Author’s response to reviews

Title: Fake facts and alternative truths in medical research

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Author’s response to reviews:

Dear Editor,

I am most thankful for the positive assessment and for the valuable comments and suggestions. All the comments have been addressed, and again I think that they have contributed to improving the manuscript. A detailed list of responses is given below. The reviewers’ comments are given in black and my responses are marked in red:

Editor Comments:

1. In regards to the reviewers first point below a full definition of 'Over diagnosis' and 'Morality Reduction' (how is it calculated, is this the yearly change for instance?) is required to make the article more accessible

RESPONSE: This is a good point. The following has now been included in the article: “«Overdiagnosis is the term used when a condition is diagnosed that would otherwise not go on to cause symptoms or death.”[20] Mortality from breast cancer is defined as deaths with breast cancer coded as the underlying cause of death and mortality reduction is defined in terms of reduced breast cancer mortality in a screened group compared to a non-screening group in the assessment of a screening program.” Moreover, the following has been included in the supplementary discussion: “Another relevant critique of this study is that the definitions of overdiagnosis and mortality reduction vary in the included studies. Those that are in favor of screening define and measure overdiagnosis and mortality reduction differently from those that are less in favor. However, this is exactly at the core of the problem: polarised interests make researchers use different models and methods. Models, outcome measures, time periods, estimates, inclusion- and exclusion criteria, corrections etc are chosen not only based on scientific merits, but also on professional interests.”
2. The Abstract needs the following subheadings - 'Background', 'Main Body' and 'Conclusion'.

RESPONSE: The main part of the abstract is rewritten in accordance to this structure.

3. Please remove the subheading 'Key message' and incorporate the text in the 'Conclusion' subheading of the abstract. Please note that the abstract should not exceed 350 words (excluding subheadings).

RESPONSE: This has been done. The word count now is 299 for the abstract.

4. Please include 3-10 keywords under the abstracts

RESPONSE: The following key words have been include: Conflict of interest, polarized research, mammography screening, breast cancer, overdiagnosis, mortality

5. Move the Quote to the below the subheading labelled 'Background'

RESPONSE: The quote has been moved under Background.

6. Change the heading labelled 'Discussion [Main Text]' to 'Main Text'

RESPONSE: 'Discussion [Main Text]' has been altered to 'Main Text.'

7. Please include a list of Abbreviations after the 'Conclusion'

RESPONSE: The following list of abbreviations have been included:

EUROSCREEN  The European Screening Network
NBCSP        The Norwegian Breast Cancer Screening Program
NRC          The Norwegian Research Council
OMRR         Overdiagnosis to Mortality Reduction Ratio
USPSTF       U.S. Preventive Services Task Force
8. Please confirm, in the declaration 'Ethics Approval and Consent to Participate' that all named contributors provided written consent to participate in the study.

RESPONSE: This has been included.

9. Please confirm, in the declaration 'Consent to Publish' that all author's consented to having their data (their opinion on screening) published.

RESPONSE: This has been included.

Reviewer reports:

Harald Schmidt (Reviewer 1): I am copying below responses to the authors' responses (and note that there was much overlap in concerns among the reviewers), and focus on 3 main points:

1. Revisions on overdiagnosis/treatment: These have been minor. As written, this would no doubt be sufficient for a specialist journal. But I rather doubt that the significance of the concepts will be apparent to a more general audience—the editor will no doubt have a good sense of what works here.

RESPONSE: This is a good point. As stated above, the following has now been included in the article: “«Overdiagnosis is the term used when a condition is diagnosed that would otherwise not go on to cause symptoms or death.”[20] Mortality from breast cancer is defined as deaths with breast cancer coded as the underlying cause of death and mortality reduction is defined in terms of reduced breast cancer mortality in a screened group compared to a non-screening group in the assessment of a screening program.” Moreover, the following has been included in the supplementary discussion: “Another relevant critique of this study is that the definitions of overdiagnosis and mortality reduction vary in the included studies. Those that are in favor of screening define and measure overdiagnosis and mortality reduction differently from those that are less in favor. However, this is exactly at the core of the problem: polarised interests make researchers use different models and methods. Models, outcome measures, time periods, estimates, inclusion- and exclusion criteria, corrections etc are chosen not only based on scientific merits, but also on professional interests.”

2. Methods of scoring bias. There is now some more information on this. A few points:
"two experts on polarized conflict of interest were asked to classify the corresponding authors of the identified publications." More should be said on how these were identified/from what pool they were recruited, specifically what inclusion and exclusion criteria were applied, and how possible polarized interests of the pool of candidates and finalists were assessed—again, very central given the primary aim of the paper, and the non-trivial difficulty of finding and Archimedean point here. Likewise, did the two assessers coincide exactly on each assessment, or are the scores in table 1 means between both?

RESPONSE:  With regard to recruitment of polarization experts, the following is stated: “Inclusion criteria were that they were experts on science ethics in general and polarised research in particular, and exclusion criteria were if they had been involved in mammography screening programs or their primary evaluations.” With respect to the pool of experts and selection bias the following is added: “Another challenge is that there is a bias in the selection of experts on polarised conflict of interest. Moreover, one could wish there to be more (than two) included experts. However, given the inclusion and exclusion criteria, the pool of experts in this field is very small. Luckily, both approached experts agreed to participate. Hopefully, the number of experts in this field will be growing, so that more thorough studies can be performed in the future. As such, this can hopefully be seen as a feasibility study.” With respect to the important point on how the assessors coincided on their assessment, the text now reads: “The experts approached each other, deliberated on the ranking, and sent a joint ranking as a response. …. more sophisticated and robust ranking systems may be applied when more experts on polarised research available.” The issue of finding an Archimedean point is addressed in the following manner: “Moreover, implicitly this study argues that we should be critical to experts in any specific scientific field and investigate their “polarised conflict of interest.” This is of cause also relevant for the author of this study and for the selected experts on polarised research. Is the author “polarised” when analyzing the data or selecting experts? Are the experts really neutral as their ranking may result from biases, preferences, and misconceptions? However important, this is a general problem, as it is difficult to find any expert that could be declared as fully objective and impartial. One may have “second order polarisations,” i.e., polarised conflict of interest amongst experts on polarised research. The point here is neither that one should ignore nor be paralyzed by such problems. By presenting assessments of polarised conflict of interest they are open for discussions and criticism. Trying to uncover covert phenomena and to make undeclared conflict of interests visible is important. No doubt, the methods for doing so may not be perfect, and may certainly need refinement. However, we should not let the lack of perfection in method stall our focus on an important issue for the application of scientific results as well as trust in science. Hopefully, this small study, and the debate article will spur fruitful debates and further research on this issue. Hence, it is certainly difficult to find an Archimedean point, but this is the core of the problem in polarized research. If such a point could be found, polarisation would be undermined.”
3. Overall feasibility of approach: Supplement 1 acknowledges a range of challenges, including the issue of rating individuals when there were groups of people involved in evidence appraisals that flagged before as an issue, "second order polarisations" and, importantly, that "the questions to identify polarised conflict of interest appear reasonable (and can be easily adapted) [but] they may not be very useful in practice" -- nonetheless it states that "Addressing the robustness of the methodology is beyond the scope of this Debate article, but is a viable and important next step in the study polarised research" Well, yes, it is hard to address this in more detail in the space available. But I am not sure that the current format is the best way of starting a debate on the issue. It suggests with rather more certainty than is possible—as noted in the Supplement, but not really reflected in equal measure in the paper itself—that the approach is feasible in principle, and that all that remains is hashing out some details in future research. Again, this will of course be for the editor to decide, but I feel that a more robust contribution would (a) either do more of the legwork upfront, or (b) remove the empirical part of the paper—that raises all the issues around how to measure this—and make a more conceptual point (in a way that would need to be distinct from prior related work such as http://www.sciencedirect.com/science/article/pii/S0895435608000048.

RESPONSE: Here I disagree with the reviewer. First, I do not state that “all that remains is hashing out some details in future research.” What I have stated is that “How exactly to assess polarised conflict of interest may need more elaboration and collaborate work.” Nonetheless, I do give some indications (proof of concept), both methodologically and empirically, that such studies are possible. I also give reasons why full-fledged empirical studies are difficult to perform at present, and I provide input for method development in order to facilitate such studies. Basing these methodological suggestions on empirical findings supports their relevance, however preliminary they may be. With regard to the referenced article, it surely mentions the “balancing of benefits and harms” and uses mammography screening as an example. However, it does not lead us to any practical procedure for handling these types of conflict of interests. The only guiding question given is: “Are the benefits of the intervention are more important than the harms and vice versa?”

I strongly endorse such studies aiming at revealing value-judgments in technology assessment (HTA), I have myself published a series of articles elaborating on this, and I have developed a method of doing so in HTA. Nonetheless, I think we need more specific approaches in the field of polarised research, and I hope that this initial study can inspire more collaborative work on this. Publishing the study will make it open to criticism. This criticism will be most welcome, because the aim is to improve the methods to identify and address; and eventually to harness; polarised research.