

# Navigating the grey areas: The Ethics of Incidental Findings in Brain Imaging Research

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## ABSTRACT

This paper explores the ethical implications of incidental findings during brain imaging research and critically examines aspects of autonomy and distributive justice in this context. Concepts of autonomy and distributive justice must be balanced with the cost effectiveness of disclosing and further investigating all incidental findings. This paper outlines arguments for and against disclosure and recommends the use of the EUSTICE framework in ethical decision making. This existing framework can aid researchers in developing an ethical protocol to disclose pathologies that carry a serious clinical significance whilst adhering to the values of distributive justice.

## INTRODUCTION

Brain imaging research can be understood as the use of non-invasive methods such as

Magnetic Resonance Imaging (MRI), Computed Tomography (CT) and Positron Emission Tomography-Computed Tomography (PET-CT) to research various pathologies such as substance misuse disorders, epilepsy and response to psychoactive agents.<sup>1, 2</sup> These techniques are becoming increasingly common in clinical research internationally due to their ability to provide an accurate assessment of disease activity and spread in a non-invasive manner.<sup>3</sup> Brain imaging research produces a large volume of scans, which in turn increase the opportunities for incidental findings to be detected, as the higher number of scans naturally lead to a greater chance of uncovering unexpected anomalies in healthy volunteers.<sup>1</sup>

Much scholarship has focused on whether it is or is not obligatory for clinicians to disclose incidental findings to participants, according to the two major principles of ethics: Beneficence and Non-Maleficence. Although these moral obligations form the bedrock of modern medical ethics, their tone is primarily theoretical in focus, and thus offers limited practical guidance to healthcare professionals in clinical settings.<sup>1</sup> Thus, it is important to consider what is owed to participants in terms of distributive justice and patient autonomy.<sup>1</sup>

### Incidental Findings and Clinical Significance

In this context, incidental findings in healthy volunteers are defined as observations that have potential clinical significance, which are unrelated to the purpose of the clinical study.<sup>1</sup> The prevalence of these in brain imaging research ranges from 2.7% to 22%, with its likelihood increasing with sensitivity of the scan and age.<sup>4</sup> Additionally, 1.4% to 8% require referral for immediate clinical evaluation due to the presence of serious abnormalities (e.g. brain tumour, demyelinating disease, aneurysm or arteriovenous malformation).<sup>1, 4</sup>

Bioethicists have reached consensus regarding incidental neuroimaging findings, based on the fact that researchers bear at least some care obligations to participants.<sup>1</sup> In most cases, three factors are relevant. Firstly, the scientific validity; referring to the occurrence and reliability of the incidental finding. Second, the clinical utility, that is, the perceived

clinical significance of the finding, and finally, actionability which refers to the potential for treatment.<sup>1</sup> An unruptured intracranial aneurysm (UIA) is exemplar of this, as it is the most common incidental finding on neuroimaging with a prevalence of 3% in the healthy adult population and is life threatening upon rupture.<sup>5</sup> Depending on lifestyle factors, site and size of aneurysm, the patient is offered management options which include definitive surgical management, e.g. coil embolisation, or conservative measures where UIAs are monitored over time and the patient is advised to avoid contact sports.<sup>1, 6</sup> Disclosure of such a finding may enhance patient autonomy as they would be empowered to discuss management options with their physician regardless of the risk of rupture. On the other hand, disclosure of nonsignificant benign calcifications that commonly occur in pineal gland or choroid plexus in older individuals may not promote patient autonomy. Sharing of nonsignificant information can create unnecessary anxiety and not add any value to awareness of their own health information.<sup>1</sup> Thus, the uncertain nature of the findings and the uncertain significance of this to the participant raises the question of whether disclosure contributes to patient autonomy.<sup>1</sup>

### Patient Autonomy

Autonomy as a concept was first originated by the Ancient Greeks and translates to self-determination.<sup>7</sup> It was legally established in medicine in 1914 by Cardozo who stated that "Every human being of adult years and sound mind has the right to determine what shall be done with his own body".<sup>8</sup> Respect for research participant's autonomy also forms a key principle in the Declaration of Helsinki of 1964 (updated in 2013), which is an ethical framework for research that involves human subjects as participants.<sup>9</sup>

Autonomy can be fulfilled by supporting a reciprocity-based obligation. Illes and colleagues<sup>11</sup> described how participants contribute to research by generating health data, and therefore, researchers are obligated to reciprocate this benefit, by providing participants with useful information relevant to them. Failure to disclose incidental findings displays a lack of respect, as researchers are treating participants as a "mere means" to accomplish research goals, instead of enhancing their ability to self-determine or contribute to their decision-making power.<sup>10, 11</sup>

Others disagree, arguing that revealing insignificant incidental findings e.g. benign calcifications might lead to participants misunderstanding its long-term implications.<sup>1</sup> For example, a participant may have an incidental finding of a benign brain cyst causing no symptoms and presenting relatively low long-term risk. However, a participant could deem this as fatal due to misunderstanding the significance of its presence and forming unsubstantiated conclusions about their health status. This participant could then proceed to spend their savings on multiple investigations and management procedures, even though the presence of pathology is of minimal significance from a medical perspective.<sup>1</sup> Autonomous self-governance cannot be promoted by distorted perceptions of information about one's clinical condition.<sup>1</sup>

Graham and colleagues<sup>1</sup> conclude that it is ethically responsible to provide consultations to those participants who've experienced incidental findings. Offering detailed

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information about their findings and arranging further investigations can enhance autonomous self-governance through the promotion of patient knowledge and involvement. However, this places significant economic pressures on researchers, and research grants often do not account for ancillary care – care that research participants need “but that is required neither to successfully answer the researchers’ scientific question nor to avoid or mitigate harm resulting from participation in the research”.<sup>10, 11</sup>

Disclosure of serious pathologies with known clinical significance (e.g. brain tumour) promote patient autonomy as they hasten clinical assessment and thus prevent life-threatening events.<sup>1</sup> However, the uncertain significance of pathologies (e.g. benign brain cysts) combined with economic pressures means that autonomy as a principle on its own does not support disclosure of information.<sup>1</sup> Thus, alongside autonomy, aspects of distributive justice must be considered.

## Distributive Justice

Distributive justice refers to the fair and equitable distribution of resources within a society.<sup>12</sup> Douglas Mackay argues that citizens are entitled to basic care as a matter of distributive justice.<sup>12</sup> Alongside moral obligations, researchers also have ‘institutional obligations’, that is professional responsibilities on behalf of the institution.<sup>12</sup>

Researchers who are sponsored by agencies or organisations that are funded by the state, have an institutional obligation to “conduct their research in a way that is consistent with the state’s duty of distributive justice to provide its citizens with access to basic health care”.<sup>14</sup> This is because the state would not sponsor agents to conduct research who do not account for its principles surrounding distributive justice.<sup>14</sup> Thus, researchers have a moral and institutional obligation to disclose

incidental findings along with providing a basic standard of care that the state would normally owe its citizens.<sup>14</sup>

Neuroimaging scans of healthy individuals to screen for abnormalities are not currently a routine requirement of basic care, and so, some would argue that institutional obligations do not apply.<sup>1</sup> Although a small minority of patients may benefit from having a significant abnormality detected earlier than would be possible with standard care, it is unjustified to consider brain imaging scans as a form of basic care, considering the risk of false positives, the costs of further investigations and existence of more effective methods of identifying brain abnormalities e.g. cranial nerve and neurological examinations.<sup>15</sup>

The philosophy of distributive justice would posit that if neuroimaging does not form a part of basic care to which healthy citizens are normally entitled, then researchers do not carry a responsibility to generate further quality scans to better visualise or detect incidental findings, in addition to those already generated for research.<sup>1</sup> Furthermore, not providing ancillary care can be further justified by fulfilling institutional obligations of basic care, through making appropriate referrals to state-based primary care facilities where necessary.<sup>1</sup>

## EUSTICE Framework

Sonu Bhaskar discusses the complexities that surround disclosure of incidental findings in brain imaging research and proposes an equity and justice informed ethical framework, known as the EUSTICE framework.<sup>13</sup> This framework outlines a step by step guide for brain imaging researchers to use along with important reminders of clauses to include in consent forms to prevent legal liabilities as a consequence of incidental findings.

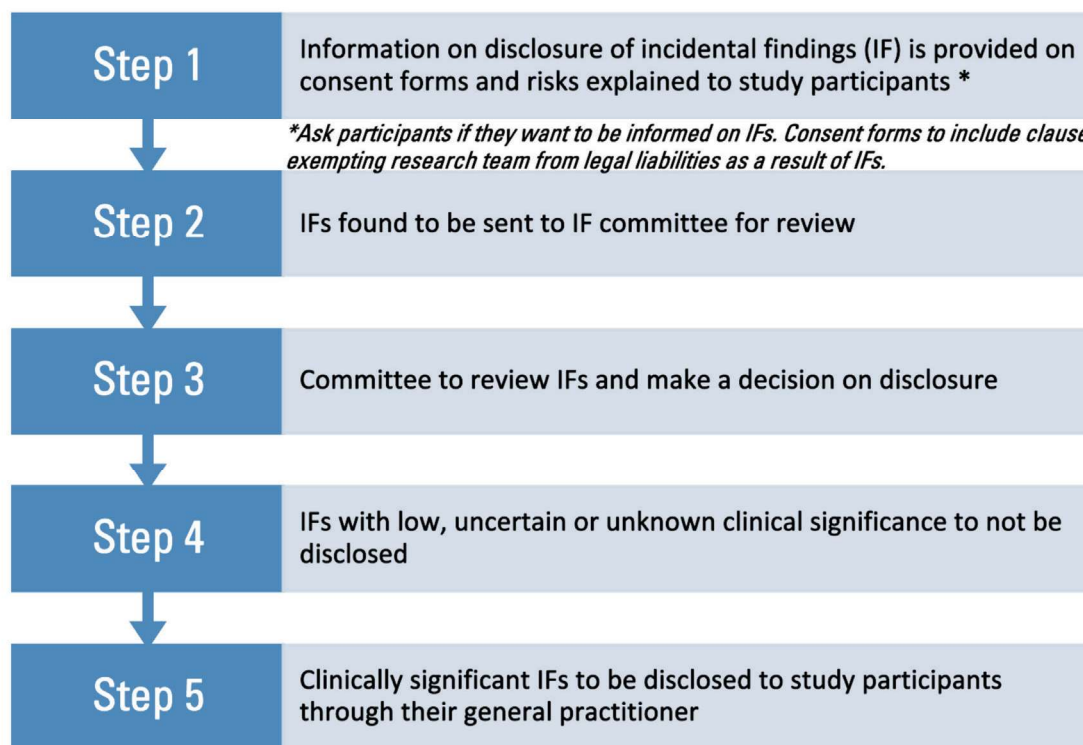


Figure 1: A diagram outlining the Ethical framework informed by distributive justice to guide brain imaging researchers in the handling and disclosure of incidental findings, adapted from the framework outlined by S Bhaskar.<sup>12</sup>

## CONCLUSION

The ethical dilemma of disclosing incidental findings is a complex topic where there is no black-and-white answer and continues to remain a grey area that researchers need to navigate. According to the Declaration of Helsinki, researchers must respect autonomy and fulfil ethical responsibilities by disclosing clinically significant pathologies that may be deemed as life-threatening. However, disclosing findings with low, uncertain or unknown significance may not promote patient autonomy and cause unnecessary negative effects on one's mental health, along with the fiscal risk of expenditure for further investigations and management.

The political philosophy of distributive justice posits that researchers have an institutional obligation to provide basic care, and therefore should facilitate primary care referrals, especially if ancillary care is not accounted for by research grants, placing economic pressures on their research projects.

The complexities of disclosure in brain imaging research present a significant challenge, necessitating a careful balance between promoting patient autonomy and addressing economic limitations imposed by the principles of distributive justice. Researchers in this field should prioritise the development and implementation of clear, comprehensive frameworks for managing incidental findings. These frameworks could be newly devised or adapted from existing models, such as the EUSTICE framework, which provides a structured approach to such issues.

A critical component of these frameworks is the precise definition of what constitutes 'significant' versus 'minimally significant' incidental findings. Establishing these definitions ensures that researchers can consistently and transparently communicate with participants about the potential implications of incidental findings. This clarity is essential for obtaining informed consent, as participants must understand the scope and nature of the information that may be disclosed to them. Informed consent is not merely a procedural formality but a cornerstone of respecting and upholding participants' rights to autonomous self-governance.

In addition to respecting individual autonomy, these frameworks must address the broader ethical imperative of distributive justice. This involves considering the economic implications of managing incidental findings and ensuring that resources are allocated fairly and efficiently. By doing so, researchers not only protect the rights and interests of individual participants but also uphold their ethical responsibilities to society at large. Implementing such comprehensive and ethically sound frameworks will ultimately enhance the integrity and trustworthiness of brain imaging research, fostering an environment where participant interests and distributive justice responsibilities are both diligently fulfilled.

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### ANSWERS TO QUIZ ON PAGE 202

- A1. Merkel cell carcinoma
- A2. Seminoma of the testis
- A3. Tinea
- A4. Small cell carcinoma
- A5. Scabies
- A6. LCIS (lobular carcinoma in situ)
- A7. Bullous pemphigoid
- A8. Serous carcinoma of the ovary