electronic searches with surveillance of electronic tables of contents in neurological journals and by hand searching the bibliographies of pertinent articles. Two authors (ZM and WNW or RA-SS) read the title and abstract of every study identified by the electronic searches and critically appraised the full text of potentially eligible studies.

We defined incidental brain findings as apparently asymptomatic intracranial abnormalities that were clinically significant because of their potential to cause symptoms or influence treatment. We divided the findings into two clinically relevant categories: neoplastic (benign and malignant tumours) and non-neoplastic (cysts, structural vascular abnormalities, inflammatory lesions, and “other” such as hydrocephalus, Arnold-Chiari malformations, and extra-axial collections). Although white matter hyperintensities, silent brain infarcts or lacune, and brain microbleeds are incidental findings, we did not focus on them because of their known increasing prevalence with age, their largely unknown role in causing symptoms, and the current uncertainty about whether or not to institute primary prevention after their detection.

We distinguished incidental brain findings from normal variants, which we defined as anatomical variants that do not have the potential to cause symptoms—for example, cavum septi pellucidi, large cisterna magna, and ventricular asymmetry.

We included studies published in full that reported the prevalence of incidental brain findings in people without neurological or psychiatric symptoms, who underwent brain MRI as research cases or controls, or as recipients of commercial, clinical, or occupational screening. We did not include studies restricted to markers of cerebrovascular disease because they have recently been the subject of systematic reviews. Disagreements about study eligibility were resolved by discussion, or arbitration by one author (RA-SS). If several publications arose from the same cohort, we only included the largest study.

Data extraction
Two authors extracted data on study design, population characteristics, and MRI parameters from each study, and extracted the overall and age specific frequencies of each type of incidental brain finding. When age specific data on prevalence were not provided in an original publication we requested these by emailing the corresponding author, who became a coauthor of this review if they extracted and supplied data.

Data analysis
We carried out a meta-analysis of prevalence data for each incidental brain finding and all incidental brain findings (excluding markers of cerebrovascular disease), using data from the studies that enabled relevant calculations. We used the I² statistic to estimate the heterogeneity of individual studies contributing to the pooled estimate, and determined whether to use a fixed or random effects model on this basis. We calculated the pooled proportion as the back transform of the weighted mean of the transformed proportions, using DerSimonian-Laird weights in a random effects model, and report 95% confidence intervals. We did subgroup analyses to explore the influence of the MRI sequences used, the specialty of the person reporting on the MRI, and participant characteristics on the pooled prevalence of all incidental brain findings (excluding markers of cerebrovascular disease). When age specific data were provided in the original publications or made available to us on request, we calculated age specific prevalence in 20 year age bands because 10 year age bands contained insufficient data. The number of asymptomatic people needed to scan to detect one incidental brain finding, or number needed to scan, was the reciprocal of the prevalence estimate. We used Confidence Interval Analysis v2.1.2 to calculate 95% confidence intervals, and StatsDirect v2.7.2 for χ² tests for trend, tests of heterogeneity, and meta-analysis of proportions with random effects models.

RESULTS
The electronic search strategy identified 1802 publications, of which 19 papers reporting data on 17 cohorts were eligible. We excluded three publications because they reported on cohorts included in this systematic review at earlier stages in their recruitment, or because it was difficult to be certain that most participants were asymptomatic for neurological conditions.

We included 16 publications reporting data between 1989 and 2008 on 16 unique cohorts (19 559 people) from Asia (n=7277), Europe (n=5942), the United States (n=5764), and Australia (n=576) who had undergone brain MRI (table). The number of people in each study ranged from 60 to 4000, with a mean age of 11 to 63 years (range 1-97 years). One study included cases (n=589) and controls (n=67), but in the rest participants were exclusively controls (six studies, n=1702), or screening attendees (six studies, n=11 118).

Critical appraisal
Participants had comorbidities in four studies, such as hypertension, diabetes mellitus, myocardial...
infarction,\textsuperscript{9,10} hyperlipidaemia,\textsuperscript{10} but they did not seem to have any comorbidities in seven studies, and no comment was made in the remainder (table). The neurological asymptomatic status of participants was determined by history,\textsuperscript{2,5,6-9,12-16} history and examination,\textsuperscript{1,11} history, examination, and investigation,\textsuperscript{11} or unspecified means.\textsuperscript{5,6} However, 21 (0.1\%) of the 19,559 participants had preceding neurological symptoms that may have been related to abnormalities found on brain MRI.\textsuperscript{1,3,6-10} Neuroradiologists were used in seven studies to interpret images (272/8,340; 3.3\%, 1.8\% to 5.7\%),\textsuperscript{1,3,6} or unspecified observers.\textsuperscript{5,6} The detection of these incidental findings in studies using neuroradiologists was not significantly higher than in studies using general radiologists (144/4,954; 2.3\%, 0.9\% to 4.4\%, \( \chi^2 = 0.3 \)).

### Influence of MRI sequences, reporting, and participant characteristics

The detection of incidental findings (excluding markers of cerebrovascular disease) was higher in studies using at least one high resolution MRI sequence (318/6,204; 5.3\%, 3.9\% to 6.7\%),\textsuperscript{9,10,12-16} higher than in studies using standard resolution sequences (176/9,355; 1.9\%, 1.3\% to 2.7\%).\textsuperscript{1,9,10,14-16} The combined prevalence of neoplastic and non-neoplastic incidental findings was 2.7\% (number needed to scan=37).

### Disease specific and overall prevalence

Disease specific prevalence was calculable for intracranial neoplasms in all 19,559 participants, but one study of 4,000 participants only described asymptomatic tumours,\textsuperscript{15} resulting in a denominator of 15,559 for prevalence of non-neoplastic incidental brain findings (fig 1). The \( \chi^2 \) statistic ranged from 0\% for low grade gliomas and cavernous malformations, to 86\% for arachnoid cysts, indicating variable degrees of heterogeneity among the included studies. We therefore used a random effects model to meta-analyse the data.
To explore the influence of the source of the participants on prevalence of incidental brain findings, the analyses were restricted to studies using at least one high resolution MRI sequence or three dimensional time of flight magnetic resonance angiography. The prevalence was higher among research cases (198/6150; 3.4%, 0.9% to 7.5%) than among attendees of commercial screening (105/4582; 2.0, 0.9% to 3.3%) and research controls (24/1635; 1.6%, 1.0% to 2.2%; $\chi^2$, P<0.001). The overall prevalence did not differ between studies in which comorbidities among participants were present (89/3074; 2.9%, 2.4% to 3.6%), absent (134/4171; 3.2%, 2.7% to 3.8%), or unknown (271/8314; 3.3%, 2.9% to 3.7%; $\chi^2$ P=0.6).

### Age specific prevalence

Of the 16 included studies, the original data were no longer available for two (totalling 5000 participants), one (2000 participants) declined to provide age specific tabular data,\(^6\) and five (totalling 1582 participants) failed to contribute data on request,\(^6\)\(^-\)\(^12\)\(^\)\(^-\)^\(^14\) leaving age specific grouped summary data on 10977 people, which were provided by six studies\(^6\)\(^-\)\(^13\)\(^-\)\(^15\) and extracted from the reports of two others with participants in just one 20 year age band.\(^6\)\(^-\)\(^13\)\(^-\)\(^15\) No age specific data were available for children aged 0-9 years, and after omitting 34 adults aged 90-99, four 20 year age bands were left for analysis of age specific prevalence (fig 2). We analysed age specific data on white matter hyperintensities and silent brain infarcts [although these data were unavailable in some studies\(^6\)\(^-\)\(^13\)\(^-\)\(^15\) ] simply to confirm that the data in the included studies showed known age specific trends in the prevalence of markers of cerebrovascular disease on brain MRI.\(^6\)

These grouped summary data showed an increasing prevalence of age for white matter hyperintensities ($\chi^2$ for linear trend=71, P<0.001) and silent brain infarcts ($\chi^2$ for linear trend=104, P<0.001), in keeping with the findings of other studies.\(^6\)\(^-\)\(^1\) The prevalence of neoplastic incidental brain findings also increased with age ($\chi^2$ for linear trend=8.8, P=0.003). The prevalence of non-neoplastic incidental brain findings, however, seemed to decline with age ($\chi^2$ for linear trend=6.9, P=0.008; fig 2), although this trend was reversed in a sensitivity analysis restricted to studies with age specific data that used at least one high resolution MRI sequence ($\chi^2$ for linear trend=66, P<0.001; see web extra appendix 2).\(^6\)\(^-\)\(^1\)\(^-\)\(^15\)

### Discussion

In this systematic review and meta-analysis of 16 studies totalling 19 559 participants, the overall prevalence of incidental brain findings on brain MRI was 2.7% (number needed to scan=37). In studies where participants underwent at least one high resolution MRI sequence—as is common practice in research using brain imaging—the prevalence of incidental brain findings [excluding markers of cerebrovascular disease] was 4.3% (number needed to scan=23) compared with 1.7% (number needed to scan=59) in studies using only low resolution sequences, which are currently most commonly used in clinical practice. Alongside an expected age related trend in white matter hyperintensities and silent brain infarcts, we found an increasing prevalence of all neoplastic incidental brain findings with age (fig 2), probably driven by the increasing prevalence of meningiomas,\(^6\)\(^-\)\(^15\) which were the most common neoplastic incidental brain finding (fig 1).

### Strengths and weaknesses of this review

By synthesising all the published data on incidental brain findings and adding unpublished data where possible, we increased the precision of existing estimates of their prevalence across the whole age range and used a novel metric of the number needed to scan to detect one incidental finding (fig 1). We included data on all abnormalities, some of which were sought but not detected by smaller studies—for example, arteriovenous malformations and colloid cysts were not detected in a recent study.\(^6\)\(^-\)\(^1\) The influence of variations in study design was diluted by pooling all the available data, and we were able to explore this heterogeneity in study characteristics and imaging sequences using

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**Fig 1** Prevalence of some incidental findings (*excluding white matter hyperintensities, microbleeds, and silent infarcts*) on brain magnetic resonance imaging.
varied considerably during the study period.

to include these data because the scanning parameters
findings and, if so, how. But the evidence is insufficient
A major dilemma is whether to treat incidental brain
Implications for clinical practice, research, and screening
Our pooled estimate provides a more precise summary
Comparison with other studies
Our pooled estimate provides a more precise summary
subgroup analyses. The provision of some unpub-
were consistent with existing population
ours were silent infarcts and white
because of the factors we have explored in sensitivity
A preferable pragmatic approach is to manage imaging
Implications for clinical practice, research, and screening
A major dilemma is whether to treat incidental brain
on what to do with most of them, partly because of the
lack of controlled trials of their treatments and partly
because the availability of MRI for only 20-30 years
means that the long term prognosis is unknown. For
example, the risk of haemorrhage from most unrup-
tured aneurysms seems to be low yet the risk of
death and stroke from interventional treatment is
sizeable. However, awareness of the presence of an
unruptured intracranial aneurysm might lead to better
modification of risk factors and potential benefits from
interventional treatment. A randomised controlled trial
is under way to address this dilemma (www.teamstudy.
org). Treatment of unruptured brain arteriovenous
malformations is independently associated with poor
outcome in the short term, which has also led to an
ongoing randomised controlled trial (www.arubastudy.
org). Although repeated scanning has become com-
onplace for asymptomatic meningiomas, about 94%
remain asymptomatic, about 63% do not grow, and sur-
gery carries a fair risk of morbidity, such that conserva-
tive management is generally recommended. Whether
treatment with surgery, radiotherapy,
or chemotherapy improves symptom free survival for
patients with low grade glioma is unknown.

Some have suggested a subdivision of incidental
brain findings by the perceived need and urgency of
referral to a specialist. But the urgency of referral is
difficult to gauge given the paucity of robust evidence
about whether and how best to treat any of the asymp-
tomatic incidental findings reported. The clinical
urgency will vary according to the age and healthiness
of the patient, and the perceived urgency may change
over time as knowledge about the effects of treatment
changes. This may explain why studies have varied—for
example, some have classified arachnoid cysts as
not requiring referral, whereas others have referred
people with these cysts for urgent clinical assessment.

A preferable pragmatic approach is to manage imaging
results with a degree of urgency on the basis of the
likely overall benefit to the study participant.

Apart from the harm that may arise from the lack of
evidence on which to base the management of inciden-
tal brain findings, the detection of such findings can
provokes considerable anxiety about a “possible
abnormality” (which might be a false positive result);
involve a costly cascade of further investigations,
with risks of complications (in the case of catheter
angiography or brain biopsy); lead to costly medical
opinions; and worry patients about the consequences
of having normal results on brain MRI are sustained
for only a few months. At the very least clinicians
The frequency of incidental findings should be discussed when obtaining consent for brain MRI. Resolution MRI sequence than studies using standard sequences (4.3% vs 1.7%).

Incidental brain findings are more likely to be detected in studies using at least one high-resolution MRI sequence, which provides more than one high-resolution MRI sequence compared to studies using standard sequences (4.3% vs 1.7%).

The crude prevalence of incidental findings on brain MRI is 2.7%, or one for every 37 neurologically asymptomatic people scanned. The frequency of incidental findings should be discussed when obtaining consent for brain MRI in research and is relevant to clinical practice, but alone does not justify health screening.

Conclusions

Doctors who request scans in clinical practice or who recommend screening for health check-ups, and researchers who obtain consent from volunteers, should provide information about the prevalence of incidental brain findings on brain MRI, the higher prevalence with high resolution MRI sequences, and the shortage of evidence to inform their management.

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Contributors: RA-SS, WW, CPW, JMW, and ZM conceived and designed the study. ZM, WW, and RA-SS collected and analysed the data. WTL, FW, Y-CL, YT, HA, and SCL extracted and contributed additional grouped summary data from studies included in this review. RA-SS, ZM, and WW wrote the paper. All authors had full access to the data in the study, can take responsibility for the integrity of the data and the accuracy of the data analysis, and edited and approved the final version. RA-SS is the guarantor.

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Ethical approval: Not required.

Implications for future research

A meta-analysis of studies on incidental brain findings using individual patient data is the only way to disentangle the various influences that we found on prevalence, including characteristics of the participants, the imaging sequences used, and who reports them. For example, reporting age specific data will help confirm the age related trends described in this review. Furthermore, future studies of the prevalence of incidental brain findings would benefit from definitions and normal variants being prespecified.

Guidance on the wide variety of ethical issues concerning the participation of healthy volunteers in brain imaging research is beginning to emerge. In future studies, volunteers should be provided with accurate information on the prevalence of incidental brain findings as part of the informed consent process, pointing out the higher detection in studies using high resolution MRI sequences. A mechanism for dealing with potential abnormalities that is appropriate to the research setting should be in place.

References

8. The American Psychological Association encourag...


