

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.

The manuscript's investigation into cardiovascular disease (CVD) mortality, with a particular focus on gender differences and the influence of early disease diagnosis and life-saving treatments, addresses a significant area of public health research. This paper applies a range of statistical models, including descriptive analyses, Cox regression, multivariate Cox-frailty, and time-varying Cox models, to assess the effects of comorbidities, gender disparities, and timing of diagnosis on CVD mortality. The consideration of national and cohort variations is valuable. Nevertheless, several aspects of the paper could benefit from refinement to enhance its focus, structure, and readability.

1. The title of your paper could be more precisely aligned with the core findings and the primary focus of your research.
2. The manuscript lists 11 keywords, which suggests a broad scope. A more concentrated selection of keywords could help to define the study's focus more clearly. This needs to be addressed not only by deleting some keywords but also by revising the text to be more focused.
2. The paper encompasses a wide array of research content, including descriptive analyses of female-to-male mortality ratios, regression analyses on CVD mortality determinants, and the presentation of a heterogeneity index across birth cohorts. The rationale and interrelation of these analyses are not fully clear. Incorporating subheadings within the results section to delineate each analysis, followed by a brief explanation of its purpose and contribution to the overarching research question, would significantly aid in understanding.
3. The citation order of tables appears inconsistent, with Table 3 mentioned in the introduction, preceding Tables 1 and 2 cited in the results section. Aligning the citation order with the tables' appearance in the text would improve the manuscript's navigability.
4. The title of Table 1, "Multivariate Cox-frailty regression model stratified by countries for circulatory-failure CODs," suggests stratifying analysis by country. However, I did not find country-specific estimates. This discrepancy might stem from a misunderstanding of the research technique on my part. To ensure clarity and alignment with the research findings, either further explanation of how the country stratification was handled or a revision of the table's presentation would be beneficial. This adjustment would help readers better understand the application and implications of your analytical approach.
5. Table 1 focuses on variables such as gender and smoking but does not explicitly mention the adjustment for potential confounders like the respondent's age, alcohol consumption, or marital status, etc. Adding a footnote detailing the

covariates included in the analysis could enhance clarity.

6. The paper concludes that males are reaping greater benefits from current life-extending techniques. While this aligns with previous findings that CVDA medical treatments tend to be more effective in men, the conclusion might be premature without direct analysis of specific interventions' effects. This paper makes this conclusion based on the observed temporal dynamics of the female-to-male ratio of mortality instead of by examining the impact of lifesaving interventions on the female-to-male ratio of CVD mortality. Hence, a more cautious interpretation of these results is advised.

7. The use of "circulatory-failure cause of death" could potentially limit the manuscript's accessibility. Adopting the more commonly understood term "cardiovascular disease mortality" could improve the paper's accessibility and alignment with existing literature.

8. Lastly, the absence of legends in Figures 2a, 2b, and 3 detracts from their interpretability. Including legends would greatly assist readers in understanding these visual representations.