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**Body:**

05-Apr-2018

Dear Dr. O'Sullivan

Manuscript ID BMJ.2018.043244 entitled "Prevalence and Outcomes of Incidental imaging findings: An Umbrella Review"

Thank you for sending us your paper. We are pleased to say that we would like to publish it in the BMJ as long you are willing and able to revise your paper as explained below in the report from the manuscript meeting. We are provisionally offering acceptance but will make the final decision when we see the revised version. The report from the manuscript meeting, the comments from the reviewers and general requirements for submission are available at the end of this letter.

There is also a technical editor checklist attached which should be adhered to - any queries please contact [papersadmin@bmj.com](mailto:papersadmin@bmj.com)

We are looking forward to reading the revised manuscript and, we hope, making a final acceptance decision.

Please note that the BMJ might choose to shorten content or replace or re-size images for the print issue.

Best wishes

Georg Roeggla  
[groggla@bmj.com](mailto:groggla@bmj.com),

**\*\*Report from The BMJ's manuscript committee meeting\*\***

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Manuscript meeting 05.04.2018

Elizabeth Loder (chair), Gary Collins (stats), Wim Weber, Jose Merino, Robin Baddeley, Georg Roggla, Tiago Villanueva, Daoxin Yin.

Decision: Provisional acceptance

The committee was interested in the topic of your research. The following concerns were mentioned:

- The committee thought heterogeneity of the included studies was rather high.
- How clinically useful it is to have this focus on the overall quantification when we're lumping together incidentalomas of variable clinical importance and there's no distinction between them.
- Some of the discrepancies between organ systems are not plausible.

- Can there be an epidemic of incidentalomas?
- This study (a review of reviews) has a very ambitious goal: identify all possible incidentaloma types with all possible imaging studies to help clinicians and patients weigh the pros and cons of imaging. I guess this means: How likely is it that my imaging study will identify a potential aetiology and should I worry? Unfortunately, the paper does not address the impact of having an incidentaloma
- The authors focus on malignant incidentalomas. What about other types? (Aneurysms, atherosclerosis, silent brain infarcts, AVMS, etc)
- Why relegate studies of patients undergone imaging studies for the evaluation of malignancy to sensitivity analyses?
- The committee had no mayor concerns regarding methods.
- Single author data extraction. Extraction 'verified' by a 2nd author. What does this mean? Did you verify all extraction form all systematic reviews and all primary studies? If so, why not double data-extract? Quality assessment was done by two reviewers.
- Some dates in the Abstract would be useful.
- Please discuss the clinical implications in more detail.

We would be thankful if you could do a quick revision: We would like to publish your paper together with a related other paper which is the editorial process for a little longer than your paper.

First, please revise your paper to respond to all of the comments by the reviewers. Their reports are available at the end of this letter, below. Please also respond to the additional comments by the committee.

In your response please provide, point by point, your replies to the comments made by the reviewers and the editors, explaining how you have dealt with them in the paper.

**\*\* Comments from the external peer reviewers\*\***

#### REFeree COMMENTS

Reviewer: 1

Recommendation:

Comments:

Nice Meta-analysis of incidental imaging findings. Publishable.

Additional Questions:

Please enter your name: Chirag Acharya

Job Title: MD

Institution: University of Mississippi Medical Center

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests <A HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='\_new'> (please see BMJ policy) </a>please declare them here:  
None

Reviewer: 2

Recommendation:

Comments:

This is a clearly written manuscript describing an umbrella review of incidentalomas. The methods are appropriate and well described. Comments and concerns are listed below:

1. While there is a clear justification for the importance of studying incidentalomas, the authors do not make a clear case for why an umbrella review is needed beyond the systematic reviews already available. On page 3, line 28, the authors state, "To assist clinicians and patients adequately weigh up pros and cons of imaging and to assist in management decisions after incidentaloma diagnosis..." (note: this sentence seems to contain several typos). However, it is not clear why it would be more helpful for clinicians and patients to have an umbrella review which looks at all types of imaging, rather than a specific systematic review which focuses on the type of imaging being considered for the particular patient. More justification for the need for this review is required in the introduction.
2. On page 4, line 34 the authors state, "All data extraction was performed by one author (JOS) and verified by a second (SG)." It is not clear from this statement whether the two listed authors independently reviewed the data and came to consensus or whether the second author only looked at and confirmed the first author's extraction decisions.
3. In the Prima Flow Diagram (Figure 1), it is not clear why the 7002 records were excluded after initial screening, prior to full text assessment. Some general reasons should be given in the diagram and/or text.

Additional Questions:

Please enter your name: L. Aubree Shay

Job Title: Assistant Professor of Health Promotion and Behavioral Sciences

Institution: UTHealth School of Public Health in San Antonio

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

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Reviewer: 3

Recommendation:

Comments:

Needs an accompanying editorial - though the methods are solid, people can run away with conclusions

Additional Questions:

Please enter your name: SAURABH JHA

Job Title: Associate Professor

Institution: University of Pennsylvania

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

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If you have any competing interests <A HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='\_new'> (please see BMJ policy) </a>please declare them here: This is a comprehensive umbrella analysis of studies about incidental findings. The methods are rigorous. Here are a few points the authors should consider.

- a) The section on "data extraction" needs clearer writing, particularly the second paragraph.
- b) The wild discrepancy between IF prevalence on chest CTs (45 %) and PE studies (2 %) does not make bioplausible sense. Can the authors comment on the explanations for this discrepancy which are statistical in nature? One explanation I have is that PE studies may omit the thyroid and adrenal gland in their field of view, but still the difference is still too large for this potential difference.
- c) Many chest CTs are done as part of a chest, abdomen and pelvis continuous run – have the authors accounted for this?
- d) Prevalence of IF in cardiac MRI is inexplicably high. How can the authors explain this? I read cardiac MRI – it doesn't make sense.
- e) Major issue is that the studies have collapsed all IFs in one group for denominator – there's clearly a spectrum – there are benign IFs and malignant IFs. There are clinically relevant IFs and clinically irrelevant IFs. Though the work is rigorous the authors place too much value on its quantitative value. How can patients use their information if they still don't know the true impact of IF, which this paper doesn't inform because the meta-analysis doesn't address the clinical significance of IFs? An incidental AAA of 5 cm may be more valuable to detect than an incidental solid breast cancer.
- f) Heterogeneity is the most important signal here, not the outcomes. Authors should expand what on the implication of heterogeneity.
- g) Paper needs an accompanying editorial to make sense of the large amount of information.

Reviewer: 4

Recommendation:

Comments:

The research question is clearly defined and appropriately answered.

The overall design of study is much elaborated and adequate for answering the research question.

The study consists of observational studies and systematic reviews which have been carefully selected and analysed. However, I miss a previous study by a Spanish group (Incidental findings in imaging diagnostic test: a systematic review, B Lumbreras et al., BJR 83 (2010), 276-289). Although this study was carried out with different statistical methods and less extensive data acquisition, the objective was quite similar.

The material and methods used are adequately described. However, the PRISMA flow diagram (Fig. 1) has not been mentioned in the Methods section.

The results are well presented and answer the research question.

The interpretation and conclusions drawn are sufficiently derived from the data. However, the implications for clinicians and policy maker should be very cautious. The evidence based approach derived from this systematic review does not reflect the need of clinicians and radiologist for caring of individual patients. Nevertheless, being aware of unexpected findings and knowledge of their nature are substantially helpful in daily routine.

References: BJR 83 (2010), 276-289 should be incorporated.

The abstract/summary/key messages are consistent with the manuscript.

Additional Questions:

Please enter your name: Martin Uffmann

Job Title: Radiologist

Institution: Department of Radiology, Landeskrankenhaus  
Neunkirchen

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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