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Biases in studying gestational weight gain and infant mortality in U.S. birth certificates

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To the Editor:

In a study recently published in the *Maternal and Child Health Journal*, Davis and Hofferth presented an analysis of the association between total gestational weight gain (GWG) and risk of infant death in a random sample of 100,000 births from the National Center for Health Statistics 2002 Birth Cohort Linked Birth/Infant Death Data file (1). We agree that investigating the link between GWG, a modifiable risk factor, and infant mortality using nationally-representative data is an important research priority. However, we believe that the data analysis as reported carries a high likelihood of bias, and that the results from this analysis should be interpreted with caution.

We have four major concerns with the analysis. First, the authors defined inadequate GWG based on the 2009 Institute of Medicine (IOM)-recommended ranges for total GWG at term (2), but applied these definitions to both preterm and term births. Preterm births in their analysis, therefore, were more likely than term births to be classified as having had 'inadequate' GWG simply because women who deliver at earlier gestational ages do not have as much time to gain weight as women who deliver at later gestational ages (3). Second, this correlation between total GWG and gestational age at delivery likely induced a spurious association between weight gain and risk of gestational-age dependent outcomes such as infant death (4). Gestational age at birth is one of the strongest known predictors of infant survival (5). It is therefore problematic that the authors only accounted for gestational age as a binary variable indicating preterm (< 36 weeks) or term status. Mortality among infants born at <32 weeks is roughly 25-fold higher than infants born at 34-36 weeks (6). Women delivering before 32 weeks would be expected to have gained 4 lb. less than women delivering at 34-36 weeks (assuming a prepregnancy BMI <25 and a pattern of weight gain recommended by the IOM guidelines) (2), introducing serious potential for residual confounding. A better approach to account for the influence of gestational age is needed to allow confident conclusions about the association between low GWG and infant mortality.

Third, the 2002 birth certificates in the U.S. did not collect data to calculate maternal prepregnancy body mass index (BMI). Lack of data on prepregnancy BMI is problematic because the 2009 IOM GWG guidelines are stratified by BMI category in recognition of its

modifying effect of GWG-adverse outcome associations (2). Using weight-gain cut-points for normal-weight women to define ‘inadequate’, ‘adequate’, and ‘excessive’ GWG in a population of births without prepregnancy BMI data will lead to substantial misclassification because there is little overlap across BMI-specific recommended GWG ranges. For example, the authors’ definition of inadequate GWG (<25 lb.) will misclassify overweight and obese women who gain within the IOM-recommended ranges (15-25 lb. and 11-20 lb., respectively). Importantly, the authors’ approach of redefining inadequate weight gain as <15 lb. in a sensitivity analysis still leads to misclassification of many obese women who gained within the recommended range. The reference group in these analyses is also a mix of inadequate-, adequate- and excessive-gainers (depending on BMI category), which further confuses comparisons.

Finally, obesity is a well-known risk factor for perinatal mortality (7, 8), and obese women typically gain less GWG than non-obese women (2, 3). We believe it likely that the lack of data on prepregnancy obesity confounds the observed relationship between gestational weight gain adequacy and infant mortality. The lack of adjustment for prepregnancy BMI is particularly concerning because comorbidities associated with both maternal obesity and infant mortality such as preeclampsia and diabetes (9, 10) also do not appear to have been accounted for.

Davis and Hofferth (1) point out that data on prepregnancy BMI will become available as states adopt the retooled birth certificate. We agree that the quality of these GWG and BMI data will need to be assessed through formal validation studies. Published methods can be used to account for the misclassification identified (11, 12).

Vital statistics data are potentially valuable to test the hypotheses posed in this paper, but future studies will need to consider the analytic issues that we describe here. Only then will it be possible to understand the potential causal link between maternal gestational weight gain, infant mortality and other adverse perinatal outcomes needed to inform evidence-based weight gain recommendations.

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