

Subject: BMJ - Decision on Manuscript ID BMJ.2016.034729.R1

Body: 03-Dec-2016

Dear Dr. Rampinelli:

Manuscript ID BMJ.2016.034729.R1 entitled "RADIATION EXPOSURE AND CANCER RISK ASSOCIATED WITH LOW-DOSE COMPUTED TOMOGRAPHY FROM LUNG CANCER SCREENING" which you submitted to BMJ,

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 address the comments of the reviewer included below. We are provisionally offering acceptance but will make the final decision when we see the revised version.

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.

https://mc.manuscriptcentral.com/bmj?URL_MASK=6d93770068364a4cae16fb10e9395b90

Yours sincerely

Jose Merino
jmerino@bmj.com,

REFEREE COMMENTS

Reviewer: 1

Recommendation:

Comments:

The authors have adequately answered my concerns from the initial review and made additions where suggested. I have no further concerns or comments

Additional Questions:

Please enter your name: James Ravenel MD

Job Title: Professor of Radiology

Institution: Medical University of South Carolina

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?: Yes

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 (please see BMJ policy) please declare them here: As my institution has a lung cancer screening program, there is a potential gain (as there would be expected for all programs of this sort) from the publication of this study

Reviewer: 2

Recommendation:

Comments:

I have reviewed this paper before and my edits are essentially unchanged. It is actually fairly straightforward, in fact straightforward enough that I am not sure it merits publication as a full peer reviewed manuscript, but may be better published as a letter or brief report.

Ultimately, this is a decision at the editorial level regarding a few things:

- Whether the extrapolation of radiation risk is robust enough to warrant publication of these results. The authors are using published and previously referenced that may well represent our best guess at risk but are controversial.

- Whether, if the results are believed to be as robust as possible based on above, that this topic is of sufficient interest and impact for the readership of BMJ. It is arguable that there is a social duty to publish data that does help provide some context of the risk-benefit from radiation that may inhibit some patients from seeking screening that may be indicated. However this article kind of boils down to a back of the envelope calculation that includes cumulative doses of radiation and controversial estimates of cancer from these compared to published benefit of screening.

Major:

As far as I am currently aware, the AAPM recommends SSDE rather than effective dose in mSv as the preferred reporting method for radiation dose from CT. This should either be changed or explicitly addressed in the discussion.

Other comments:

Abstract

Would consider using "estimate" rather than "assess" in objective, given the uncertainty in the risk model.

Design/ setting: The primary result in this paper utilized radiation data from a prospective CT lung cancer screening trial and could really be considered a secondary analysis of this data rather than retrospective. The secondary outcome is a risk-benefit estimate and as this is an important part of the results and conclusions; it should be mentioned as a risk-benefit analysis in the study design and setting.

This is not an interventional trial so I am not sure the abstract should be structured to make it look like this.

Additional Questions:

Please enter your name: Chris Moore

Job Title: MD

Institution: Yale

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: Yes

Funds for a member of staff?: Yes

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 (please see BMJ policy) please declare them here: AHRQ funding for research in dissemination of reduced dose CT.

****Information for submitting a revision****

Deadline: Your revised manuscript should be returned within one month.

How to submit your revised article: Log into <http://mc.manuscriptcentral.com/bmj> and enter your Author Center, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Once the revised manuscript is prepared, you can upload it and submit it through your Author Center. When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) and Committee in the space provided. You can use this space to document any changes you make to the original manuscript and to explain your responses. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s). As well as submitting your revised manuscript, we also require a copy of the manuscript with changes highlighted. Please upload this as a supplemental file with file designation 'Revised Manuscript Marked copy'. Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

When you revise and return your manuscript, please take note of all the following points about revising your article. Even if an item, such as a competing interests statement, was present and correct in the original draft of your paper, please check that it has not slipped out during revision. Please include these items in the revised manuscript to comply with BMJ style (see: <http://www.bmj.com/about-bmj/resources-authors/article-submission/article-requirements> and <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists>).

Items to include with your revision (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>):

1. What this paper adds/what is already known box (as described at <http://resources.bmj.com/bmj/authors/types-of-article/research>)
2. Name of the ethics committee or IRB, ID# of the approval, and a statement that participants gave informed consent before taking part. If ethics committee approval was not required, please state so clearly and explain the reasons why (see <http://resources.bmj.com/bmj/authors/editorial-policies/guidelines>.)
3. Patient confidentiality forms when appropriate (see http://resources.bmj.com/bmj/authors/editorial-policies/copy_of_patient-confidentiality).
4. Competing interests statement (see <http://resources.bmj.com/bmj/authors/editorial-policies/competing-interests>)
5. Contributorship statement+ guarantor (see <http://resources.bmj.com/bmj/authors/article-submission/authorship-contributorship>)
6. Transparency statement: (see <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/transparency-policy>)
7. Copyright statement/licence for publication (see <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse>)
8. Data sharing statement (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>)
9. Funding statement and statement of the independence of researchers from funders (see <http://resources.bmj.com/bmj/authors/article-submission/article-requirements>).
10. Patient involvement statement (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>).
11. Please ensure the paper complies with The BMJ's style, as detailed below:
 - a. Title: this should include the study design eg "systematic review and meta-analysis."
 - b. Abstract: Please include a structured abstract with key summary statistics, as explained below (also see <http://resources.bmj.com/bmj/authors/types-of-article/research>). For every clinical trial - and for

any other registered study- the last line of the abstract must list the study registration number and the name of the register.

c. Introduction: This should cover no more than three paragraphs, focusing on the research question and your reasons for asking it now.

d. Methods: For an intervention study the manuscript should include enough information about the intervention(s) and comparator(s) (even if this was usual care) for reviewers and readers to understand fully what happened in the study. To enable readers to replicate your work or implement the interventions in their own practice please also provide (uploaded as one or more supplemental files, including video and audio files where appropriate) any relevant detailed descriptions and materials. Alternatively, please provide in the manuscript urls to openly accessible websites where these materials can be found.

e. Results: Please report statistical aspects of the study in line with the Statistical Analyses and Methods in the Published Literature (SAMPL) guidelines <http://www.equator-network.org/reporting-guidelines/sampl/>. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:

- i. For a clinical trial: Absolute event rates among experimental and control groups; RRR (relative risk reduction); NNT or NNH (number needed to treat or harm) and its 95% confidence interval (or, if the trial is of a public health intervention, number helped per 1000 or 100,000.)
- ii. For a cohort study: Absolute event rates over time (eg 10 years) among exposed and non-exposed groups; RRR (relative risk reduction.)
- iii. For a case control study:OR (odds ratio) for strength of association between exposure and outcome.
- iv. For a study of a diagnostic test: Sensitivity and specificity; PPV and NPV (positive and negative predictive values.)
- v. For a systematic review and/or meta-analysis: Point estimates and confidence intervals for the main results; one or more references for the statistical package(s) used to analyse the data, eg RevMan for a systematic review. There is no need to provide a formal reference for a very widely used package that will be very familiar to general readers eg STATA, but please say in the text which version you used. For articles that include explicit statements of the quality of evidence and strength of recommendations, we prefer reporting using the GRADE system.

f. Discussion: To minimise the risk of careful explanation giving way to polemic, please write the discussion section of your paper in a structured way. Please follow this structure: i) statement of principal findings of the study; ii) strengths and weaknesses of the study; iii) strengths and weaknesses in relation to other studies, discussing important differences in results; iv) what your study adds (whenever possible please discuss your study in the light of relevant systematic reviews and meta-analyses); v) meaning of the study, including possible explanations and implications for clinicians and policymakers and other researchers; vi) how your study could promote better decisions; vi) unanswered questions and future research

g. Footnotes and statements

Online and print publication: All original research in The BMJ is published with open access. Our open access policy is detailed here: <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse>. The full text online version of your article, if accepted after revision, will be the indexed citable version (full details are at <http://resources.bmj.com/bmj/about-bmj/the-bmjs-publishing-model>). The print and iPad BMJ will carry an abridged version of your article. This abridged version of the article is essentially an evidence abstract called BMJ pico, which we would like you to write using the template downloadable at <http://resources.bmj.com/bmj/authors/bmj-pico>. Publication of research on [bmj.com](http://www.bmj.com) is definitive and is not simply interim "epublication ahead of print", so if you do not wish to abridge your article using BMJ pico, you will be able to opt for online only publication. Please let us know if you would prefer this option. If your article is accepted we will invite you to submit a video abstract, lasting no longer than 4 minutes, and based on the information in your paper's BMJ pico evidence abstract. The content and focus of the video must relate directly to the study that has been accepted for publication by The BMJ, and should not stray beyond the data.

Date Sent: 03-Dec-2016

configure instructions