



Re: addressing mortality in mothers of infants with congenital anomalies

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In their commentary on the article “*Associations between the birth of an infant with major congenital anomalies and subsequent risk of mortality in their mothers* (1)”, Drs. Romeo and Lamm note that they were surprised that the adjusted hazard ratio (aHR) was not elevated for endocrine/nutritional/metabolic disease, for nervous system disease and for death by unnatural causes. They note that each of these might contribute to stress-related death.

There may indeed be no association between our exposure (having an infant with major anomalies) and each of these cause-of-death outcomes. An association between chronic stress and disease has been described primarily in cardiovascular diseases and depression (2). Evidence for a direct association is weaker for other conditions. An alternative explanation is that there may be an association that we were unable to detect. The number of events for common outcomes was high (e.g., death from cancer or cardiovascular death), allowing for much more precise estimates of aHR for these outcomes than for causes of death with low event rates like deaths from endocrine/nutritional/metabolic disease, nervous system disease and unnatural causes. For instance, the estimate for deaths from unnatural causes was an aHR (95% CI) of 1.12 (0.92–1.36). This point estimate is not markedly different than the overall aHR of 1.22 for the study. Misclassification bias may also lead to erroneous attribution of death; cause-of-death is frequently based on physician reporting in the absence of autopsy data (3).

We agree that there are other explanations for the findings reported besides chronic stress. The decision to focus the study on major congenital anomalies allowed for unambiguous ascertainment of the timing of the exposure, minimal risk of diagnostic misclassification, and facility in defining an appropriate comparison group. Replication of the study results in other populations such as mothers of children with neurodevelopmental conditions may be more challenging, but can be very illuminating.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

1. Cohen E, Horváth-Puhó E, Ray JG, et al. Association Between the Birth of an Infant With Major Congenital Anomalies and Subsequent Risk of Mortality in Their Mothers. *JAMA* 2016;316:2515-24.
2. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. *JAMA* 2007;298:1685-7.
3. Helweg-Larsen K. The Danish Register of Causes of Death. *Scand J Public Health* 2011;39:26-9.

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