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Managing incidental findings in total body PET/CT studies: balancing ethical considerations and resource constraints

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Abstract

Total body positron emission tomography (TB-PET) represents a major advancement in molecular imaging. While this technology expands the capabilities of PET imaging for both research and clinical applications, it also introduces significant ethical and operational challenges, particularly in the management of incidental findings. Current ethical and regulatory guidance acknowledge the need to address incidental findings that arise during research studies, but often provides ambiguous or insufficient direction. This leaves institutions to independently balance participant safety, ethical responsibilities, and resource constraints. Using the Australian National Total Body PET Facility as a case study, this article explores strategies for managing incidental findings in PET/CT research. By comparing research workflows with clinical practices, we highlight critical differences and propose a practical framework to help institutions establish ethically sound and feasible protocols. This framework aims to balance the duty of care to the participant with the logistical demands of PET research, contributing to the ongoing discourse on ethical imaging practices and offering guidance for managers of TB-PET research facilities.

Keywords: Incidental findings, Total body PET, Risk-cost analysis, Nuclear medicine

Introduction

Incidental findings are not uncommon in medical imaging research, with their prevalence and significance largely depending on the imaging modality and the population being studied (Morin et al. 2009; Graham et al. 2021; O'Sullivan et al. 2018). The term *incidental finding*, or *incidentaloma*, is typically defined in the literature as *"a finding that has potential health or reproductive importance, unknown to the participant, which is discovered unexpectedly in the course of conducting research, but is unrelated to the purpose and beyond the aims of the study"* (Wolf et al. 2008; Booth et al. 2014; Schaare et al. 2022). The prevalence of such unexpected findings is influenced by the specificity of the radiopharmaceutical used, as well as the clinical context of the imaging procedure. For example, in a general patient population undergoing positron emission tomography (PET) for any clinical indication, with a non-specific tracer like [^{18}F]FDG, whole-body scans can reveal unexpected new

pathologies in up to 75% of scans (e.g., Adams et al. 2018). However, while the majority of these findings are benign or clinically insignificant, a small but notable proportion (3–8%) may represent previously undiagnosed malignancies (Casselden et al. 2019; Bentestuen et al. 2022).

These incidental findings often present major ethical and logistical challenges that are not always clearly addressed in current regulatory guidelines and there is no global consensus on their appropriate management (Booth et al. 2014; Wardlaw et al. 2015; Kwee et al. 2023; RCR 2011). With the increasing use of total body (TB) PET scanners in both clinical and research settings (Daube-Witherspoon et al. 2022), the issue of incidental findings is likely to become increasingly prevalent. Long axial field of view (AFOV) scanners capture images of the entire body (or from most of the major organs), regardless of whether the primary focus is on neuroscience, cardiovascular, or other specific organ systems and, therefore, the potential for detecting unexpected or unrelated abnormalities is significantly increased (Hicks et al. 2024; Ng et al. 2022). However, managing incidental findings can divert limited resources from the primary objectives of a study, straining tight research budgets and complicating the achievement of research outcomes. Moreover, even beyond the budgetary considerations, there is no clear consensus on the risk-benefit balance of informing research participants about every incidental finding (RCR 2011). Determining where to draw the line - what findings warrant disclosure based on their potential clinical significance - is inherently complex. As a result, incidental findings in research settings present unique challenges that may require decisions about the detection, disclosure, follow-up, and management of these findings (Graham et al. 2021; Vanderschaeghe et al. 2018), which often differ from standard clinical decision pathways.

The management of incidental findings in PET/CT research facilities differs substantially from that in purely clinical settings, largely due to differences in resource availability, such as funding the cost of clinical reviews and access to trained radiologists. In clinical practice, imaging is performed to address a specific clinical question, with each scan systematically reviewed by trained radiologists as part of routine care. Incidental findings are promptly flagged and managed within the same clinical framework. In research settings, however, resource constraints often limit the capacity for comprehensive clinical review. For example, some research facilities operate under an integrated operating model, where clinical and research teams overlap. Although resources are shared, this approach may strain overburdened radiologists, as research scans are performed on top of busy clinical workloads. Other facilities operate entirely independently from clinical settings, requiring most tasks, such as operating the scanner or clinical reporting, to be outsourced to external staff or collaborators. Our research facility, on the other hand, has adopted a hybrid operating model whereby research and clinical services coexist, but operate separately. For example, our PET/CT scanner, whose capacity is shared equally between research (managed by the University of Sydney) and routine clinical operations (managed by Royal North Shore Hospital), operates within a clinical environment (with access to nurses and technologists), but without access to hospital radiological resources for research scans, which are fully allocated to the clinical service. Consequently, radiological reviews of research scans (when required) are outsourced, increasing the costs and potentially delaying research outcomes.

A review of current ethical and regulatory guidelines suggests the need for a clear plan to manage findings from research imaging, including protocols for identifying, communicating, and addressing incidental findings (Scott et al. 2024). However, guidance is often not explicit, and difficult to locate within ethics and regulatory frameworks (RCR 2011). For example, in Australia, the ethical obligation is not necessarily to disclose findings, but on the need to prepare a thoroughly reviewed and approved plan to manage such findings, whether that involves disclosure, non-disclosure, or another course of action (National Health and Medical Research Council 2023). This plan must be reviewed by a Human Research Ethics Committee (HREC) and institutional governance committees. The section "Communication of research findings or results to participants" of the National Statement (National Health and Medical Research Council 2023) is fundamental to understanding the ethical obligations and the considerations to inform preparation of an ethically defensible plan. Internationally, organizations such as the U.S. National Institutes of Health (NIH) and the World Health Organization (WHO) provide similar guidelines (Seleiro et al. 2018), advocating for transparency, ethical management, and balancing participant rights with researcher obligations. However, these guidelines leave room for interpretation, especially regarding whether findings should be disclosed and the extent of responsibility researchers or service providers have in ensuring research participants receive appropriate follow-up care.

This article aims to explore the ethical and operational challenges arising from PET/CT imaging research, with a particular focus on the Australian National Total Body PET Facility in Sydney as a case study, but discussed within a broader context and general applicability. By examining the workflows and processes within our Facility and contrasting them with those in clinical PET settings, we offer an insight into how the research environments may affect the management of incidental findings. We aim to propose a robust framework and set of guidelines that research institutions can adopt when establishing their incidental findings protocol. Within the constraints of a research environment the proposed framework prioritizes participant well-being by establishing clear, ethically defensible pathways for managing incidental findings while safeguarding the integrity of the research process. This includes addressing resource limitations, defining the scope of responsibility for reporting findings, and providing strategies to minimize the impact of incidental findings on study timelines and budgets.

Incidental findings: challenges with PET/CT imaging research

Long axial field of view PET

Extended AFOV PET scanners, such as the Siemens Biograph Vision Quadra (Prenosil et al. 2022) and the United Imaging uEXPLORER (Spencer et al. 2021), have transformed clinical and research PET imaging, by enabling shorter scans and/or reduced radiation exposure without compromising image quality, as well as dynamic whole body studies. However, these benefits also introduce a new set of challenges, particularly regarding the management of incidental findings (Ng et al. 2022). Conventional PET/CT scanners typically focus on specific anatomical regions, such as the brain, heart, or a localized tumour site, limiting the scope for detecting incidental findings outside of these targeted areas. In contrast, long AFOV scanners capture images of most, or all, of the body in one acquisition, substantially increasing the likelihood of identifying unexpected

abnormalities across various organs and tissues that are unrelated to the study's primary objectives. This introduces a complex ethical question: are researchers obliged to thoroughly review the entire whole-body dataset or focus only on the region of interest and disregard the rest (Kwee et al. 2023)?

Non-diagnostic or non-clinically approved protocols

While clinically approved protocols are typically optimised for diagnostic image quality and radiation exposure for both PET and CT modalities (Bertolini et al. 2020; Huang et al. 2023), experimental research protocols often incorporate quite different acquisition and reconstruction parameters optimised to address specific research goals. These may include dynamic imaging with increased temporal resolution or unconventional dosing regimens to improve the characterisation of pharmacokinetics and tracer uptake (Chalampalakis et al. 2021). The exploratory nature of these protocols can impact the interpretability and diagnostic utility of the images, potentially influencing the detection or clinical characterization of incidental findings. Suspected incidental findings may be deemed inconclusive, creating a need for additional diagnostic tests or follow-up imaging. This additional imaging not only increases the financial and logistical burden on the research team (and potentially the participant), but also raises ethical concerns by potentially exposing participants to more radiation than initially intended, as well as causing increased anxiety from follow-up procedures.

Complementary whole body CT scans

While incidental findings in FDG-PET imaging are well documented (Adams et al. 2018), less attention has been given to abnormalities detected on associated CT scans. A complementary CT scan is always performed for attenuation correction and anatomical localisation, typically with low or ultra-low dose protocols, which prioritise minimal radiation exposure over diagnostic evaluation (Prieto et al. 2021). Techniques such as tin filtration may be also be used in experimental protocols or in studies with vulnerable populations (e.g. paediatrics) to substantially reduce the delivered radiation dose, but making them suboptimal for detailed diagnostic evaluation (Mostafapour et al. 2024). If a scan reveals a possible abnormality but lacks sufficient image quality for confident diagnosis, there is an ethical dilemma: should the participant be informed and a follow-up diagnostic CT be performed, or would this cause undue distress over an uncertain finding? Additionally, researchers may not have the expertise to interpret such findings, placing further responsibility on radiologists or clinical specialists who were not originally part of the study protocol. This challenge is further compounded with long AFOV PET/CT scanners, where a whole-body CT scan is now almost always acquired.

Novel radiopharmaceuticals

The use of novel radiopharmaceuticals which have not yet been established in clinical practice and may not even have been previously evaluated in human subjects, presents significant challenges in the interpretation and management of incidental findings in research studies. Unlike commonly used radiotracers, such as [18F]FDG, for which extensive data exist on normal and abnormal uptake patterns in a wide variety of clinical conditions, novel tracers typically lack a well-characterized biodistribution, making it

difficult to determine whether an unexpected finding is clinically relevant. For example, PSMA expression is known to occur in several non-prostatic tissues (Siva et al. 2020), potentially resulting in incidental detection of conditions unrelated to the primary research question. Similarly, PET radiopharmaceuticals used in neurological research may reveal findings beyond their intended scope. Novel amyloid imaging agents, commonly used to assess Alzheimer's disease pathology, have been reported to highlight extracerebral amyloid deposits, including those seen in cardiac amyloidosis (Genovesi et al. 2021). While such findings may have clinical relevance, their significance in asymptomatic individuals remains uncertain (Zhao and Fang 2016). This uncertainty complicates the ethical obligations of researchers regarding the reporting of suspected findings, as it is unclear whether these findings represent disease or normal physiological variability. This is particularly relevant to experimental tracers for novel molecular targets. Enhanced uptake outside the intended target region may be unexpected, leading to potential over-interpretation or unnecessary follow-up testing, which increases patient risk and healthcare costs, as well as putting extra pressure on what is often an already stretched healthcare system.

Limited resources

Research studies often face tight financial constraints, focusing resources on specific scientific goals rather than managing incidental findings. Unlike clinical settings, where imaging data are routinely reviewed by radiologists, research imaging aims to collect data for study objectives, with scans processed collectively and typically analysed by non-clinical experts. Routine radiological review of research scans is impractical due to high costs, logistical challenges, and the limited availability of trained radiologists, who are already overburdened with clinical work. The growing volume of research imaging data, particularly with advanced technologies like TB PET, further exceeds the capacity of the current radiology workforce (RCR 2011). These challenges underscore the need for scalable, cost-effective strategies to manage incidental findings in research imaging.

Lack of participant's clinical history

The lack of a comprehensive clinical history for study participants, presents a significant challenge when interpreting research PET/CT scans. Without a detailed medical record, physiological changes or other benign processes, can be misinterpreted as pathological (Pijl et al. 2021), leading to an increased risk of false-positive findings. Benign processes like post-surgical inflammation, reactive lymph nodes, or recent vaccinations can mimic serious conditions such as metastases, potentially prompting unnecessary follow-ups, additional imaging, or invasive procedures, causing participant stress. The consequences of such over-diagnosis are far-reaching (Pini et al. 2024; Brodersen et al. 2020). Over-diagnosis also burdens healthcare systems with unwarranted interventions, diverting resources from those in need and delaying research timelines as participants are sidetracked by incidental findings.

Ethical considerations

Likelihood of false positives

Although exploratory imaging protocols can occasionally result in suboptimal PET or CT image quality, potentially impacting the diagnostic utility of the images, long AFOV

PET/CT systems are typically capable of producing images with substantially superior quality compared to conventional PET/CT scanners. The enhanced signal-to-noise in reconstructed PET images may also increase the likelihood of detecting small lesions that may or may not be clinically relevant (Chen et al. 2024; Ng et al. 2022). While the superior sensitivity and image quality are invaluable for advancing research objectives (e.g., enabling the detection of subtle physiological or molecular changes), they also introduce challenges in managing suspected incidental findings.

Obligation to inform participants

Despite challenges, there is a widely acknowledged ethical obligation to inform research participants of incidental findings that are clinically significant, especially if treatable and potentially life-threatening (Graham et al. 2021). Failing to disclose such findings risks harm to the participants, conflicting with the ethical obligation to avoid harm and to exercise reasonable care (Koplin et al. 2020). Participants have the right to be informed, as early intervention could have a significant impact on their health outcomes. As such, the informed consent process is essential in managing expectations around incidental findings (Bunnik et al. 2017). Even with clear consent, there remains an ethical obligation to disclose findings that could have serious health implications. However, disclosing findings without clear medical context or guidance can cause psychological distress, particularly if the significance of the finding is uncertain.

Balancing resources and enabling research

To address this tension between resource constraints and ethical obligations, several strategies can be employed (see Table 1). Establishing a clear protocol for the management of incidental findings helps streamline decision-making and clarifies the study's obligations to participants. Also, partnering with clinical specialists or medical centres allows for the referral of participants when incidental findings are identified. While the research team may not have the resources to address findings directly, collaboration with healthcare providers can ensure that participants are guided toward appropriate follow-up care. However, the question of who bears the cost of follow-up investigations and care related to incidental findings remains contentious and jurisdiction-dependent (Wardlaw et al. 2015). For example, in countries such as the USA, which lacks a universal healthcare system, managing these costs often falls to participants, raising equity concerns.

Participant consent and expectations

One of the foremost ethical challenges in managing incidental findings during TB PET studies is setting realistic expectations for participants. Long AFOV scanners offer whole-body imaging, which often leads research participants to assume they are receiving a comprehensive health check-up. However, it is essential to clarify that these studies are designed for research purposes, not for clinical diagnosis. Participants may consent to the research under the impression that any health abnormalities will be identified and communicated to them (Kirschen et al. 2006), which creates a delicate balance between transparency and the intended scope of the study. Researchers must emphasize in the consent process that the imaging is for research, and incidental findings

Table 1 Strategies for managing incidental findings within a research environment

ID	Strategy	Short description	Ethical risk	Financial cost	Risk	Cost
A	Thorough review of all scans for incidental findings by expert radiologists	All PET/CT scans undergo review by specialist radiologists. Incidental findings are flagged, reported, and managed through clinical follow-up.	Very low risk of missing significant findings, but may lead to over-diagnosis, patient anxiety, and unnecessary follow-ups.	Very high cost due to radiologist fees and follow-up tests. Increased pressure on potentially already stretched resources.	1	9
B	Selective review of clinically significant findings determined by trained radiologist	Incidental findings are only reported if deemed clinically significant by a radiologist. Less critical findings are ignored unless they are suspicious.	Low to moderate risk of missing subtle or evolving conditions, but ensures better resource allocation.	Moderate to high cost as fewer scans are reviewed and fewer follow-ups are needed.	3	7
C	AI-assisted detection of incidental findings for all scans	AI tools are used to pre-screen scans for incidental findings, highlighting areas of concern for further review by either researchers or radiologists.	Moderate risk as AI may have limitations in detecting rare or subtle findings. Model bias could be an example of increased risk.	High upfront cost for AI development and integration, but moderate long-term human resource costs.	5	6
D	Trained radiologists review only the low-dose CT images for incidental findings	Only the low-dose CT image is reviewed, primarily for gross abnormalities. The PET image is ignored unless something specific is seen on CT.	Moderate to high risk. Some issues may be missed on PET or low-dose CT, but highly significant issues will be caught on CT.	Moderate cost since only CT is reviewed. Costs could be higher for long axial FOV systems where the whole body is reported.	7	5
E	Targeted review only for high-risk participants or projects	Only participants (or projects) with known risk factors (e.g., family history of cancer, previous surgeries) have their scans reviewed by a radiologist.	Moderate to high risk, as serious conditions may be missed on healthy volunteers.	Moderate to low cost, as reviews are limited to high-risk individuals.	7	3
F	Research team reviews all scans with radiologist consultation and escalation	Research staff systematically screen all scans specifically for identifying any incidental findings, escalating any suspicious cases to an expert radiologist.	Low to moderate, risks mitigated by radiologist oversight. Initial non-specialist screening may lead to missed cases.	Moderate with lower radiologist involvement but increased research staff workload.	4	5
G	No review of scans. Participant-informed consent for incidental findings	Scans are used strictly for research purposes, and no one reviews them for clinical abnormalities. Participants are informed that no clinical evaluation will be provided.	Very high risk of missing potentially life-threatening, but treatable, findings.	Very low (or no) costs incurred for radiological reviews.	9	1
H	Proposed framework	All scans are briefly reviewed for standard QA by a technologist or a researcher who flag any suspected incidental findings. These are followed up by expert radiologists.	Moderate risk. Subtle findings may be overlooked, but significant issues will be addressed. Non-specialist screening may lead to missed cases.	Low to moderate, depending on the frequency and expertise needed for expert radiological reviews.	5	3

For each strategy we assign a relative estimate for the associated risk and expected cost. Data are shown on an arbitrary 0–10 grading scale

will only be addressed within the framework outlined by the study protocol. Ensuring that participants provide informed consent, with a clear understanding of whether or not incidental findings will be addressed and how they will be addressed, is crucial.

Potential for psychological harm

Even when incidental findings are communicated to participants, there is a risk of causing psychological harm, especially if the findings are clinically insignificant or cannot be clearly interpreted. The discovery of incidental findings in a research setting can have substantial psychological effects on participants, particularly for healthy volunteers. When incidental lesions are detected – often with no immediate clinical relevance – participants may experience unnecessary stress or anxiety, fearing that they have a serious health issue (Ganguli et al. 2019). This risk is compounded by the fact that many incidental findings, such as benign tumours or inflammatory lymph nodes, may mimic malignant conditions, leading to further diagnostic investigations. These follow-ups could involve additional exposure to radiation or other invasive tests, creating a cascade of potentially avoidable harm.

Ethical and legal responsibility

The ethical and legal landscape surrounding the management of incidental findings in research is complex and often unclear (Scott et al. 2024; RCR 2011). Researchers have an ethical obligation to ensure the well-being of participants, which includes informing them of any incidental findings that may have clinical significance. However, there is no consistent legal framework that defines the extent of this duty of care in research contexts. For example, research institutions follow guidelines established by the National Health and Medical Research Council (in Australia), the Medical Research Council or the Wellcome Trust (in the UK), or the National Institutes of Health or Office for Human Research Protections (in the US). However, these guidelines are not universally prescriptive when it comes to incidental findings. While a researcher's primary responsibility is to conduct the study, they are also expected to act reasonably in addressing clinically significant findings, especially if these findings could affect a participant's health. The legal landscape remains underdeveloped in this area, with few cases providing precedents for how far the obligation extends, leaving many research centres to navigate these challenges through institutional review boards and human ethics committees (Fig. 1).

Informed consent

In a comprehensive report, the UK Royal College of Radiologists and Scottish Imaging Network recommend (RCR 2011) that participant information sheets and consent forms for any imaging research studies clearly outline: (a) whether images have diagnostic content, (b) if and by whom they will be reviewed, (c) procedures for incidental findings, and (d) what information will be shared with participants. Research teams must ensure participants understand the limitations of research PET scans and the image review process. In keeping with the principles of Informed Consent in research, typical examples of common incidental findings are recommended to be provided and the process for managing incidental findings must be explained to the participant. This

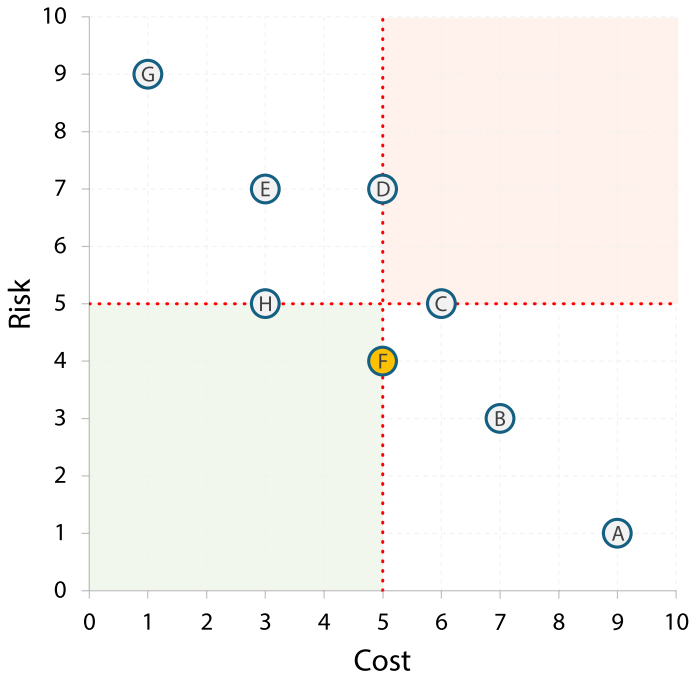

Fig. 1 Estimated risk versus cost for each of the incidental findings management scenarios listed in Table 1; data are shown on an arbitrary 0–10 grading scale. Risks represent undetected significant findings, legal liabilities or reputational damage, while costs represent direct expenses (e.g., personnel, technology), or indirect/opportunity costs. An ethically sound and resource-efficient framework should ideally fall within the green bottom-left quadrant, i.e. strike a balance between minimising risk and costs. The orange circle (F) indicates the approach chosen at the Australian national total body PET facility

may include: (a) the notification to their general practitioner (GP) or another nominated healthcare professional if any incidental findings are found, (b) the potential that additional investigations or tests may be requested by their GP to confirm the findings. These investigations do not form part of the research study and may incur out-of-pocket costs, (c) participants should also be informed of the possibility that the detection of such an abnormality may be a false positive (particularly due to the use of low dose CT scanning), which may cause unnecessary anxiety.

Proposed framework

Our guidelines aim to balance the participant's right to be informed with the practical constraints of research resources, ensuring an approach that upholds ethical and legal standards without compromising research objectives. Designed for the Australian National Total Body PET Facility, these guidelines offer a robust framework for managing incidental findings in human research studies and could be adapted for use in PET research facilities worldwide based on the risk-cost balance they chose to strike. Specifically, we recommend that research teams: (a) incorporate a clear, ethically defensible escalation pathway within their Study Protocol for handling incidental findings, outlining a step-by-step process for review and action when a potentially significant finding arises; and (b) transparently inform Study Participants that the PET scan is conducted solely for experimental research purposes – not as a diagnostic tool for their healthcare. Participants should be made aware that while their scan is not

intended to provide clinical information, in rare instances where something concerning is noticed, the study team will be alerted and will act in alignment with the protocol and the participant's consent, as documented in a signed Patient Information Consent Form (PICF). This framework provides a structured yet flexible approach that encourages participant trust while safeguarding the research process. Further details on these principles are discussed below.

Incidental findings management at the Australian national total body PET facility

Except when explicitly requested by the research user (e.g. study team lead), and at an extra cost, the service provided by the Research Facility does not include a full clinical review and report, as most research studies are exploratory and do not have a clinical outcome. When a research user specifically requests it or if the study is part of a clinical trial which mandates it, the Research Facility shall arrange for a clinical review and report to be performed by a suitably qualified nuclear medicine physician or radiologist and provided to the research user. Any Incidental Findings identified during the clinical review shall be included in the clinical report sent to the research user, who will then follow the escalation process described below.

In all other cases, i.e. when a clinical review and report is not requested by the research user, incidental findings are recommended to be managed as follows (Fig. 2). If a person undertaking a routine review of the scans identifies anything in an image that, in their professional opinion, may meet the above definition of an incidental finding, it is recommended that they flag the finding to the Research Facility representative, who in turn will inform the research user or study team lead, who will then follow the process outlined in the escalation process described below. People that may routinely review research scans include:

(a) A nuclear medicine technologist who will acquire and reconstruct research scans and review the quality of PET/CT images prior to transferring them to a storage server (which may be part of the standard data storage). It is normal practice, even for all clinical PET scans, for images to be checked for quality assurance (e.g., gross motion artefacts, etc) prior to releasing the patient.
(b) Members of the study team undertaking an initial review of the images prior to more in depth data analysis.
(c) Members of the Research Facility team who may review the reconstructed images for quality assurance or during an initial pre-processing analysis.

As part of these processes, an incidental (or possible incidental) finding might be noted or suspected.

Escalation pathway

In the event of a suspected incidental finding, it is the responsibility of the research user and more specifically, the study team lead, to request an appropriate clinical review to confirm (or not) the finding. If the research user requires assistance for organising a clinical review, the Research Facility may, on request, arrange for a clinical review and report to be performed by a suitably qualified nuclear medicine physician or radiologist for the research

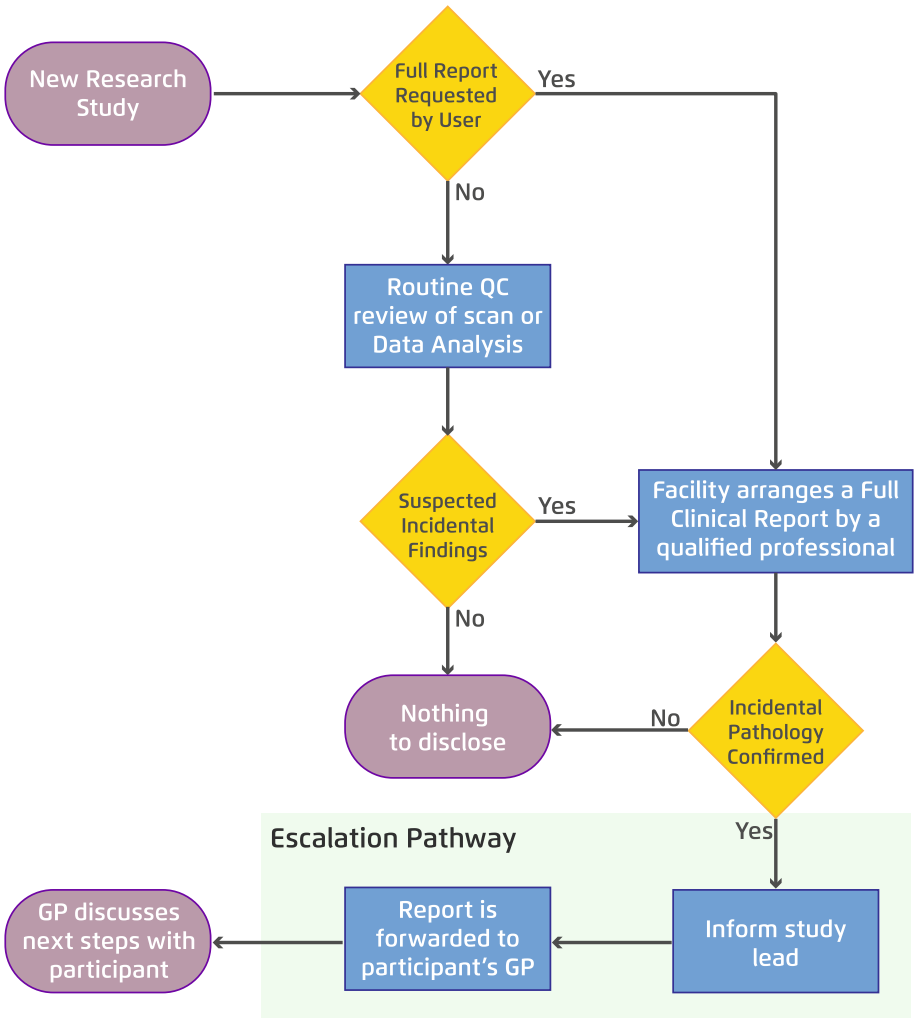

Fig. 2 Proposed framework for managing incidental findings at the Australian national total body PET facility. The escalation pathway outlined in the green box may vary across studies, but must always align with the ethically approved study protocol and participant information sheet. Ultimately the participant will be informed of any unexpected pathology and will discuss the next steps with a health care professional

user. Any incidental findings identified during this clinical review are expected to be included in the clinical report sent to the study team lead as the nominated representative of the research user. If an incidental finding is identified in the clinical review, the study team lead will follow the escalation pathway identified in the ethically approved study protocol and the PICF. This may generally include forwarding the report to promptly disclose the incidental findings to the study participant's GP or another suitable healthcare professional. The responsibility for discussing the incidental finding with the Study Participant usually rests with the participant's GP or referring healthcare professional, as appropriate.

Discussion

Establishing an appropriate and ethically justifiable process for managing incidental findings in human PET/CT research studies presents significant challenges, particularly in the absence of clear guidelines and consensus within the field. In this article

we reviewed and discussed key ethical, operational, and practical considerations surrounding the management of incidental findings within a research facility and proposed a framework aimed at balancing participant well-being, research integrity, and the logistical constraints of imaging research (Fig. 3).

When considering the various approaches to managing incidental findings in PET/CT research, a critical balance must be struck between cost, risk, and ethical obligations (Fig. 1). Research studies typically operate under tight budgets and limited resources, so any strategy to manage incidental findings must be cost-efficient while minimizing risk to participants. Each approach offers distinct advantages and disadvantages that impact both the feasibility of the research and the duty to protect participant welfare.

Comprehensively reviewing all scans by trained radiologists can nearly eliminate the risk of missing potential life-threatening conditions (Case A, Table 1). However, this approach incurs significant financial costs and logistical delays, especially in large-scale research studies. The expense of involving radiologists for reviewing every scan could easily exceed research budgets, making this approach unsustainable for many institutions. However, even with sufficient funding, this approach may prove impractical due to the heavy workloads radiologists already face, as they balance routine clinical responsibilities with the additional burden of reporting large volumes of research scans. The high cost of comprehensive review, while ethically robust, is not practical for most research settings, especially when the scans are non-diagnostic.

On the opposite end of the spectrum, opting for no radiological review and allowing the research team to use their discretion greatly reduces costs but introduces a higher level of risk (Case G, Table 1). Research personnel, often without specialized training in radiology, may overlook or misinterpret significant findings. While this approach preserves financial and human resources and enables research to proceed unencumbered, the ethical implications are concerning. Participants are left vulnerable to undetected conditions, and the obligation to inform them of potential health risks is not adequately fulfilled. The lack of proper review also raises legal and ethical risks

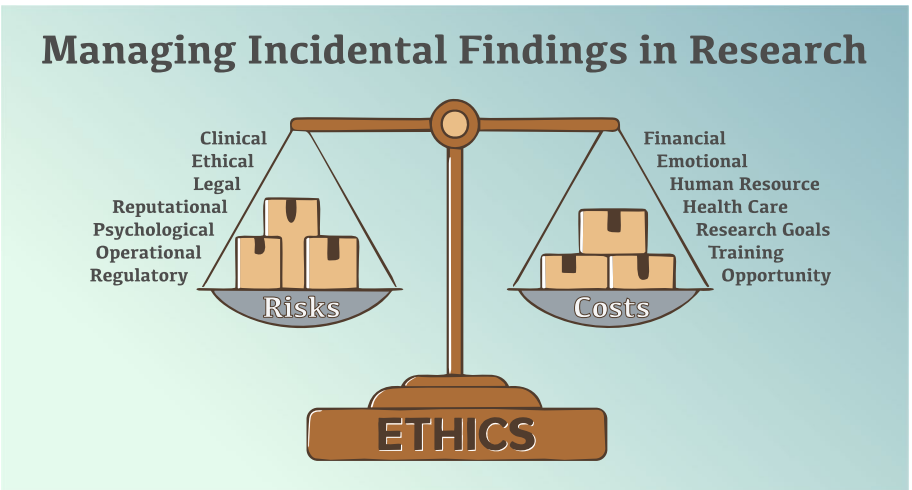

Fig. 3 Managing incidental findings in PET/CT imaging research is a balancing act of risks and costs, approached from an ethics and duty of care perspective

for the research institution, making this approach undesirable despite its low financial burden.

Artificial Inteligence (AI) assisted detection can offer a resource efficient solution by flagging suspicious cases for further review (Case C, Table 1). However, while AI can reduce the workload and costs associated with human review, it is not infallible. False positives or false negatives could occur, which poses ethical risks and adds uncertainty. Additionally, model bias presents another significant challenge, as the training data and methodologies used to develop AI systems can influence their performance, potentially increasing risks. This approach is a promising tool for managing incidental findings in resource-constrained environments, but it still requires human oversight to ensure clinical relevance. The investment in AI infrastructure, while high initially, may pay off over time as AI systems improve, making this a feasible middle-ground solution for research centres, once reliable AI models become available.

A more nuanced approach is to review only the low-dose CT component of PET/CT, which reduces costs and focuses on anatomical abnormalities (Case D, Table 1). This approach avoids the need for dual qualified radiologists and the uncertainty with the clinical significance of novel radiopharmaceuticals. While this strategy manages costs better than full radiological review, it misses potential functional abnormalities on PET scans, raising the risk of overlooking critical findings. The cost-benefit ratio here leans toward research feasibility, but the risk of incomplete diagnosis still exists. Although this approach satisfies ethical concerns to some extent, it remains an imperfect solution.

The preferred approach in our Facility (Case F, Table 1) involves the review of all images primarily for quality assurance purposes, such as assessing for patient motion or other factors affecting image quality. During this process, any suspected incidental findings are flagged for further evaluation by experienced radiologists only when necessary. This strategy provides a pragmatic balance between cost and risk by focusing resources where they are most needed. The initial review by research personnel minimizes financial and logistical burdens, while the selective escalation of suspected significant findings ensures appropriate clinical oversight. Ethically, this method fulfils the obligation to inform participants of clinically relevant findings while avoiding unnecessary strain on resources. Through a clear informed consent process, outlined in the signed Patient Information Consent Form, participants are made aware of this approach and its limitations, ensuring their expectations align with the research context.

The guidance offered here could be a valuable template for adoption by other research centres. By establishing a standardized approach, we can encourage consistency across PET research facilities, ensuring that incidental findings are managed uniformly regardless of regional or institutional differences. Such national guidelines would not only provide clarity for researchers and participants alike but could also aid in streamlining research protocols, enhancing public trust, and supporting the growth of imaging research in ethically responsible ways. Our hope is that this framework will serve as a foundation for developing policies that support participant safety and respect institutional limitations, ultimately enabling scientific progress in a manner that is both ethical and sustainable. To ensure this approach remains effective and relevant over time, we recommend periodic reviews, ideally every 1–2 years, to evaluate its applicability and address any unforeseen challenges that may arise.

Conclusion

Our proposed framework balances cost, risk, and ethical responsibility, offering a resource-efficient and participant-focused approach suitable for research centres worldwide. By minimizing unnecessary reviews, while ensuring that significant findings are appropriately escalated, this approach aligns ethical imperatives with the practical constraints of large-scale studies. This framework offers a model for other research facilities, in an area that currently lacks guidelines and consensus, providing a scalable and responsible solution to the challenge of managing incidental findings in PET/CT imaging.

Abbreviations

AFOV	Axial field of view
AI	Artificial intelligence
CT	Computed tomography
FDG	Fluorodeoxyglucose
GP	General practitioner
HREC	Human research ethics committee
NIH	National institutes of health
PET	Positron emission tomography
PICF	Participant information consent form
TB	Total body
WHO	World Health Organisation

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Author Contributions

The initial manuscript was drafted by GA, FC, and SM. The proposed framework was developed collaboratively by GA, FC, SM, and KO. All authors reviewed and approved the final manuscript.

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Data availability

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Declarations

Conflict of interest

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

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Not applicable.

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