Author’s response to reviews

Title: Multiplicative Disadvantage of Being an Unmarried and Inadequately Insured Woman Living in Poverty with Colon Cancer: Historical Cohort in California

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Author’s response to reviews: see over
Dear Dr. Bertone-Johnson:

This letter may serve as my formal resubmission of the above noted manuscript on behalf of all co-authors. Our responses to the two reviewers’ editorial comments/criticisms/suggestions as well as yours are outlined in point-counterpoint fashion below. We greatly appreciate their peer review guidance and your editorial direction. Our revised manuscript seems to us to be a much clearer scholarly presentation because of it.

Thank you for helping us to clarify the science-based story that our research findings tell. We hope that our revised manuscript will now meet with your editorial approval for publication.

Sincerely,

Kevin Gorey

Peer-Reviewers’ and Editor’s Comments/Criticisms/Suggestions with Bulleted Responses

MAJOR
Reviewer 1: Dr. Nele Brusselaers
1. “How did the authors manage missing data?”
   - The following was added to the Methods section (lines 148-149). All variables except tumor grade (6.3% missing) had less than 2% missing data, none of which were confounding so missing data were imputed from full regression models.
   - This and other methods of handling missing data (e.g., complete case analysis) produced nearly identical findings.

2. “Last sentence of results: gender? I thought paper/analyses…based on women only?”
   - We agree that this was confusing. Previously, we included a preliminary/exploratory analysis of women and men. For clarity, this was removed so that this paper does indeed focus on women only. Consequently, textual changes were required throughout the manuscript: abstract, background/hypothesis, methods, results and discussion/summary.
   - To rationalize why this study focuses on women, our preliminary analysis of women and men is briefly mentioned in the Methods section (lines 131-134).

3. “Maybe the results of the cox regression model should be presented as well. Now the authors mention only that there is no difference.”
   - We added some more results details (two critical Cox-based findings) to the last paragraph of the Results section (lines 179-183).
   - We thought that this served to greatly clarify the clinical significance of the logistic-based chemotherapy findings (thank you). As we wished for those to remain this work’s centerpiece and we already added another table with more details relevant to the logistic regression (and its 3-way interaction term) we chose not to go into more detailed presentations and interpretations related to the Cox model.
Reviewer 2: Dr. Melissa Clark
4. “More information would be helpful…Why colon cancer/chemotherapy? For example, why not treatment for heart disease?”
   • We probably overstated our case in the original. We have toned down the language and aimed to make the case that chemotherapy for colon cancer is an (not the only) important such sentinel exemplar. This was done by adding a key sentence to the first paragraph of the Background section (lines 79-83).

5. “The authors use the term secondary analysis on line 131, which implies that they intended for there to be a primary analysis…”
   • This concern relates to concern #2 above, and we agree that it was confusing. Such language of secondary analysis was removed here and throughout the manuscript.

6. “…there is concern about the construction and interpretation of the health insurance variable (paraphrased: especially potential confounding of Medicare and private coverages given that the majority of the sample is over 65, lines 115-116).”
   • A more detailed variable definition was added to the Methods section for clarification (now lines 126-129).

7. Paraphrased: “The following last sentence of the Discussion section’s first paragraph was confusing on two points (lines 172-175).” This study also provided direct evidence that the receipt of CT is intimately related to survival chances among those with non-localized and non-metastasized disease, while more indirectly it suggested CT’s association with quality of life among those with metastasized disease.
   • We replaced the above with the following, simpler sentence. We also found evidence that the receipt of chemotherapy can explain any difference in the survival chances between married and unmarried women.

Editor: Dr. Elizabeth Bertone-Johnson
8. “I have questions about the appropriateness of considering the observed results as evidence of a 3-way interaction.” “…do not present results from a statistical test of this interaction.”
   • A statistical test was run. Its central finding is displayed in a new table (Table 2 and end-note) along with accompanying changes to Methods and Results sections text.
   • Related to concern #2 above, analysis of the 4-way interaction was removed as gender is not a variable (the 4th term) in this specific analysis/study.

MINOR
Reviewer 1:
1. “Numerous abbreviations hamper readability (paraphrased).”
   • Throughout the manuscript we have now spelled out all of those in regular English language usage: AA, ACA, CCR, CT, HI, MS, NHWA and US.
   • Only abbreviations related to statistical terms have been retained: CI, OR, PR, RD and RR (see List of Abbreviations, lines 276-278).

2. “Should be previously married, instead of previously unmarried (line 190).”
   • The suggested change was made to the sentence that is now on lines 211-212.
Reviewer 2:
3. “What do the authors mean by the fact that they “serendipitously” explore the 4-way hypothesis (line 104)?”
   • Again, this concern relates to concern #2 (major) above and was removed in that major edit of the entire text (would now be line 114).

4. “Is the…power analysis for the survival analyses specifically or for all analyses?”
   • It’s all. We clarified this in the Methods section (lines 146-147).

5. “…there are other potential explanations that warrant mention…social networks. Addition of some of this literature would strengthen the Discussion.”
   • Discussion of this research literature was added to the Potential Limitations subsection of the Discussion section. Its new first paragraph integrates that field’s knowledge with this study’s findings with four additional references [33-36], a germinal book chapter and three systematic reviews/meta-analyses that synthesize the findings of more than 250 primary studies.

6. “What are gold, platinum, bronze and silver health plans (lines 91-93)?”
   • A more detailed explanatory sentence (now lines 101-103) was added to this part of the Background section.

7. “Categories used for socioeconomic status are not clear. Words…missing (lines 111-112).”
   • A more detailed descriptive sentence was written (now lines 121-124).

Editor’s Suggestion Respectfully Declined
1. These were interrelated to the findings now presented in table 3 (was table 2). “Confidence intervals for the three groups overlap, indicating that they are not statistically different.” “By combining categories…the interaction they are testing is 2-way.” Paraphrase: “Suggest showing all four combinations. As shown it is impossible for the reader to tease apart the separate effects of poverty and insurance status.”
   • First, we have now statistically tested the 3-way interaction (see response to major comment #8 above). Table 3’s display is mean to be a descriptive depiction; an interpretive aid, rather than a statistical test.
   • After redoing the table as suggested, we believe that our original is a simpler and more vivid depiction. However, we have now clarified that the two “intermediate groups” did not differ (see table end-note) so no information of practical/clinical/policy significance was lost by displaying three, rather than four groups.
   • Finally, after having tested the interaction statistically, we are not surprised that the confidence intervals overlap. After all, we could not possible stratify and internally adjust rates for all of the main and interacting factors in the logistical regression model that tested the interaction. We still think that (after having applied a statistical test and applying further descriptive epidemiologic techniques within strata including the basic adjusted rates that themselves seem quite telling) the table tells an important story. That is, that the multiplicative barrier to colon cancer care of being inadequately insured and poor is worst for unmarried women.