Response to Invited Commentary

Hernández-Díaz et al. Respond to “The Perils of Birth Weight”

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Abbreviation: DAG, directed acyclic graph.

In his commentary (1), Dr. Allen Wilcox is interested in two distinct though related questions: 1) do we have to adjust for birth weight when evaluating the effect of prenatal risk factors on infant mortality? and 2) is low birth weight a cause of infant mortality?

In our paper (2), we provided an answer to the first question under several possible scenarios represented by causal directed acyclic graphs (DAGs) (3). The most realistic of these scenarios, depicted in parts 3.4 and 3.6 of our figure 3 (2), included an effect of prenatal factors (i.e., maternal smoking) on birth weight, as well as common causes of low birth weight and infant mortality. The answer to Wilcox’s second question was assumed to be affirmative in part 3.4 of the figure and negative in part 3.6. In both cases, we concluded that adjustment for birth weight was unnecessary to adjust for confounding of the effect of prenatal factors on mortality (there is no such confounding under our DAGs) and that birth weight adjustment could introduce selection bias (4).

Thus, our article is agnostic with respect to Wilcox’s second question. We did not need to address it, because our conclusions regarding the bias induced by birth weight adjustment were insensitive to the answer. In fact, only if investigators were interested in the direct effect (i.e., not mediated through birth weight) of prenatal factors on mortality would they need to even consider any sort of adjustment for birth weight. However, as Wilcox notes (1), whether there is an effect of birth weight on mortality is an important public health question. The strong association between birth weight and infant mortality could be explained by a direct effect of birth weight on mortality, by the presence of common causes of low birth weight and infant mortality (confounding), or by a combination of both. Here and elsewhere (5, 6), Wilcox and his colleagues have argued for confounding as the main explanation and hence for public health interventions that target well-known causes of mortality rather than low birth weight.

Interestingly, adjustment for birth weight results in estimates of the effect of prenatal factors that may be opposite in sign to the unadjusted estimates. This extreme divergence of adjusted and unadjusted estimates is often referred to as “Simpson’s Paradox” (7) when the adjustment factor is a confounder. As Wilcox explains, a similar situation may occur when the adjustment factor is not a confounder but, like birth weight, a factor affected by prior exposure. In this case, adjustment may introduce selection bias (4). As always, the choice between the adjusted (for birth weight) estimate and the unadjusted estimate depends on the causal structure. Causal DAGs help us represent this causal structure, but only subject-matter knowledge can help us propose plausible causal structures to be represented by DAGs (8). We therefore join Wilcox in recommending that investigators “never adjust for covariates just because they are handy” (1, p. 000), even if adjusting for them changes one’s estimate (8).

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