Review of: "The Pandora Box from 12 Countries: Who Benefits More from Modern Interventions?"

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Potential competing interests: No potential competing interests to declare.

Peer Review Comments on the Manuscript

The Pandora Box from 12 countries : Who benefits more from modern interventions.

Revision by Jacob Pástor-Paz

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Research Question Clarification: The manuscript poses an intriguing research question: "Do life-saving interventions benefit women more than men?" This question is fundamental in understanding gender disparities in healthcare outcomes.

Hypothesis Refinement: The hypothesis suggests that "Disparities in mortality trends may be influenced by gender-specific variations in the administration of life-saving and life-extending interventions." This hypothesis effectively sets the stage for investigating the nuanced dynamics of gender differences in health interventions.

Objective Enhancement: The objective to explore the reversal in age-specific mortality rate ratios between genders across studied countries is commendably clear. It targets a gap in existing literature, focusing on how these ratios have shifted over time, potentially due to differential impacts of health interventions on men and women.

Methodological Clarifications:

- The manuscript would benefit from a clearer explanation of how the hazard baseline is established at the study's outset. Understanding the baseline hazard determination method would enhance the reader's comprehension of the initial risk assessment process.
- Including mathematical specifications for each model used in the study would significantly improve the manuscript's technical rigor. Detailed equations for the Cox Proportional Hazards Model, Cox Frailty Model with Gamma Distribution, and other variations would provide clarity on the analytical approaches employed.
- Clarification on whether each country, individual, or strata has distinct parametrizations to account for heterogeneity would be invaluable. This detail is crucial for understanding the models' flexibility in capturing diverse risk profiles.

Model Implementations and Insights:

- The manuscript hints at the implementation of various Cox model extensions without specifying or detailing their unique contributions. Introducing a summary table that outlines different models, their implementations, and the insights each provides would greatly enhance the narrative clarity and underscore the study's comprehensive analytical framework.

Contribution Highlight:

- The manuscript's contribution appears to be the application of frailty terms within Cox models to test the hypothesis regarding gender differences in mortality benefits from interventions, rather than the identification of unobserved heterogeneity itself. Emphasizing this application as the novel contribution, especially its role in advancing our understanding of gender disparities in health outcomes, would better highlight the manuscript's significance.

Structural Suggestions:

- Consider relocating detailed methodological diagrams, like the flow chart of depleting wave studies, to an annex. This could streamline the narrative for enhanced readability.
- Defining key concepts and methodologies upon introduction, such as Cox regression and predictor variables, would make the manuscript more accessible to readers with varying levels of expertise. Additionally, reordering sections for logical flow could aid in better comprehension and engagement with the study's findings.