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Interpregnancy Interval and Adverse Pregnancy Outcomes: An Analysis of Successive Pregnancies

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Hanley et al[1] present a compelling analysis of interpregnancy intervals and adverse pregnancy outcomes using a case-crossover design to analyze data from Canadian women with at least three deliveries between 2000 and 2015. Consistent with a previous analysis,[2] the authors found that adverse associations between short interpregnancy interval and neonatal outcomes commonly reported in studies using unmatched analyses were erased (or even reversed) after conducting a case-crossover analysis. Although we agree with Hanley et al that time-invariant confounding is most likely reduced when using a within-woman study design such as case-crossover analysis, it may be at the expense of generalizability.

As the study authors point out, unmatched designs use information from all women, whereas case-crossover analyses use information only from women with discordant exposures and outcomes.[1,3] According to the article's appendix tables, of the 38,178 women with at least three deliveries included in the unmatched analysis, 14% had discordant preterm birth outcomes (n = 5,195). Because 27% of women overall had discordant interpregnancy intervals (one in the reference group, one not in the reference group), approximately 3.8% (n = 1,457) of the total cohort presumably provided data for the case-crossover analysis on preterm birth. Although the authors note that their results may not generalize to other settings, further work on the generalizability of case-crossover analyses, which by design exclude individuals who have not experienced the outcome under study, to the broader target population would be welcome.[4]

A second point is that it would be helpful to calculate the unmatched odds ratio after restricting the data set to the women included in the case-crossover analysis, such as was done by Brotman et al.[5] Otherwise, comparisons of unmatched and case-crossover odds ratios reflect both different analytical methods and different study populations.

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We agree with Hanley et al that the relationship between interpregnancy interval and pregnancy outcomes is confounded by many factors; even after decades of research, the causal effects of interpregnancy interval on pregnancy outcomes remain unclear. Novel analytic approaches, such as that employed by Hanley et al, as well as natural-experiment designs or instrumental variable analyses, may lead to a better understanding of the role that interpregnancy interval plays in adverse pregnancy outcomes.

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