Reviewer's report

Title: Estimating the Cumulative Risk of False Positive Cancer Screenings

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Reviewer: Martin C Mahoney

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Accept after discretionary revisions

Manuscript Review - BMC Medical Research Methodology
Baker, et al.

This paper by Baker, et al, examines an interesting question regarding a mathematical estimate of the risks of false positive results for mammograms. With some modest revisions, and consideration given to the points raised below, this paper would be suitable for publication.

Comments:

1. In the abstract, the authors should specify the age ranges of the subjects included in the data set as well as the years of the study. Since they use the HIP data set, it would be important to describe patient characteristics. In addition, the author should specify whether "screening number" refers to the number of mammography examinations.

2. Several places throughout the text, including line 4 of the results section within the abstract, the authors make use of the term "unnecessary biopsy". When an abnormality is found on mammograms a prudent work-up would include a FNA or an open biopsy. Therefore, these sections of the text should probably not use the phrase "unnecessary biopsy" but rather "negative biopsy". The FNA/biopsy is medically necessary but results from this are negative.

3. The authors might add some discussion about who is most likely to have a false positive mammogram since they have demographic data such as age, race, etc.; they might make a unique contribution through these analysis.

4. Background section of text Paragraph 2 - non-sequitor; incomplete text citing references 3 & 4.

5. While this manuscript is being submitted for a mathematically oriented journal. Some consideration to moving much of the mathematical formulas into an appendix ought to be strongly considered. This would improve the overall flow of the manuscript, make the presentation much more comprehensible to a diverse audience and allow the authors to focus on some of the more practical/public health implications of the information that they report on. Furthermore, this would also allow the authors to further describe some demographic correlates of the probability of false positives mammography results (see #3).
6. Within the results section, there ought to be some consideration for including basic economic analysis. For example, what would economic implications of the false positive rates reported in this paper.

7. Within the discussion, the author should restate what these proportions are regarding these two questions that they pose. This is the most important information from this manuscript.

8. In paragraph two of the discussion the author states that their methodology is applicable to any screening test recommended on a periodic basis. While this is true, there is likely to be some impact based upon the sensitivity and specificity of a particular screening test. Within this context, the authors need to address some further comments regarding strengths and limitations of this particular data set. For example, what are the potential implications of 1) subsequent improvements in technology as it relates to mammographic imaging and 2) improvements in radiologic interpretations by mammographers whose sole practice is mammographic review compared radiologists with a broader scope of practice who view a smaller number of mammograms.

9. Might it be possible to construct a curve showing the probability of false positive results according to the number of screening tests completed and/or a similar curve for negative biopsies following screenings. How does the curve shift if screening is extended to once every two years? Such figures would likely aid in interpretation of results.

10. please elaboration on public health implications of these findings. Will it increase or decrease breast cancer screening rates? How might clinicians represent this to their patients?

**Competing interests:**

None declared.