First do no harm in responding to incidental imaging findings

You order a computed tomography pulmonary angiogram (CTPA) for a patient with suspected pulmonary thromboembolism. The radiology report states that no pulmonary thromboembolism is seen but notes an unrelated lung nodule. What should you do with this incidental finding, or "incidentaloma"?

Incidentalomas are lesions, usually asymptomatic, serendipitously detected in patients undergoing imaging for an unrelated reason.[1] They occur in about 15–30% of all diagnostic imaging tests and 20–40% of computed tomography (CT) and magnetic resonance imaging (MRI) scans.[1-3] Increasing use of these imaging tests, an ageing population, and enhanced image resolution of modern machines are driving a surge in incidentalomas.[1,4,5] How to best manage these lesions, avoiding both underinvestigation of potentially serious lesions and overinvestigation and overdiagnosis of benign lesions, is often unclear. Here we discuss the benefits and harms of detecting incidentalomas, examine current management guidelines, and propose recommendations for radiologists and referring clinicians in minimising incidentaloma-induced low value care.

Benefits and harms of early detection

Although early detection of progressive or malignant disease is beneficial, most incidentalomas prove benign but incur patient anxiety and harms from investigation cascades, including complications of invasive procedures such as biopsies, radiation risk from follow-up imaging, and opportunity costs and resource use for health care systems.[6] Incidentalomas result from an imaging modality inadvertently screening bodily organs that were not the target organs of interest. In this regard, imaging of non-target organs shares several analogies with other forms of screening (Box). Such screening can bias towards detecting benign, asymptomatic abnormalities. For example, in a study of CTPAs performed in a tertiary hospital emergency department on patients with suspected pulmonary thromboembolism, one in four revealed an incidental finding (pulmonary nodule or enlarged lymph gland), whereas pulmonary thromboembolism was seen in only one in ten patients.[7] On the basis of other studies, the majority of these nodules (85% or more) will prove to be benign.[8,9]

So the question becomes one of risk stratification of each incidentaloma based on patient risk factors, clinical context and image morphology. A dense, spiculated pulmonary nodule on a CTPA from a 58-year-old heavy smoker is likely to be malignant and warrants intervention. However, an ill-defined soft opacity in a 30-year-old non-smoker undergoing CTPA would most likely be benign and intervention may cause harm.

Despite the predominance of benign over clinically important disease, diagnostic uncertainty, inaccurate estimates of disease risk,[10] discounting of potential downstream harms,[11] defensive medicine,[12] patient and clinician fear,[13] professional norms,[14] and cognitive biases[15] all drive radiologists and referring clinicians to "play it safe" and favour intervention. For an individual, detecting and removing an incidental mass thought to be benign but later confirmed as cancerous is seen as a clear benefit. But at the population level, studies showing a substantial increase in renal cancer diagnoses over the past 20 years from increased imaging report no reductions in cancer-related mortality and instead increased rates of nephrectomies for suspected cancer.[16,17]

Characterising incidentalomas and assessing their potential to progress to serious disease has proved challenging. The reported frequency of incidentalomas detected in the same organs varies considerably.[1-3] This may reflect different incidentaloma prevalence in different patient populations (eg, ethnicity and age), or differences in how radiologists take images of, classify and report incidentalomas. The proportion of incidentalomas that prove malignant also varies widely, due to variation in duration and type of follow-up and the extent of histological confirmation driven by investigative bias.[18] Less than 5% of lesions involving brain, parotid and adrenal gland prove malignant, whereas renal, thyroid, ovarian, pancreatic and breast incidentalomas are classified as malignant in 25–40% of cases.[1,2,19] However, cancers range from indolent or *in situ* to rapidly growing tumours, so the binary cancer/non-cancer categorisation is prognostically misleading and promotes overtreatment of non-progressive cancers.

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Analogies between imaging of non-target organs and screening tests

Ideally, an imaging investigation which may detect an incidentaloma in a non-target organ should confer benefit similar to that of an effective screening test, in that the imaging:
- accurately identifies true pathology (ie, few false positives or false negatives);
- involves patients with higher disease prevalence in non-target organs;
- detects preclinical disease that would otherwise progress and manifest clinically;
- allows earlier administration of an effective intervention that alters the natural history of the disease;
- yields a better patient outcome than would have occurred without imaging (screening); and
- is cost-effective

Managing incidentalomas

Advice from radiologists to referring clinicians on how to manage an incidentaloma should rest on accurate risk prediction and consideration of benefit–harm trade-offs of further investigation and procedures, patient preferences, anticipated life span, comorbidity burden[20] and resource use. Often missing is an understanding of the natural history and prognostic features of many incidentalomas (few long term cohort studies),[21] and of the benefits, harms and cost-effectiveness of specific management (few controlled trials).[22]

Guidelines for managing incidentalomas, non-existent for many organs, are usually directed at radiologists and emphasise lesion size, location and anatomy in estimating the likelihood of malignancy.[23] However, this likelihood is no more quantified in most reports than "likely benign", "suspicious" or "highly suspicious". For certain lesions, such as pancreatic cysts, "likely benign" reports will still frequently feature recommendations for more sensitive imaging for greater granular characterisation, serial scans to assess structural change over time, or even whole-body imaging to exclude metastases.[24] In cases involving other organs, radiologists can issue very different recommendations, reflecting ongoing uncertainty around prognosis. Highly suspicious lesions, or those with markedly elevated biomarkers (eg, prostate-specific antigen in prostate cancer, hormonal levels in adrenal cancers), clearly warrant intervention, but these are the rare exceptions rather than the rule.[1-3]

Recommendations for reducing incidentaloma-induced low value care

Avoid unwarranted imaging

Incidentalomas will be fewer if less imaging is requested in situations where validated decision rules can rule out certain diagnoses without the need for imaging. In a study at one hospital, 55% of CTPAs ordered to exclude pulmonary thromboembolism were avoidable by using Wells scores and D-dimer assays.[25] Having radiologists adopt more of a gatekeeper role in advising what imaging should, or should not, be ordered for certain scenarios may also reduce overuse.

Raise awareness of potential for harm

Clinicians must appreciate potential for harm from using sensitive imaging and explicitly discuss this with patients who are currently rarely informed of the chance of incidental findings when radiological tests are ordered.[26]

Improve incidentaloma characterisation and risk stratification

All radiologists should familiarise themselves with systematically developed reviews for common, organ-specific incidentalomas that emphasise features distinguishing benign from clinically important lesions, according to imaging modality. Several such reviews have recently been published.[27] Multivariable risk prediction models that integrate lesion and

patient characteristics warrant greater use, while new machine learning-based imaging applications may perform even better in predicting malignancy among, for example, thyroid and lung nodules.[28,29] At a more basic level, when interpreting a new image, retrieving past images or reports aids in identifying pre-existing incidentalomas and any interval change suggesting progressive disease. This requires greater networking and interoperability of different electronic radiology systems enabling seamless transfer of such information. Radiologist access to electronic medical records can also make relevant risk factors more visible to radiologists (eg, smoker, past cancers) when interpreting incidentalomas, rather than rely on request forms which may at times be cryptic.

Optimise management recommendations

At the system level, radiologists and organ-system specialists should collaborate in developing explicit recommendations for managing specific incidentalomas,[30] rather than leave such decisions to referring clinicians. In the United States, the American College of Radiology has established an Incidental Findings Committee, which to date has produced 14 guidelines for incidentalomas, created by consensus of imaging and clinical specialists.[31] When applied to practice, in one study targeting incidental ovarian cysts, such collaboration saw guideline adherence increase from 50% to 80%, with overmanagement of cases (ie, unnecessary or too frequent follow-up) decreasing from 34% to 10%.[32] At the individual patient level, management of indeterminate lesions could involve a multidisciplinary team of radiologist, organ specialists and referring clinician in which sharing of information about patient risk factors and other contextual variables may aid radiologist interpretation and advice and ensure timely diagnostic work-up of incidentalomas warranting such action.[33] Such efforts may be assisted by networked software whereby standardised radiology reports, with highlighted text relating to incidentalomas and their management, can be transmitted to referring clinicians and personnel tasked to ensure patient follow-up.[34]

Adopt conservative, specific reporting

Radiology guidelines often fail to recommend how incidentalomas should be reported in ways that avoid referrer confusion and anxiety.[35] Incidentalomas considered likely benign should be explicitly reported as such, with no inference of malignant potential. Recommendations to referrers to pursue additional imaging should, where possible, cite the relevant guideline, while taking patient preference into account.

Include incidentaloma outcome reporting in clinical trials

Clinical trials involving imaging tests (eg, using CT coronary angiography to risk stratify patients with chest pain) should capture data about identified incidentalomas and patient outcomes resulting from their investigation, thus providing additional prospective data about their characteristics and natural history.

Conclusion

Increasing use of medical imaging will likely detect more incidentalomas, which may prompt inappropriate intervention. Greater clinician and patient awareness of this risk and applying a more evidence-informed, risk-based approach to imaging requests and incidentaloma reporting are potential remedial strategies. As interpretive certainty for all incidentalomas will remain elusive, all parties involved may have to accept a certain level of risk in deciding the need for further investigation. Preventing psychological and physical harm to patients from overdetection and overinvestigation of imaging incidentalomas is an imperative, as is the need to limit the opportunity costs of such practices that may inevitably make health care harder to access for other patients who have greater need.

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1 Lumbreras B, Donat L, Hernández-Aguado I. Incidental findings in imaging diagnostic tests: a systematic review. *Br J Radiol* 2010; 83: 276-289.

2 O'Sullivan JW, Muntinga T, Grigg S, Ioannidis JPA. Prevalence and outcomes of incidental imaging findings: umbrella review. *BMJ* 2018; 361: k2387.

3 Evans CS, Arthur R, Kane M, et al. Incidental radiology findings on computed tomography studies in emergency department patients: a systematic review and meta-analysis. *Ann Emerg Med* 2022; 80: 243-256.

4 Smith-Bindman R, Miglioretti DL, Larson EB. Rising use of diagnostic medical imaging in a large integrated health system. *Health Aff (Millwood)* 2008; 27: 1491-502.

5 Deyo R. Cascade effects of medical technology. *Annu Rev Public Health* 2002; 23: 23-44.

6 Ganguli I, Simpkin AL, Lupo C, et al. Cascades of care after incidental findings in a US national survey of physicians. *JAMA Netw Open* 2019; 2: e1913325.

7 Hall WB, Truitt SG, Scheunemann LP, et al. The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. *Arch Intern Med* 2009; 169: 1961-1965.

8 Benjamin MS, Drucker EA, McLoud TC, Shepard JA. Small pulmonary nodules: detection at chest CT and outcome. *Radiology* 2003; 226: 489-493.

9 Iribarren C, Hlatky MA, Chandra M, et al. Incidental pulmonary nodules on cardiac computed tomography: prognosis and use. *Am J Med* 2008; 121: 989-996.

10 O'Neill CJ, Spence A, Logan B, et al. Adrenal incidentalomas: risk of adrenocortical carcinoma and clinical outcomes. *J Surg Oncol* 2010; 102: 450-453.

11 de González SAB, Mahesh M, Kim KP, et al. Projected cancer risks from computed tomographic scans performed in the United States in 2007. *Arch Intern Med* 2009; 169: 2071-2077.

12 Berlin L. The incidentaloma: a medicolegal dilemma. *Radiol Clin North Am* 2011; 49: 245-255.

13 Ganguli I, Simpkin AL, Colla CH, et al. Why do physicians pursue cascades of care after incidental findings? A national survey. *J Gen Intern Med* 2020; 35: 1352-1354.

14 Brown SD. Professional norms regarding how radiologists handle incidental findings. *J Am Coll Radiol* 2013; 10: 253-257.

15 Busby LP, Courtier JL, Glastonbury CM. Bias in radiology: the how and why of misses and misinterpretations. *Radiographics* 2018; 38: 236-247.

16 Turner RM, Morgan TM, Jacobs BL. Epidemiology of the small renal mass and the treatment disconnect phenomenon. *Urol Clin North Am* 2017; 44: 147-154.

17 Welch HG, Skinner JS, Schroek FR, et al. Regional variation of computed tomographic imaging in the United States and the risk of nephrectomy. *JAMA Intern Med* 2018; 178: 221-227.

18 Fu T, Plecha D, Sommer J. System-driven longitudinal follow-up of incidental imaging findings. *Br J Radiol* 2023; 96: 20220573.

19 Glasziou PP, Jones MA, Pathirana T, et al. Estimating the magnitude of cancer overdiagnosis in Australia. *Med J Aust* 2020; 212: 163-168. https://www.mja.com.au/journal/2020/212/4/estimating-magnitude-cancer-overdiagnosis-australia#:~:text=An%20estimated%2022%25%20of%20breast,%25%20of%20invasive%20cancer%20diagnoses

20 Raphel TJ, Weaver DT, Berland LL, et al. Imaging follow-up of low-risk incidental pancreas and kidney findings: effects of patient age and comorbidity on projected life expectancy. *Radiology* 2018; 287: 504-514.

21 Podbregar A, Kocjan T, Rakuša M, et al. Natural history of nonfunctioning adrenal incidentalomas: a 10-year longitudinal follow-up study. *Endocr Connect* 2021; 10: 637-645.

22 Lee RA, Uzzo RG, Anaokar J, et al. Pathological and clinical outcomes in a large surveillance and intervention cohort of radiographically cystic renal masses. *J Urol* 2023; 209: 686-693.

23 Johnson PT, Horton KM, Megibow AJ, et al. Common incidental findings on MDCT: survey of radiologist recommendations for patient management. *J Am Coll Radiol* 2011; 8: 762-767.

24 Bobbin MD, Ip IK, Sahni VA, et al. Focal cystic pancreatic lesion follow-up recommendations after publication of ACR white paper on managing incidental findings. *J Am Coll Radiol* 2017; 14: 757-764.

25 Perera M, Aggarwal L, Scott IA, Cocks N. Underuse of risk assessment and overuse of computed tomography pulmonary angiography in patients with suspected pulmonary thromboembolism. *Intern Med J* 2017; 47: 1154-1160.

26 Kole J, Fiester A. Incidental findings and the need for a revised informed consent process. *AJR Am J Roentgenol* 2013; 201: 1064-1068.

27 Given-Wilson R, Screaton N, Taylor SA. Incidental imaging findings from head to toe: challenges and management: introductory editorial. *Br J Radiol* 2023; 96: 20239002.

28 Peng S, Liu Y, Lv W, et al. Deep learning-based artificial intelligence model to assist thyroid nodule diagnosis and management: a multicentre diagnostic study. *Lancet Digit Health* 2021; 3: e250-e259.

29 Baldwin DR, Gustafson J, Pickup L, et al. External validation of a convolutional neural network artificial intelligence tool to predict malignancy in pulmonary nodules. *Thorax* 2020; 75: 306-312.

30 Fassnacht M, Arlt W, Bancos J, et al. Management of adrenal incidentalomas: European Society of Endocrinology clinical practice guideline in collaboration with the European Network for the Study of Adrenal Tumors. *Eur J Endocrinol* 2016; 175: G1-G34.

31 American College of Radiology. Incidental findings. Reston (VA): ACR, 2023. https://www.acr.org/Clinical-Resources/Incidental-Findings (viewed Nov 2023).

32 Kim DC, Bennett GL, Somberg M, et al. A multidisciplinary approach to improving appropriate follow-up imaging of ovarian cysts: A quality improvement initiative. *J Am Coll Radiol* 2016; 13: 535-541.

33 Farmer CI, Bourne AM, O'Connor D, et al. Enhancing clinician and patient understanding of radiology reports: a scoping review of international guidelines. *Insights Imag* 2020; 11: 62.

34 Emerman CL, Gallagher MA, Diaz PJ. Incidental radiology findings: effectiveness of a radiology–electronic medical records interface system for improving communication. *J Clin Outcomes Manag* 2012; 19: 111-115.

35 Crable EL, Feeney T, Harvey J, et al. Management strategies to promote follow-up care for incidental findings: a scoping review. *J Am Coll Radiol* 2021; 18: 566-579. ∎