Obesity

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LETTER TO THE EDITOR

Response to "Stratification Bias in Associations Between Prepregnancy BMI and Neonatal Outcomes Following Extremely Preterm Birth"

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Received: 8 October 2025 | **Accepted:** 15 October 2025

We thank Wu et al. for their letter about our article "Impact of maternal prepregnancy body mass index on neonatal outcomes following extremely preterm birth" [1]. We agree with them that there are important differences between a "fetuses-at-risk" (FAR) and a births-based approach. There is a longstanding debate among perinatal epidemiologists about the application of both approaches to research questions regarding outcomes affecting live births. Indeed, there are benefits to both approaches, but the choice of approach should be tailored to the research question [2, 3].

In our study, we sought to establish whether maternal prepregnancy body mass index (BMI) influenced neonatal survival without severe morbidity for fetuses alive at maternal admission to hospital and subsequently born before 27 weeks of gestation—an event affecting about 5 per 1000 births [4]. This question has clinical significance for identifying and understanding the pregnancy characteristics that may determine prognosis after extremely preterm birth and for counseling women at immediate risk of extremely preterm delivery and families of children who are born extremely preterm. Our hypothesis was that maternal prepregnancy obesity could lead to worse outcomes in these fragile infants given that increased BMI has been linked with inflammation and oxidative stress in offspring.

Using previously harmonized data [5] from three of the largest extremely preterm (birth at 22–26 completed weeks of gestation) national birth cohorts that exist, we found that extremes of maternal prepregnancy BMI did not affect outcomes. The absence of association was seen overall and in all three cohorts that had varying maternal characteristics, care patterns, and outcomes. This research question required a birth-based approach, but we nonetheless considered pregnancy complications and gestational age as mediators of the relationship between prepregnancy BMI and neonatal outcomes after live birth.

Our study design does not allow inference about the overall effect of maternal prepregnancy obesity on the risk of having an extremely preterm infant with severe morbidity. In general, as prepregnancy obesity increases risks of extremely preterm birth, overall risks will be higher [6]. The value of applying the FAR approach to understand better the overall risks of survival without severe morbidity in very preterm populations has been shown when comparing differences by race/ethnicity [7].

Wu et al. pinpoint a limitation of current and past research on very preterm birth. Because of the logistic complexities and financial costs of setting up extremely or very (< 32 weeks of gestation) preterm cohort studies, these studies do not include information on later preterm or term births. Consequently, this body of research cannot take into consideration overall population risks. This is a major limit for prevention research and

the broader set of questions that could be answered using a FAR framework, as well as a good justification for a change in paradigm which would embed very preterm cohorts in routine population registers.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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