Reviewer's report

Title: An Investigation of the Apparent Breast Cancer Epidemic in France: Screening and incidence trends in birth cohorts

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Reviewer: Montserrat Rue

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General comments

This study examines the relation of screening activity to the incidence and mortality of breast cancer (BC) in France. The question posed by the authors is well defined. In general, overdiagnosis estimation is a complex problem and most of the approaches have biases and limitations. The authors take an indirect approach that gives very high overdiagnosis estimates, compared to data in the literature. The manuscript is well written.

The study compares aged-matched cohorts 15 years apart. It uses population data on screening mammography, BC incidence and mortality, hormone replacement therapy, alcohol consumption and obesity. There are some limitations that should be better described and addressed.

Specific comments

Major compulsory revisions

1. The Methods section is comprehensive but it would help the readers to include more specific details in the Appendix. For instance, age and time specific exposure to the studied risk factors HRT, alcohol and obesity were estimated using different published data sources. The Appendix 2 should be more extensive and discuss how possible synergies among risk factors were or should be addressed or what are the assumptions about independence or sequence in the risk factors that the authors made to estimate accurately the attributable fractions.

2. It is not clear how the authors accounted for changes in the mortality proportion to obtain an estimate of overdiagnosis. This should be clarified.

3. The discussion section would benefit from a Limitations section that summarized the shortcomings of the study. Issues that this section should include are:

   a) The existence of other BC risk factors, like age at first birth, nulliparity or socioeconomic status, that may have experienced changes during the studied period.

   b) The fact that BC incidence was estimated from existing cancer registries that
covered only 7% of the total population in the middle of the study period.

(c) BC mortality depends on incidence and survival time after the diagnosis of BC. The authors conclude that given that mortality did not change correspondingly, increase in adjusted incidence proportion was considered as an estimate of overdiagnosis. There is a potential bias here due to the fact that changes in BC survival or in competing risks during the studied period are not taken into account. This issue should be discussed.

Minor revisions

4. In the second paragraph of the Introduction, the sentence "Both screening and improvements in treatment should have reduced cancer mortality substantially unless the true incidence in breast cancer has increased over time" is not clear to me. Either "increase" should be "decrease" or "unless" should be another word.

5. In the Results section in Changes over time in breast-cancer incidence and breast-cancer mortality, the second paragraph presents information that is not very clear to which figure corresponds. It seems to me that it corresponds to Figure 3. If yes, Figure 3 should be cited there.

6. Paragraph in the discussion that starts with "Undetected invasive breast", 3rd sentence, add "who" to "women died".

7. Reference 21: there is a typo (ecoomie). Reference 38 should be presented without capital letters.

Discretionary Revisions

8. The Design section in the abstract should specify better which cohorts are compared.

9. In the Appendix 1 the sentence "When making use of equation [k] for replacing I'" could be replaced by "Subtracting I to both sides of equation [l]".

10. We published a paper last year with overdiagnosis estimates in Catalonia. In case that the authors want to check it out, the reference is:

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests