Response to Invited Commentary

Basu and Malig Respond to “Case-Crossover Methods and Preterm Birth”

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Our study in this issue of the Journal (1) indicated an increased risk of preterm delivery with higher ambient temperature. Since this study is the first, to our knowledge, to report such an association, we agree with Dr. Darrow (2) that a review of the case-crossover method we used is appropriate.

Among the key issues raised was the selection of control periods. Since the probability of delivery increases with gestational age, a bias may result if control periods are systematically chosen before (or after) the corresponding case periods. Time-stratified selection of control periods, however, can help minimize such a bias because control periods are selected both prior to the case period (when the probability of giving birth is typically lower) and after the case period (when the probability of giving birth is typically higher). The ideal situation is to have control periods equally balanced before and after the case periods. As discussed in the Results section of our study (1), preterm births were found to have a similar frequency each week during any given month; thus, the selection of control periods was not likely to be biased.

An additional concern was that the observed positive association of high temperature with preterm delivery was not causal but may have been explained by coincidental higher overall frequency of births during warmer months (i.e., seasonal pattern of births). To alleviate the effect of seasonality of preterm births, we limited our analysis to the warmer months of May through September, and we found that the number of preterm births during these months remained stable. Furthermore, as is often done in time-stratified case-crossover analyses to prevent seasonality effects, control periods were selected during the same month as case periods. Thus, it is not likely that seasonal patterns of preterm births significantly impacted the results of our study (1).

Finally, Dr. Darrow (2) offered the time-series analysis as an alternative for studies in which the baseline risk may change over time. Previous studies, however, of temperature and mortality have demonstrated that time-series and case-crossover studies have produced nearly identical results (3, 4). Depending on the assumptions of the model in a time-series analysis, such as the degrees of freedom selected to adjust for changes over time, the estimates may be biased (5). The case-crossover analysis involves fewer assumptions, and time trends and other confounders are inherently controlled for by study design. Because the unit of analysis is each case in the case-crossover study, individual-level characteristics can be considered and exposure misclassification can be minimized. The time-series analysis, on the other hand, usually relies on aggregated ecologic measures (e.g., metropolitan area).

This discussion of the case-crossover study reinforces that it is essential to check the assumptions of the method, even when using the preferred time-stratified approach. As rates of preterm delivery continue to rise (6), further studies of high ambient temperature and preterm delivery using various analytical techniques and different study populations are warranted. If the association is confirmed, this finding has important public health implications because it targets pregnant women as a subgroup vulnerable to heat exposure.

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REFERENCES


