Workup and Management of Incidental Findings on Imging

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Key Points

- Incidental findings are *apparently asymptomatic intracranial abnormalities of potential clinical significance*.
- Incidental findings are common. For every 100 apparently normal asymptomatic subjects scanned, on average about 3 will have an incidental finding, giving a "number needed to scan" (NNS) of 37 (strong evidence).
- Nonneoplastic incidental findings in apparently normal subjects (excluding leukoaraiosis) have a prevalence of 2.0% (95% CI 1.13–3.10) and neoplastic incidental findings have a prevalence of 0.7% (95% CI 0.47–0.98%) (strong evidence).
- Including silent infarcts increases the incidence to above 10% (moderate evidence).
- The frequency of incidental findings increases with age (even after excluding leukoaraiosis) and with the use of more sensitive imaging sequences (sensitive imaging techniques reveal an incidence of 4.3% [CI 3.0–5.8%] versus 1.7% [CI 1.1 to 2.4%] with conventional imaging) (strong evidence).
- Detection of incidental findings is increasing due to overzealous investigation in clinical practice, increasingly easy access to more and more complex neuroimaging, the rise in easy access by the public to commercial imaging health centers (for-profit health screening), and widespread use of neuroimaging in research (moderate evidence).
- Incidental findings vary in their importance, from those that are worth noting in a report but are unlikely to be of any clinical consequence (e.g., small temporal arachnoid cyst) (limited evidence) to those which may be imminently life threatening (8-mm diameter basilar tip aneurysm) (strong evidence).
- Many incidental findings, regardless of whether they are an immediate threat to health, carry implications for insurance (travel, employment, life) as well as ability to obtain a mortgage and other financial risk ramifications (moderate evidence).
- For many incidental findings, there are inadequate data on appropriate management. These require sympathetic management to minimize anxiety in the subject and to minimize their impact on health status (insufficient evidence).

Definition and Pathophysiology

The definition of an incidental finding is an *apparently asymptomatic intracranial abnormality of potential clinical significance*. Common examples include both non-neoplastic lesions such as arachnoid cysts, pineal cysts, cavernous hemangiomas, developmental venous anomalies, aneurysms, inflammatory white matter lesions, and neoplastic lesions such as meningiomas, gliomas, pituitary adenomas, and vestibular schwannoma (Table 3.1) [1].

The pathophysiology varies from lesions that are unlikely ever to be clinically significant to those which are likely to cause symptoms or may already have done so, but that the subject has ignored to those which could be imminently life threatening. Examples of the first group include small temporal arachnoid cysts, of the second group include demyelination or an arteriovenous malformation, and of the third group include large intracranial aneurysms or gliomas. Figures 3.1 and 3.2 show examples of abnormalities discovered in control subjects for research studies.

Epidemiology

Incidental findings are not new [2–4], but awareness has increased in recent years. The likelihood of detection has increased due to a combination of factors which include greater availability of, and referral for, imaging in clinical practice, improved quality of clinical imaging protocols, availability of multiple images through PACS (compared with more limited imaging available on printed films) [5], increased use of imaging in research, and the availability of imaging-based for-profit screening programs.

Some studies have found the prevalence of incidental findings on research brain scans to be as high as 10–28%, ([4, 6, 7]; however, these included all incidental findings, including age-related white matter changes and findings with little or no clinical significance (Table 3.1). Most studies indicate that incidental findings of potential clinical significance are present on neuroimaging in approximately 3% of the apparently normal population [8–11]. In a meta-analysis of 16 studies (published up until May 2008) comprising 19,559 apparently normal asymptomatic subjects, the prevalence of brain neoplasms, silent infarcts, and white matter lesions all increased with age but of nonneoplastic lesions (excluding silent infarcts and white matter lesions) was similar across age groups from 10–29 to 70–89 years [8] (strong evidence). The neoplasms identified were meningiomas (0.29%, 95% CI 0.13–0.51%), pituitary adenomas (0.15%, 95% CI 0.09–0.22%), low-grade gliomas (0.05%, 95% CI 0.02–0.09%), vestibular schwannomas, lipomas and epidermoids (all around 0.03%, 95% CI 0.01–0.07%), and other unspecified neoplastic lesions (0.09%, 95% CI 0.03–0.17). The prevalence of demyelination (definite or possible) was 0.06% (95% CI 0.02–0.15) and 0.03% (95% CI 0.00–0.07%), respectively. Aneurysms (0.35%, 95% CI 0.13–0.67), arachnoid cysts (0.50%, 95% CI 0.21–0.87%), and Chiari malformations (0.24%, 95% CI 0.04–0.58%) were the most frequent non-neoplastic lesions (excluding silent infarcts and leukoaraiosis). Other findings included colloid cysts (0.04%), hydrocephalus (0.10%), extra-axial collections (0.04%), and arteriovenous malformations (0.05%). Two papers published since the systematic review found similar prevalences of neoplastic and non-neoplastic incidental findings. Hartwigsen et al. [10] found incidental findings in 19 of 206 young healthy volunteers (9.2%) undergoing research neuroimaging on a 3-T magnet, of which about half had some clinical implication (pituitary or pineal lesions, cavernomas, or AVMs). Orme et al. [9] reviewed 231 head scans on which they identified 136 incidental findings (42.9%). Of these, five cases (2.2%) were of sufficient significance to required further action.

Silent infarcts occur in 20% of healthy elderly people and increase in prevalence with age [12]. One large study of 1,890 normal elderly subjects described a slightly higher prevalence of 13% in subjects aged 60–64 and 23% in those between 65 and 70 [13]. White matter lesions (WMLs) attributed to cerebral small vessel disease (leukoaraiosis) are not usually present in people under the age of 40–50 years (at least not more than three to five small lesions) but increase in number and extent thereafter. Morris et al. [8] found a prevalence of 2.5% of people aged 30–49, 7% of people aged 50–69, and 17% of people aged 70–89 years. When the amount of WMLs is expressed as a volume of affected tissue, most people aged 45–59 years had less than 5 ml (median 1.8, IQR 1.06–3.17 ml); of those aged 60–74 years, most had less than 7.5 ml (median 3.05, IQR 1.87–5.49 ml); and of those aged 75–97 years, most had less than 15 ml (median 7.74, IQR 2.64–16.49 ml) but some had as much as 50 ml [6].

Microhemorrhage is also described in normal subjects; a recent meta-analysis including 4,641 normal subjects found a prevalence of 5% (95% CI 4–6%) in apparently healthy adults increasing with advancing age [14] (moderate evidence); however, these studies showed significant variation in the scanning sequences employed, and true incidences may be higher with currently available susceptibility imaging sequences [15, 16].

In spinal imaging, there may be incidental findings outside the spinal column or cord, in addition to common findings such as disc degeneration that may not be relevant to the patient's symptoms [5]. Incidental findings on body imaging may be even more frequent than on brain imaging, but a detailed discussion of this is outside the scope of this chapter [11, 17–19].

The prevalence of incidental findings varies with the sensitivity of the investigative process. Thus, studies using higher sensitivity sequences found more clinically significant incidental findings (4.3%) than did studies using less sensitive MR sequences (1.7%) [8] (strong evidence). Prospective studies using angiographic sequences found higher prevalences of asymptomatic intracranial aneurysms than studies with conventional MRI protocols or comparable postmortem studies (0.35% for conventional MRI, 3.6% for autopsy studies, and 6% for MR angiography studies) [8, 20–22].

Finally, incidental findings are apparently more common in imaging studies performed in research subjects (3.4%) than for inpatients undergoing for-profit screening examinations (2%), or in research controls (1.0%), Chi squared $p < 0.001$.8 (moderate evidence). The reason for this is unknown.

Use of neuroimaging in research is increasing [23]. Incidental findings are not uncommon in research, as one would expect from the above summary, and this raises important ethical and management issues [24–28]. The problem of what to do about incidental findings in research is discussed in a later section.

Overall Cost to Society

No studies have addressed the cost of incidental finding to society which depends on the balance between the benefits of early treatment and the risks associated with the investigation and treatment, plus the impact on the subject's ability to work, drive, obtain insurance, anxiety levels, etc., and the costs incurred by all those steps.

The health-care cost implications will vary in different countries depending on the health-care funding model. In social systems such as the UK National Health Service, there is no financial incentive for the physician to overinvestigate or overtreat the finding. In for-profit health-care systems, there is a possible temptation to perform further investigations and to treat, even when the evidence for intervention may be poor. Examples include the current vogue for stenting of asymptomatic intracranial arterial atheromatous stenosis [29] or for asymptomatic internal carotid stenosis. The danger is that increasing use of imaging to reassure the patient (or the doctor) that there is nothing wrong increases the risk of identifying incidental and irrelevant findings that the patient (and doctor) then worry about. However, there is little evidence that performing investigations is reassuring, even when the results are resoundingly negative [30–33] (moderate evidence).

Many of the consequences and the impact of an incidental finding are outside mainstream medical practice and would be even harder to quantify [34]. These include both direct and indirect factors. The individual's ability to obtain life, health, and travel insurance may be affected with serious consequences. The individual's employment may be put at risk either through increasing time off work due to their anxiety at the discovery or directly because of the loss of insurance or other liability [35, 36]. They may not be able to drive or obtain a mortgage. Their health may suffer through anxiety at knowing they have a "time bomb" through the consequences of overinvestigation or the complications of unnecessary treatment [37, 38].

Goals of Imaging

A physician portrayed by Groucho Marx in *A Day at the Races* was described by his patient (in the film) as "*One of the finest doctors I have known. Why, I didn't know there was anything wrong with me until I met him.*" The overall goal in the management of incidental findings must be to manage them without harm to the subject. Nonmaleficence is a basic guiding principle of all medical care and can be stated as:

> given an existing problem, it may be better not to do something, or even to do nothing, than to risk causing more harm than good.

Some of these findings will have been present since birth or for many years prior to discovery and would be unlikely to cause the subject harm. More harm may be caused to the subject through overzealous reaction to the finding, investigation, and treatment. Referring the anxious only makes them more anxious [39]. Until better evidence is available from more long-term epidemiology studies and intervention randomized clinical trials, the authors believe that the approach should be cautious [34].

Methodology

We updated a recent systematic review of incidental findings in neuroimaging [8], by searching from end of December 2008 to end of December 2010 in MEDLINE using PubMed (National Library of Medicine, Bethesda, Maryland) for original research publications on incidental findings in the brain or spinal cord on imaging. We also identified studies on potential adverse effects of neuroimaging used in research and commercial applications through two related projects, the first on the wider societal implications of neuroimaging held at the Scottish Universities Insight Institute in 2010 (http://www.scottishinsight.ac.uk/, details of organizations involved provided in report) and the second on the management of incidental findings in research imaging held at the Wellcome Trust, London, in 2010 (http://www.sinapse.ac.uk/media/events/ethics_management. asp; report available at http://www.rcr.ac.uk/docs/radiology/pdf/BFCR(11)8_Ethics.pdf) [40]. The search therefore covered the years 1950 to December of 2010. The search strategy employed different combinations of the following terms: (1) neuroimaging, (2) radiography OR imaging OR computed tomography OR CT OR MR OR MRI OR magnetic resonance imaging, (3) cranial OR brain OR spine OR neuro, (4) brain OR brain diseases OR spine diseases, (5) humans, and (6) ethics. Reviewing the reference lists of relevant papers identified additional articles. This review was limited to human studies and mainly the English language literature. The authors performed an initial review of the titles and abstracts of the identified articles followed by review of the full text in articles that were relevant. Articles identified in the review presented above or in the related projects [8] were handled in a similar way by the investigators of those projects, and as both authors were lead organizers of one or both of those projects, we did not repeat that work.

Discussion of Issues

How to Minimize the Chances of Incidental Findings in Clinical Practice and Why Is this Important?

Summary
The more investigations health-care providers do, the more likely they are to identify incidental findings. Incidental findings have adverse effects: they worry the patient, often unnecessarily [41]; they divert attention away from the original suspected disease of interest, potentially leading to mismanagement of the latter; and they use up additional health-care resources through further investigations and consultations, increasing the cost of health care [34]. These risks are encapsulated in the term "victims of modern imaging technology (VOMIT)" coined by Hayward in 2003 [41].

Consequently, in clinical practice, patients should be referred for neuroimaging only if clinical indications for the presence of the disease of concern, or the need to exclude it, are strong. Evidence-based guidelines help to focus the use of neuroimaging on patients who are, according to the best current evidence, likely to benefit from and not be harmed by the results. Utilization guidelines are provided by radiological societies and by disease-oriented organizations. A comprehensive list of national and international sources for imaging guidelines is available through the NHS National Library of Guidelines (http://www.library.nhs.uk/) and the Agency for Healthcare Research and Quality (http://www.guidelines.gov/). Performing scans only for reassurance increases the risk of incidental findings, encourages the patient to expect investigations the next time they consult [33] (moderate evidence), and there is little evidence that use of investigations in this situation is anxiolytic [32].

Imaging-based for-profit screening is increasingly available [37], and use of imaging in research is common. In both situations, subjects should be warned in advance of the likely risk and the medical and non-medical implications of an incidental finding [27]. Imaging-based for-profit screening is likely to remain a significant factor because the activities of commercial screening organizations and the widespread media attention given to high-profile scientific publications, such as the paper by Vernooij and colleagues in the New England Journal of Medicine, [6] risk raising concern among the public [42]. People, concerned about their health and personal well-being, may develop the impression that they too should seek reassurance that they do not have a "ticking time bomb" [43].

Supporting Evidence

Until recently, access to investigations was limited so that only patients with good justification for the test were referred; in addition, investigations were less sensitive for the identification of small or subtle incidental findings. This is all changing. Investigations are now widely available, and the barrier to advanced imaging investigation of suspected disease has been lowered [43, 44]. In 1993, the American College of Radiology issued the ACR appropriateness criteria, scientific based guidelines for referring physicians about the appropriate use of diagnostic radiology in given situations [45]. A study, 15 years later, showed that the uptake and application of these guidelines and of other formal guidelines among referring clinicians were very low [46]. Unfortunately there is little firm evidence on how many patients are now referred for neuroimaging investigation solely for reassurance.

Most national colleges and organizations produce guidelines on the use of imaging investigations for clinical purposes based on the best evidence available at the time and regularly update these recommendations. The American College of Radiology (ACR) in the USA and the Royal College of Radiologists (RCR) in the UK produce guidelines on who to refer for imaging, what type, and when (Table 3.2). Readers should refer to their relevant national guidance, as that is most likely to be geared to the resources and practices in their country. Referral to guidelines may also help explain to the patient why investigations should be avoided unless there is very good reason.

The stress of being screened is difficult to quantify and probably depends in part upon the seriousness (in the mind of the screened population) of the disease being sought. Getting a normal test result is not necessarily as anxiolytic as some doctors might assume, although opinion concerning this remains mixed. McDonald et al. [30] assessed patient reassurance after a normal test result in patients undergoing echocardiography for symptoms or an asymptomatic murmur. All those presenting with symptoms remained anxious despite the normal test result and 39/52 people (75%) presenting with an asymptomatic murmur became anxious after detection of the murmur. Over half of these (21/39) remained anxious despite the normal echocardiogram result [30]. Similarly, a study of the effects of investigating cases of possible and probable MS, where diagnosis would not affect management, found that although anxiety seemed to be reduced by testing, overall anxiety levels did not decrease as much as anticipated. Patients also became less optimistic about their future health after testing. Subgroups of patients differed in their response to diagnostic information. Those in whom no definitive diagnosis emerged tend to be more anxious rather than being reassured by the "negative" workup. Individuals with "positive" workups became less anxious and expressed favorable feelings about the diagnostic workup even though they often faced a chronic disease [47]. In contrast, Sox et al. [48] measured clinical outcomes of 176 patients thought clinically to have nonspecific chest pain who were randomly allocated either to have a routine electrocardiogram and serum creatine phosphokinase tests (test group) or to have all diagnostic tests withheld (no-test group). Fewer patients in the tests group (20%) reported short-term disability than patients in the no-test group (46%) ($p = 0.001$). The use of diagnostic tests was an independent predictor of recovery. Patients in the test group felt that care was "better than usual" more often (57%) than patients in the no-test group (31%) ($p = 0.001$).

Some commercial screening organizations provide results of investigations in an unhelpful way to the individual, for example, which suggest that there may be an abnormality of concern when in fact there is not, which the screened individual then has to take to their family doctor for advice and treatment [38].

What Is the Expectation of Research Studies in Identifying and Reporting Incidental Findings?

Summary

Use of imaging in research is a common source of incidental findings and the subject of much debate about how best to manage them.

Guidance on how to manage incidental findings detected during research imaging is less well developed. Advice from national and international ethics and regulatory research bodies is limited and variable [27] and likely to change with evolving attempts to minimize the administration burden involved in research [49]. A large group of imaging experts, professional, grant funding, ethics, and regulatory bodies recently formulated guidance on best practice for the UK [40]. However, the evidence on which to base much practice related to incidental findings in research is lacking.

Points for consideration requiring further evaluation methods include the following. Full radiological review of all research examinations, preferably by a specialist neuroradiologist, is attractive but carries significant cost implications. Neuroradiology and radiology resource is finite and limited so that full review of all research scans is impractical in most institutions. Indeed, many imaging-based research studies are conducted in nonclinical centers with principal investigators who are not necessarily clinically qualified. Despite this, some legal authorities have stated that the reactive model, where incidental findings noted by investigators are referred for further assessment, ignores the duties owed to the subject of research and may invite litigation [50]. In addition, studies in the US showed that the institutional review board at 22% of research centers required involvement of a neuroradiologist in neuroimaging studies [51]. A further issue of importance is that many research scans, such as those used for functional MRI, would be considered entirely inadequate for diagnostic use [27]. Current opinion varies considerably [27, 52], and review of current practice reveals a wide range of methods for dealing with incidental findings in research studies. Management models range from no radiology reporting at all through "reactive radiology" where suspicious findings noticed by investigators are referred to a radiologist for an opinion, "proactive radiology" where all research images are reported, and "very proactive radiology," where images additional to those required for the research may be acquired routinely to improve detection or characterization of any incidental findings [27].

Whatever model is employed, it is important to understand that many volunteers will expect expert examination of research images to be routine. In one study which sought research volunteers opinion, the majority of volunteers expected that their images would be examined and medical anomalies would be disclosed to them, *regardless of the written information they were given during the consent process or whether the research took place in a medical on nonmedical environment* [53]. There is currently no consensus on the appropriate model to employ, and clear legal and ethical guidance is either conflicting or incomplete [27].

Supporting Evidence

Researchers have a clear and legally binding duty of care to their research subjects that includes dealing with problems arising from incidental findings [40, 54]. It has been stated that systems which rely on the identification of significant incidental findings by inadequately qualified personnel ignore the duties owed to the subject by the investigator [40, 55] and may invite litigation [50]. A review of legal precedent in the USA found only two cases related to incidental findings [56]. In the first, a control group participant in a neuroimaging study was found to have a severe AVM; the patient was referred for treatment which was unsuccessful and led to a lawsuit aimed at the treating clinicians rather than the researchers who identified the original abnormality. In the second case, failure to identify an incidental finding on a liver scan led to delayed treatment and the successful prosecution of the radiologist. The authors conclude that these legal holdings do not dictate that a researcher who fails to detect or report a potentially dangerous incidental finding on a research scan can be held to the same standard of care as radiologists or other physicians who read clinical scans for specific patients in a clinical setting. However, they do suggest that individuals whose condition worsens, or their survivors, may seek to impose liability on the person who first reviewed the scan if earlier treatment would have yielded a better clinical outcome. Other legal opinions have concluded that the relationship between the investigator and subject does not carry the same degree of fiduciary responsibility as that between clinician and his patient [55, 57], although the legal position remains relatively untested in case law [58].

Current guidance for researchers, ethics committees, and institutional review boards on how to manage incidental findings is rare or difficult to find with little or no consensus. National and supranational ethics and human rights guidance is given in various research documents but is also hard to find [27, 40].

Having a radiologist review images is likely to provide the most accurate interpretation. In general, nonradiological researchers are not used to identifying lesions that are outside their immediate sphere of knowledge (or even within it) and in addition are prone to mistaking artifacts or completely insignificant findings (e.g., falx calcification) for clinically significant abnormalities. Thus, they may cause undue alarm to research subjects. Despite this there is evidence of widespread use of variations of the "reactive radiology" approach that have been widely supported [52, 59] and implemented. Some workers have suggested that reporting of incidental findings is unnecessary or inappropriate [60, 61], whereas others believe that all research scans on healthy controls should undergo expert review [50]. Cramer and colleagues [52] described a system for the management of incidental findings in neuroimaging studies where investigators who suspected an abnormality would refer the images on a web-based system for specialist review. Over a 5-year period, 27 scans were submitted to review from an estimated 5,000. Interestingly, the abnormalities identified by the investigators showed only limited agreement with the specialist review. The authors argue that this is a cost-effective ($50 per scan reviewed) system for the management of suspected incidental findings. However, the referral rate of half a percent observed in this study must raise significant anxieties that the referral process overlooked other and potentially significant incidental findings. Interestingly, the authors state, "some investigators at our institution used this facility more than others," raising the possibility that there is wide variation in the ability of nonradiological investigators to identify potentially important incidental findings.

There is clear evidence that most research subjects expect that their images will be looked at by a competent trained individual [62]. Furthermore, this belief is not affected by information given in the consent process. However, most imaging research is not done by radiologists or even near to a radiology department and not looked at by a radiologist, so there are genuine practical difficulties and costs in obtaining review of the images. In fact, one survey showed that the most senior person who examined any images obtained during neuroimaging research examinations was usually a junior postdoctoral assistant [51]. It is somewhat unlikely that someone who has only recently completed a PhD in a focused scientific aspect of neuroimaging (e.g., fMRI or tractography) will be adequately trained to recognize or accurately interpret and manage incidental findings.

Thus, while publications from many countries suggest that many agree that research imaging should be reported by radiologists [24, 28, 53, 63–65] (strong evidence), it is less clear as to how this should be achieved in practice [66]. Although it seems unlikely that any would disagree that abnormal scans should be reviewed by specialist radiologist, there is a clear problem in developing systems that will allow sufficiently sensitive and appropriately specific identification of those examinations that need specialist review. Having a protocol in place for recognition, review and management of incidental findings is important, and this must include clear guidelines on construction of consent, the consent process and methods, and policies for disclosure [40, 59].

These issues were discussed at a UK national (with international participants) meeting on management of incidental abnormalities found on research scans held on 1st June 2010 [40] and further information, including videos and transcripts, can be accessed at http://www.sinapse.ac.uk/media/events/ethics_management.asp and the report at http://www.rcr.ac.uk/docs/radiology/pdf/BFCR(11)8_Ethics.pdf.

How to Manage Incidental Findings

Summary

Discovery of an incidental finding whose management experience is outside the expertise of the investigator should be referred for an expert opinion. It is worthwhile doing this at an early stage since it may preempt the need for further investigation and resolve anxiety. The situation should be discussed with the patient as early as possible, and subsequent investigations should be expedited.

With a few exceptions (intracranial aneurysms [67], internal carotid stenosis [68]), the management of many incidental findings is not guided by good evidence, often because the natural history of the condition is not adequately understood. In some cases, there is guidance available in literature about the management of individual conditions, which may commonly be found as incidental findings. However, the majority of these studies do not deal with the management of potentially asymptomatic incidental findings but rather with the management of the same disease when it has been discovered due to clinical presentation.

The potential negative impact on the individual subject with an incidental finding whose potential importance is unclear, or incorrectly assessed, must also be considered [24, 60]. For example, Royal et al.[60] illustrate an example of a normal subject with an abnormality of unknown significance, thought most likely to be a normal variant, which led to the participant being advised to undergo a course of periodic additional MRI exams with significant associated expense and anxiety.

Supporting Evidence

In the majority of cases, there are no randomized clinical trials describing the natural history or optimal management of asymptomatic incidental findings so that the majority must be managed on an individual basis. Table 3.3 gives a brief description of the clinical management appropriate to common asymptomatic incidental findings, together with appropriate references where possible. However, the majority of these are retrospective case reviews of symptomatic cases and may not be directly applicable in the case of an incidental finding.

There is often considerable debate in the literature concerning the optimal treatment of apparently asymptomatic disorders. One interesting example is in the management of minimally or apparently asymptomatic arachnoid cyst. Typically, surgeons have been reluctant to decompress arachnoid cyst in the absence of significant or dramatic symptoms. However, in recent years there have been a number of studies suggesting that cyst decompression improved the function of adjacent brain tissue, supporting the view that patients with clinically silent cysts may profit from decompression [69–71]. Partly in response to this, some neurosurgeons have adopted a far more aggressive approach with apparently substantial clinical benefits and a low risk of complications [72] (limited evidence).

Special Case: Applicability to Children

Summary

The majority of neuroimaging research is performed in adults, although this may change with the rising interest in use of neuroimaging to study behavioral responses and educational abilities that might predict future antisocial behavior, learning difficulties, or job-related skills [73]. Although there are relatively few studies specific to the detection of incidental findings in children, it has been shown that there is a higher prevalence of incidental findings relating to otitis, mastoid items, and sinusitis in the pediatric population (approximately 20–25%). Furthermore, investigation of the subjects shows that many are suffering from clinically significant but unsuspected pathology so that identification of signal abnormalities within the ear and mastoid cavity should stimulate referral for ENT review [74, 75]. Other pathologies appear to have similar incidence to adults so that similar concerns apply. However, the range of intracerebral incidental findings in children is less well documented than in adults, and management strategies for many pathologies differ significantly. Under these circumstances, it would seem reasonable to propose a more active form of review for studies in pediatric populations.

Supporting Evidence

There is very little information about incidental neuroradiological findings specifically in children. One small retrospective study ($n = 225$) found that the prevalence of those requiring clinical referral was low (around 7%) and only one required urgent referral [76] (moderate evidence). Other studies have identified a higher prevalence in the pediatric population. In a Japanese cohort study of 110 children, incidental findings were seen in 36.4%; however, 26.4% were due to sinusitis and/or otitis media [61]. The prevalence of incidental findings when these are excluded was 10.9%, but only one patient required urgent referral for assessment. A similar study of 666 children with a mean age of 9.8 years found incidental findings in 25.7%; 17% represented normal variants and only one patient required referral for further assessment [77]. A study of 953 children aged 5–14 years suffering from sickle-cell disease found a 6.6% prevalence of incidental findings, but again only three patients required urgent referral and over half were considered normal variants which did not require further assessment [78]. The high prevalence of middle ear and mastoid abnormalities in children, usually represented as high signal on T2-weighted images, has also been studied by two groups [74, 75], both of whom found significant prevalence of MR abnormalities (12% and 27%). Both found that in a significant proportion of these groups MR findings were paralleled by previously unidentified clinical symptoms, and both concluded that incidental findings of this kind should prompt a referral for clinical assessment. Incidental findings in the pediatric age group are likely to be little different from the prevalence of non-neoplastic findings in young adults, that is, 2.0% [8]. A major difference to adults is that most neoplasms that present in childhood need to be treated, so there is likely to be less uncertainty about whether or not to treat and when than with, for example, meningiomas in adults. Here the issue is that there are three parties affected by the finding – doctor, patient, and their parents, with substantially more anxiolytic potential.

Special Case: What Benefits Arise from Detection of Incidental Findings?

Summary

There is little evidence about the potential benefits from detention of incidental findings on brain imaging. Although early detection of abnormalities such as cerebral aneurysms or neoplastic lesions would appear to be desirable, the incidence of these is small, and definitive evidence-based guidance concerning optimal management of asymptomatic lesions is commonly unavailable. Even the benefits of identifying unruptured cerebral aneurysms are uncertain, and the benefit of treatment continues to be contentious. A large study published in 1998 showed that the annual rate of rupture of unruptured aneurysms was lower than had previously been believed [79]. Following this, the Stroke Council of the American Heart Association issued guidelines in 2000, [80] which concluded that screening for cerebral aneurysms was not warranted even in subjects where a family member had died from aneurysmal subarachnoid hemorrhage. When unruptured cerebral aneurysms are identified incidentally, current practice suggests that those less than 5 mm should be managed conservatively, those greater than 5 mm in patients below 60 years of age should be considered for surgery, and only those greater than 10 mm in diameter should be treated under any circumstances [80].

Supporting Evidence

In their large meta-analysis, Morris et al. [8] examined only the prevalence of incidental findings but reviewing the subsequent impact was beyond the remit of the study. Other studies also provide only limited information concerning the benefits or harm derived from the identification of incidental findings. Orme et al. [9] found abnormalities in 136 of 231 scans but referred only five of these for further investigation, of whom one had a sphenoid sinus aspergillus infection and the other a cerebral ependymoma. Vernooij and colleagues [6] described a particularly high incidence of brain abnormalities in a sample of 2,000 normal individuals over the age of 45. The most common abnormalities were asymptomatic infarction (7.2%), cerebral aneurysm (1.8%), meningioma (1.6%), and arachnoid cyst (1.1%). It is interesting therefore to note that of almost 250 patients with reported abnormalities surgery was performed in only two [6]. These were a single patient with a subdural hematoma and one of 35 patients with cerebral aneurysms. Although other details concerning treatment and further management are not given, the authors do state that all aneurysms except for three were less than 7 mm in diameter.

Special Case: Should Image Based For-Profit Health Screening Be Avoided

Summary

Over the past 10 years, an increasing number of companies have begun to offer for-profit clinical screening services using either whole-body CT or increasingly MRI. These services have been particularly popular in the USA and are increasingly available in Europe. They have been highly contentious largely due to the paucity of evidence showing benefit but also due to the risks of over-investigation that we have described above. In particular, whole-body CT has been heavily criticized for its radiation dose which has led to increasing availability of whole-body MRI. There has also been extensive criticism of the increasing social inequality arising from the availability of improved health care to those who can afford to pay for screening.

Supporting Evidence

The arguments concerning the potential benefit/hazards of screening, which have been discussed extensively above, apply equally to commercial screening procedures. Many correspondents [37, 81] and national organizations, including the FDA and the US National Institutes of Health, have been cautious or even critical of these services [82, 83]. Particular criticism has been directed at the use of screening investigations in the brain. Several authors have examined the potential benefits and hazards of an incidental finding of cerebral aneurysm, cerebral tumor, or common incidental findings such as Chiari malformations [37, 81]. Each has reached the conclusion that the benefits, if any, are outweighed by the potential risks of investigation and treatment. In a commentary in the Mayo Clinic Proceedings, Komotar, and colleagues state [81]:

> In New York City, brain MRI screening can be performed for less than $200, regardless of age or medical history, so that brain lesions can be detected at an earlier stage. Although this program appears to have great benefits, closer analysis shows that brain MRI scans should not be recommended for screening healthy populations because of unequal accessibility, disproportionate allocation of health care resources, screening bias, low prevalence, poor predictive value, and limited need and effectiveness of intervention. Further, early detection programs often have negative consequences, and benefit that justifies possible sequelae has not been demonstrated.

There has been little published concerning the incidence of incidental findings in attendees of commercial screening services. The available data suggest that the reported incidence is lower than in research cases with a prevalence of 2% compared to 3.4% in research subjects (weak evidence). The reason for this is extremely unclear. Dr Barnett Kramer, director of the US National Institutes of Health Office of Disease Prevention, said:

> for every 100 healthy people who undergo a scan, somewhere between 30 and 18 of them will be told that there is something that needs a workup and it will turn out to be nothing.

This represents a major apparent dichotomy between the reported incidence of incidental findings and the apparent detection rate of abnormalities which may represent a trend to overinvestigate insignificant incidental findings in patients attending screening programs. Interestingly, popularity for these services appears to have waned in the USA with closure of some companies [84].

Take-Home Tables

Tables 3.1 through 3.3 highlight prevalence of incidental findings, guidelines on use of imaging investigations from radiological societies and disease-oriented organizations, and options for management of common incidental findings, respectively.

Imaging Case Studies

Case 1: Asymptomatic 64-year-old scanned as a control subject in a study of vascular depression (Fig. 3.1a, b)

Case 2: A 56-year-old woman scanned as a control subject in a study of cerebral vascular disease (Fig. 3.2a, b)

Table 3.1 Prevalence of incidental findings

Incidental finding	Prevalence (%)
Arachnoid cyst	0.5
Aneurysm	0.35
Meningioma	0.29
Cavernous malformation	0.16
Hydrocephalus	0.1
White matter lesions suggestive of an inflammatory disorder	0.06
Low-grade glioma	0.05
Arteriovenous malformation	0.05
Common developmental variants, rarely of medical importance	Precise unknown

Adapted with permission from Morris Z, Whiteley WN, Longstreth WT, Jr et al. Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. Br Med J. 2009;339:b3016

Table 3.2 Guidelines on use of imaging investigations from radiological societies and disease-oriented organizations

Radiological Societies
American College of Radiologists http://www.acr.org/secondarymainmenucategories/quality_safety/guidelines.aspx
Royal College of Radiologists http://www.rcr.ac.uk/content.aspx?PageID=995
Canadian Association of Radiologists http://www.car.ca/en/standards-guidelines/guidelines.aspx
British Society of Paediatric Radiologists http://www.bspr.org.uk/guidelines.htm
National Organizations
Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/guidelines/published/index.html
National Institute for Clinical Excellence http://guidance.nice.org.uk/
UK National Guideline on Management of Incidental Findings in Research Imaging http://www.rcr.ac.uk/docs/radiology/pdf/BFCR(11)8_Ethics.pdf [40]
Disease-Oriented Organizations
European Stroke Organization http://www.eso-stroke.org/recommendations.php?cid=9&sid=1
American Heart Association (cardiac disease and stroke) http://www.americanheart.org/presenter.jhtml?identifier=2158
European Federation of Neurological Societies http://www.efns.org/Guideline-Archive-by-topic.389.0.html

Table 3.3 Summary of the management options for common incidental findings

Incidental finding	Commonest potential complications	Treatment of asymptomatic findings
Arachnoid cyst	Pressure on adjacent brain structures	Neurosurgical decompression is not indicated for asymptomatic cysts (no RCTs [72])
Aneurysm	Hemorrhage (risk influenced by aneurysm site and size)	Endovascular coiling or neurosurgical clipping is available, but there is uncertainty about their use because of the lack of published RCTs comparing treatment with conservative management for asymptomatic aneurysms
Meningioma	Pressure on adjacent brain structures	Neurosurgical excision and radiotherapy tend to be used when meningiomas cause symptoms (no RCTs [85])
Cavernous malformation	Hemorrhage and epileptic seizure(s)	Neurosurgical excision and stereotactic radiosurgery are available, but there are no case series or RCTs supporting their use for asymptomatic cavernous malformations [86]
Hydrocephalus	Headache and drowsiness	Intervention is often not indicated for people without symptoms [87]
White matter lesions suggestive of an inflammatory disorder	Later development of multiple sclerosis	Immunological treatments are not indicated. Cautious medical review and advice may be needed [88]
Low-grade glioma	Pressure on adjacent brain structures and epileptic seizure(s)	Neurosurgical excision may be used, but who to treat and when are uncertain (no RCTs). Occasionally more malignant primary brain tumors like glioblastomas have been reported as first presenting during scanning for other purposes
Arteriovenous malformation	Hemorrhage and epileptic seizure(s)	Endovascular embolization, neurosurgical excision, and stereotactic radiosurgery are available. There is an ongoing RCT comparing treatment with conservative management for unruptured AVMs
Common developmental variants, rarely of medical importance[a]		May alarm nonexpert

RCT randomized controlled trial

[a]Additional common developmental or normal variants that are of little health relevance but may alarm the untrained observer include mega cisterna magna, callosal lipoma, asymmetrical ventricles, and enlarged perivascular spaces. Other anomalies that may sometimes be of health relevance and that are not listed above include Arnold Chiari malformations, cerebellar atrophy, and pineal cysts

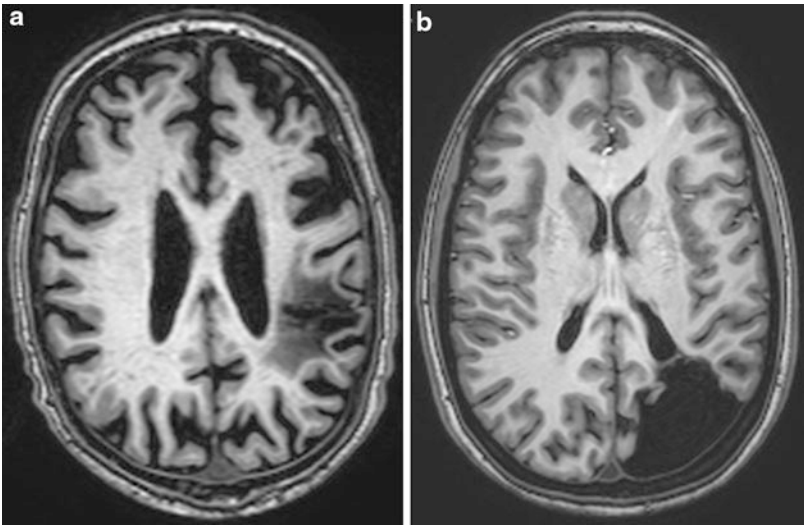

Fig. 3.1 (**a**) An asymptomatic 64-year-old scanned as a control subject in a study of vascular depression. The scan reveals a large long-standing left-sided cerebral infarction. (**b**) A 24-year-old normal volunteer for a functional MR study. Scan shows a large left-sided posterior abnormality believed to represent a long-standing ischemic insult. The patient was referred for clinical assessment and no significant neurological deficit could be demonstrated

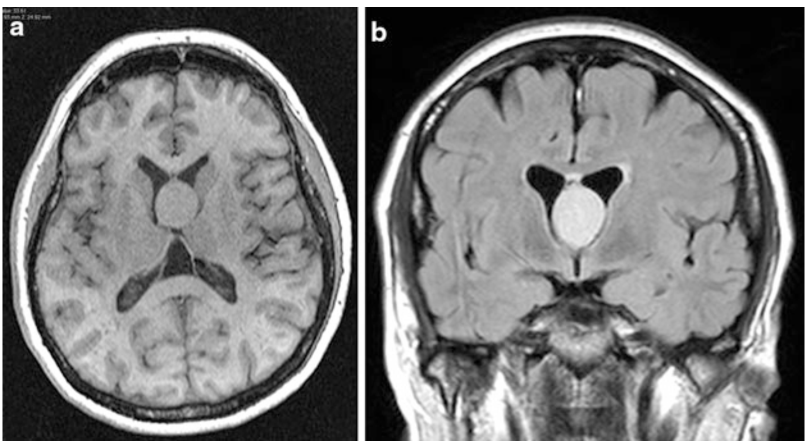

Fig. 3.2 Images from a 56-year-old woman scanned as a control subject in a study of cerebral vascular disease. The scans show a large intraventricular tumor thought most likely to be a colloid cyst. The patient was referred for a neurosurgical opinion, and although she was entirely asymptomatic, the lesion was treated by surgical excision, largely due to the patient's underlying anxiety concerning the diagnosis

Future Research

It should be clear from the forgoing that there are many unanswered questions concerning the incidence and management of incidental findings in clinical practice, health services or commercial screening, and research. The incidence of many incidental findings varies with age, as some conditions are simply more common at some ages than others, but as yet there are too few age-specific studies that published this data.

Population-based imaging studies, health-care providers, and other organizations should endeavor to record and publish information on their incidental finding rates, the medical consequences, and any personal consequences for the patients or volunteers.

For many incidental findings, there is a lack of evidence from well-conducted population studies on the natural history or the finding, the likelihood of progressing to symptoms, or any life-threatening consequences. More information on, for example, vascular malformations such as cavernomas, aneurysms, and developmental lesions should continue to be collected. Centralized health-care statistics could play a key role in facilitating this, where such exist. Consideration should be given to establishing incidental findings registries, making use of internet and image banking expertise that is now emerging. Without better information on natural history, it will be difficult to provide good advice and appropriate medical management.

As a result of the lack of the above, and for many other reasons, there is also a lack of information on the best medical management in relation to specific treatment or the need for regular monitoring if it is decided that no treatment is necessary at the time of detection. This is not a problem that is unique to incidental findings but also affects other conditions like prostate cancer where it is still unclear whether early detection of marginally raised prostate-specific antigen by screening and then treatment is beneficial for the majority or not.

The impact of the additional workload generated by injudicious requests for imaging by clinicians, or use by for-profit screening companies, or in research, on private or publicly funded health-care services has not been quantified but is likely to be considerable. It is also likely to further overload already overloaded health-care providers, detracting from the evidence-based care that they are funded to provide to symptomatic patients, particularly in publicly funded health-care systems. Imaging requests should always be kept to a minimum to help avoid spurious findings and, in the case of CT scanning, to reduce radiation doses. Cost estimates of the likely impact of incidental findings would help health-care providers to manage their use of imaging investigations better.

There is little information on volunteers and patients attitudes toward, or awareness of, incidental findings. It is probably fair to assume that most people would rather not have an incidental finding as it is likely to raise anxieties even if it turns out to be of no medical consequence. Nonetheless, how best to manage these from the patient or volunteer's point of view is currently largely based on speculation and a few case reports. Further studies are needed to determine the best ways of managing incidental findings to minimize anxiety to patients or volunteers as this would help develop policies for imaging research and clinical practice.

The true full extent of the wider implications of incidental findings, such as employment, insurance (health, travel, life, etc.), and mortgages for house purchase, is not well known and probably varies. However, with the increasing use of imaging, it will be important for insurance companies and employers to develop thoughtful, equitable, and sensible approaches to otherwise healthy individuals.

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