May 20, 2020

### Dr. C.B. Lambalk, Editor-in-Chief

*Human Reproduction*

Dear Dr. Lambalk,

Enclosed please find a manuscript entitled “Parity is not associated with multiple measures of biological age: Evidence from NHANES 1999-2010” for publication consideration in *Human Reproduction* as an original research article. We believe the manuscript fits well with the journal’s goals and audience given its focus on how parity may affect biological processes related to morbidity and mortality, and its analysis of nationally-representative, epidemiological data to provide estimates of such effects (or lack thereof).

We present analyses using National Health and Nutrition Examination Survey data collected between 1999 and 2010 in the United States to examine the relationship between parity and clinical-based measures of biological age. Though some studies have described relationships between parity and cellular measures of aging (including Pollack, Rivers, & Ahrens, published in *Human Reproduction* in 2018), cellular measures of aging display weak correlations with well-established composites of biological age based on clinical biomarker data. Here, we present the first analyses using these previously validated, clinical-based composites of biological age to elucidate putative costs of reproduction in women.

We find that parity does not significantly affect biological age across all three biological age composites, and that the lack of this association is robust to the inclusion or exclusion of covariates that modulate biological age, like smoking and BMI. The lack of this association is also robust to the inclusion of months or years since last live birth; further, time since last live birth does not independently predict biological age, nor does the time since last live birth modulate the relationship between parity and biological age. These results have implications for our understanding of the chronic and acute physiological changes associated with increasing parity, and suggestions for future research based on these findings are discussed.

We confirm that this work has not been previously published and the manuscript has been submitted solely to *Human Reproduction*. We have complied with all relevant ethical guidelines in conducting this project. All authors have been involved in the data analysis and manuscript writing, and have approved all files submitted for review. No authors have any conflicts of interest to report.

Thank you in advance for your consideration of this work. We look forward to hearing from you.

Sincerely,

Talia N. Shirazi, MA