Reviewer’s report

Title: Do we know enough about the effect of low dose computed tomography screening for lung cancer on survival to act? A systematic review, meta-analysis and network meta-analysis of randomised controlled trials.

Version: 0 Date: 30 Mar 2019

Reviewer: Thom Howard

Reviewer's report:

General comment.

Thank you for the opportunity to review this interesting and concisely written manuscript. Although I have some concerns about the presentation of results (e.g. p-values, cross-tables) and description of methods (i.e. what model was used for network meta-analysis) I believe the review is comprehensive. The conclusion that, on balance, we should wait for further evidence seems justified if considering only the narrow grounds of preventable deaths, rather than wider effectiveness and cost-effectiveness.

Specific comments.

1. The authors repeatedly refer to statistical significance but don't report any of the p-values. The recent American Statistical Association statement on p-values advises against the use of the arbitrary 5% threshold for decision making and that p-values themselves should always be reported (American Statistical Association 2016). Please include these in the abstract and wherever in the text a statement on significance is being made. Ideally, the authors would instead refer to weak or strong evidence in support of hypotheses(Sterne and Davey Smith 2001).

2. On page 5 the authors present the methods for network meta-analysis (NMA) but do not specify the link function or likelihood. The National Institute for Health and Care Excellence provide guidance on the appropriate model for binomial outcomes where follow-up varies across trials (i.e. binomial likelihood and complementary log log link). As the authors present risk ratios, and not hazard ratios, it is unlikely the NICE TSD model was adopted. Please be clear what model was used.

3. On page 8 is reported the confidence interval for LDCT screening vs controls on all-cause mortality (0.89 to 1.00). This is interpreted as "not-statistically significant" and is dismissed. This illustrates the danger of using the arbitrary 5% threshold for decision making as this is only marginally non-significant and really provides weak evidence that LDCT screening reduces all-cause mortality.
4. On page 8 specific risk ratios estimated by the NMA are presented. Please provide a cross-table with all pairwise comparisons of screening methods on both all-cause and lung cancer mortality.

5. Page 9 of the discussion gives an interesting discussion of numbers needed to screen to avoid one lung cancer death (which is 357). This would be boosted by giving the proportion of patients in the high risk group and proportion likely to turn up for screening. A mention of the actual cost of screening would provide further useful context.

6. Cost-effectiveness modelling is only mentioned at the end of the conclusions. The findings of this analysis (now published, and to the effect that there is evidence a single round of screening could be cost-effective) should be reported and discussed. It would follow on naturally from the discussion on numbers needed to screen.

References

American Statistical Association (2016). "AMERICAN STATISTICAL ASSOCIATION RELEASES STATEMENT ON STATISTICAL SIGNIFICANCE AND P-VALUES. Provides Principles to Improve the Conduct and Interpretation of Quantitative Science March 7, 2016 ".


Level of interest

Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English

Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.