Author’s response to reviews

Title: Fake facts and alternative truths in medical research

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Author’s response to reviews:

[Please see the attached file for easier (color coded) reading of the responses]

Dear Editor,

I am most thankful for the valuable comments and suggestions and for the opportunity to submit a revised version of the manuscript. All the comments have been addressed, and I think that they have contributed to improving the manuscript. A detailed list of responses is given below. Several of the comments are on the methods of the empirical parts of this submission as a Debate article. In order to provide more details about the methods without diverting the attention from the content of the article (i.e., polarized research), I have provided a supplementary file with a more detailed description and discussion of the method. I hope that this addresses several of the comments without violating the formal requirements for Debate articles. Please let me know if you know of other and better ways to handle this.

Here follow the reviewers’ comments (in black) and my responses (marked in red):

Reviewer reports:

Harald Schmidt (Reviewer 1): Fake facts and alternative truths in medical research argues that researchers frequently have undisclosed "polarized conflicts of interest" that lead to biased reports. This undesirable situation should be overcome through three measures: editors should "a) make researchers state their "polarised conflict of interest" when submitting manuscripts, b) make reviewers explicitly assess polarisation, and c) apply external experts to assess polarisation when reviewers (and/or editors) are too ingrained in the research to be able to make the assessment."
This is a timely paper, and the case of breast cancer screening is a particularly fitting one, in principle. If the aim is to convince not only those already believing, but also those needing persuasion, it would be helpful to address the following points:

1. "Overdiagnosis to Mortality Reduction Ratio (OMRR) in publicly funded mammography screening programs of women aged 50-69 years old"
   → the significance of this ratio needs to be explained—while, as noted, I find it in principle eminently useful, I doubt the brief introduction can make sense to anyone who is not yet familiar with the basic concept of overdiagnosis/detection/treatment.

RESPONSE: This certainly is an important point. I have elaborated on this and specifically included a closer explanation of and motivation for using the OMRR. This now reads as follows: “Let me use mammography screening as an example to illustrate how polarized facts can be investigated. In this field there are two main points of disagreement: a) What is the benefit of mammography screening, e.g., on the reduction of breast cancer mortality, and b) what is the harm of this type of screening, e.g., in terms of overdiagnosis? Some researchers tend to claim that the mortality reduction is high, while the overdiagnosis rate is low,[18] while others claim that the mortality reduction rate is moderate, while overdiagnosis is high.[19] What is at stake is the risk/benefit-ratio in a utilitarian perspective. Hence, one way to illustrate the polarization in the field is the divergence in the Overdiagnosis to Mortality Reduction Ratio (OMRR), that is the ratio of overdiagnosis over the rate of mortality reduction.

Accordingly, the research questions of this brief study used as a point of departure are: What is the OMRR in publicly funded mammography screening programs of women aged 50-69 years old? How is this related to the corresponding authors’ attitudes towards screening? A straightforward literature search identifies 8 studies who have addressed the first question. The studies and their results are shown in Table 1.”

2. "as assessed by experts in polarised research (1: Very negative to screening, 2: Negative to screening, 3: Neutral to screening, 4: Positive to screening, 5: Very positive to screening)."
   → A reference should be provided here how/where these scores were obtained—rather critical, given the author's point of departure is that experts can’t be trusted.

I am pretty familiar with Marmot Review, USPSTF, and Cochrane/Gotsche, and can broadly follow the ranking here, but as described the analysis lacks robustness.

RESPONSE: This is a very important point. In the Supplementary file (S1) it is explained that “experts on polarized conflict of interest were selected by approaching scholars who had
published on this type of conflict of interest, and who had not been involved in mammography screening programs or their evaluations. These experts were asked to classify the risk of polarized conflict of interest of the corresponding authors of the identified publications on a 5-level Likert scale. 1: Very negative to screening, 2: Negative to screening, 3: Neutral to screening, 4: Positive to screening, 5: Very positive to screening.” Moreover, to address the issue of not trusting the experts of polarised research, S1 reads: “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.”

3. Related, something needs to be said about the (unfacted, objective, measureable) fact, that the Marmot Review, USPSTF, and Cochrane/Gotsche are not single authored papers, but done by large groups. Is the assertion here indeed that, in the case of Marmot and USPSTF, the chairmen strong-armed all committee members into accepting their views? If so, that should be stated explicitly. On Gotsche: a major part of what explains the skepticism is that many studies others include in meta reviews are excluded on methodological grounds—eg no double blinding, etc. This—as all Cochrane reviews gives chapter and verse on this, using GRADE and other frameworks. It's obviously interesting that there is a thin line between being methodologically rigid irrespective of where the results lead, on the one hand, and, on the other, starting from a position where one picks methods so they best support findings that gel with ones predetermined worldview. But the framing here is too broad brush, and it seems the author suggest the only things that drive disparate findings are "self-interest… intellectual laziness… mental shortcuts, or hyper-partisanism, financial conflicts". In terms of substance, that seems rather too quick. And, to restate, in terms of methods it is necessary to address the point that at least 3 major reviews included here are the result of committee work, and not single author publications, so more need to be said about how the ranking was determined.
RESPONSE: This is an important point. The issue is addressed on several occasions in S1. First, the question of committee is addressed in the methods section: “Moreover, some of the included studies were reviews, making the questions less clear. Several of the studies were also the outcome of group work or committee work. Some of the committee members were selected because they had not published on the topic before. Hence, although the suggested questions appeared reasonable to identify polarised conflict of interests, they did not work well in this case. As acknowledged by Ploug and Holm themselves: “researchers within a polarised group in a polarised field may not themselves be able to identify the field as polarised or see themselves as belonging to a polarised group.”[17]"

The question of representativeness is addressed in the following manner: “Another challenge lies in the fact that only the corresponding authors were assessed by the experts. They may not be representative for the rest of the authors. One could of course assess all co-authors (or all committee members in external committees) and make a joint score for the whole group. Applying the corresponding author is pragmatic and assumes that the person is a suitable representative of the group, but not that the person has any special influence or power. 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.”

The last point is addressed by the following: “Polarisation may be a general trend resulting from disagreements on research methodology or assessment of evidence (according to GRADE or other). However, it may also result from self-interest[29], intellectual laziness[30, 31], mental shortcuts, or hyper-partisanism.[32] Moreover, emotional conflicts of interests are more difficult to handle than financial conflicts.[33]”

4. Directly related: "An adapted version of these questions was sent to the corresponding authors of the identified publications."
   → By whom? The author? If so, should state so, as well as when and how
   → this was fielded, what the response rate was, who responded (and on
   → behalf of whom, if relevant), etc  Both for review purposes and for
   → the benefit of readers, it would be helpful to add a table with
   → responses to the 2 questions stated in footnote [ii]

RESPONSE: I am most thankful for this point and these questions. They have been explicitly addressed in Supplement S1. As the response rate for this piloting part of the study was 50% and the results are not relevant to the argument of the debate, I have not added a table in the
manuscript. The reason why I still have decided not to delete but rather to refer to this part of the study is because it illustrates that even though the questions to identify polarised conflict of interest appear reasonable (and can be easily adapted) they may not be very useful in practice. In S1 it now reads: “One may also argue that the questions sent to the corresponding authors should not be mentioned in the study, as the responses were not of any value for the study as such. However, the reason for reporting on this is that it illustrates that even though the suggested questions to identify polarised conflict of interest [17] appear reasonable (and can be easily adapted), they may not be very useful in practice. It may make future researchers on polarised research avoid dead ends. Besides, reporting on this avoids reporting bias (only reporting positive findings).”

I am open to delete this part if the reviewers or the Editor finds it distracting from the main argument of the manuscript.

5. By a) making researchers state their "polarised conflict of interest" when submitting manuscripts, b) making reviewers explicitly assess polarisation, and c) apply external experts to assess polarisation when reviewers (and/or editors) are too ingrained in the research to be able to make the assessment.

→ These recommendations are concrete in one sense, but also lack considerable detail on how exactly this would be done. Both in terms of the fact that many guidelines etc are established by committees, as noted above under (3) and, that aside, practically,

RESPONSE: This is a very important point also made by reviewer 2. Although it may be too early to elaborate detailed guidelines, and this should be the result from a joint work rather than the work of a single author, I have tried to elaborate on this at the end of the manuscript:

“How exactly to assess polarised conflict of interest may need more elaboration and collaborate work. However, Box 1 suggests some questions to ask when assessing polarised conflict of interest.
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<th>Box 1</th>
<th>Relevant questions to ask when assessing polarised conflict of interest.</th>
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<td><strong>Addressee</strong></td>
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<td>Editors</td>
<td>Is the topic of the submitted manuscript subject to significant controversy (with respect to methods, results, conclusions, or recommendations)?</td>
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<td>Which are the groups (the “poles”) and what do they disagree on?</td>
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<td>Do the authors state their polarised conflict of interest?</td>
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<td>Do you or co-editors have a specific stance on the controversy? If yes, how will you handle this? (stating conflict of interest, using alternative editors etc)</td>
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<td>Reviewers and Editors</td>
<td>Based on your expertise in this field, are there groups with competing views on methods, theories, outcomes, or/and policies in the field (of the manuscript)? (Polarisation awareness)</td>
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<td>If yes, do you and the author(s) belong to the same group? (Polarisation identification)</td>
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<td>Based on your reading of the manuscript, if the results, conclusion or recommendations of the study were the opposite (data an methods being the same) would you assess the manuscript differently? (Own stance in polarisation)</td>
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<tr>
<td>Researchers</td>
<td>“If the results of your current (well planned and well conducted) project point in the opposite direction of the results of your previous research on this topic, would your first reaction be to reanalyze the data and reconsider your methods, or to reconsider your previous conclusions?”[17] (Result polarisation)</td>
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<td>“If your findings were the exact same as the opposing researchers in this field of research, would your policy recommendations be any different from the recommendations of the opposing group?”[17] (Interpretation polarisation)</td>
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<td>When calculating outcome measures from your results (e.g., risk/benefit ratios) and these result from the methods, models or evidence criteria that you use, would you still use the same methods, models or evidence criteria if the outcome measures were very different (opposing)? (Methods polarisation)</td>
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<td>Is your institution, department, or organization is providing services related to your research? If yes, do you find it appropriate to proclaim “nothing to declare” in the conflict of interest statement? (Affiliation polarisation)”</td>
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6. On a more minor point, the following statement seemed like a needless and likely counterproductive overgeneralization: "While philosophers of science and sociologists long have acknowledged the value of disinterestedness in science[11], scientists and researchers in medicine have not."

RESPONSE: This is a good point, as the sentence certainly can be misinterpreted. This is rewritten, and now reads: “While philosophers of science and sociologists long have revealed the challenges of value-laden facts and underscored the constitutive value of disinterestedness in science[12], it is high time we scientists acknowledge this in practice.”

Wendy lipworth (Reviewer 2): This is a provocative and interesting short article on the issue of polarised scientific opinions and their effect on the generation, interpretation and presentation of scientific evidence. I think that the article should be published but that the authors need to include some more information about
- What exactly a polarised group is
- How an individual member of such a group might be recognised by, for example, a reviewer -what a declaration of a polarised interest might look like

Polarisation is the key concept underpinning the whole article and at present the reader is left with only a vague idea of what it actually means and how it might be detected and declared in publication.

RESPONSE: I fully agree with this comment, which is in line with the comments from Reviewer 1. This has been addressed in the Discussion (main text), in the conclusion, and in the Supplementary file S1.

Minor points:
- P3 Line 23: Not sure what is meant by "certain facts are exalted empirical testing" (is there a word missing here)?

RESPONSE: Good point. This sentence now reads: “One source of crisis in science is when facts are based on confirmative empirical testing[14] or that research hypotheses, models, and approaches are directed by strong interests.”
David Shaw (Reviewer 3): This is a very interesting paper on an important topic but it is very brief and needs more much explanation in general - regarding background, but particularly on methods and results.

1. I'm familiar with the breast screening debate but many readers won't be - more explanation of the debate and context of it is required.

RESPONSE: This is an important point. The following is now included in the text: “Let me use mammography screening as an example to illustrate how polarized facts can be investigated. In this field there are two main points of disagreement: a) What is the benefit of mammography screening, e.g., in terms of reduced breast cancer mortality, and b) what is the harm of this type of screening, e.g., in terms of overdiagnosis? Some researchers tend to claim that the mortality reduction is high, while the overdiagnosis rate is low,[18] while others claim that the mortality reduction rate is moderate, while overdiagnosis is high.[19] What is at stake is the risk/benefit-ratio in a utilitarian perspective. Hence, one way to illustrate the polarization in this field is to scrutinize the divergence in the Overdiagnosis to Mortality Reduction Ratio (OMRR), that is, the ratio of overdiagnosis over the rate of mortality reduction.”

2. More explanation needs to be given of the attempted survey. The questions sent to the experts are interesting but all we are told is that they had trouble answering them. The questions seem easy enough to answer but we are not even told why they had trouble. Did all experts reply? What reasons did they give for having difficulty? Why are no results of that survey reported at all?

RESPONSE: This is addressed in the following way in Supplement S1: “The questions were sent to the corresponding authors of the identified studies by e-mail, and they were asked to address the questions with respect to the specific study. Four of the eight corresponding authors responded and their answers were very divergent and not conclusive with respect to polarisation. As one of the authors replied: “I consider it difficult to answer yes or no”.” And later in the methods discussion: “One may also argue that the questions sent to the authors should not be mentioned in this study, as the responses were not of any value for the study as such. However, the reason for reporting on this is that it illustrates that even though the suggested questions to identify polarised conflict of interest [17] appear reasonable (and can be easily adapted), they may not be very useful in practice. It may make future researchers on polarised research aware of and avoid such practical problems. Besides, reporting on such failures avoids reporting bias (only reporting positive findings).”

3. Two experts on polarised CoI were asked to rate the experts in terms of bias. No information is given about what evidence was used by these two experts to inform their ratings. Were the
experts familiar with all the published works of the experts they were rating? If not, it hardly seems a fair or robust approach.

RESPONSE: This is an excellent point. The experts were very familiar with the debate on mammography screening, but have themselves not been involved in the explicit assessment of such programs. As explained in S1: “In order to overcome this problem, two experts on polarised conflict of interest were selected by approaching scholars who had published on this type of conflict of interest, and who had not been involved in mammography screening programs or their primary evaluations. These experts were asked to classify the risk of polarized conflict of interest of the corresponding authors of the identified publications on a 5-level Likert scale. 1: Very negative to screening, 2: Negative to screening, 3: Neutral to screening, 4: Positive to screening, 5: Very positive to screening.” … and elaborated on later: “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.”