Yet another paradox?

TO THE EDITORS: Gardella et al\textsuperscript{1} selectively reported on placental fetal vascular malperfusion and concluded that in preterm neonates with intrauterine growth restriction (IUGR), fetal vascular malperfusion is correlated with an increased risk of abnormal neurodevelopmental outcomes in children at 2 years of age, even in the absence of brain lesions or neurologic abnormalities at discharge from the neonatal intensive care unit. One of the eligibility criteria of the study was delivery of a viable very-low-birthweight (≤1500 g) neonate before 34 weeks’ gestation. Furthermore, they only considered neonates discharged alive with normal head ultrasound findings who had complete 2-year neurodevelopmental data. We have major concerns about the methodology of this study. We believe that there is a high risk of selection bias. Making conclusions based on complete data is a mechanism of selection bias.\textsuperscript{2} Another mechanism is collider stratification. When one draws a directed acyclic graph, it becomes clear that “IUGR in viable preterm neonates” is a collider (Figure 1). Looking only at preterm neonates

![Directed acyclic graph of placental lesions and neurodevelopmental outcome](image1)

FIGURE 1
Directed acyclic graph of placental lesions and neurodevelopmental outcome

![Directed acyclic graph of the birthweight paradox](image2)

FIGURE 2
Directed acyclic graph of the birthweight paradox

Adapted from Whicomb et al.\textsuperscript{3}

born alive with IUGR results in collider stratification bias. IUGR in viable preterm neonates can be caused by other causes than placental lesions, and these other causes can influence the neurodevelopmental outcome. When the other causes have a more important negative effect on the neurodevelopmental outcome than the placental lesions, placental fetal vascular malperfusion might even become protective of a negative outcome in viable preterm neonates with IUGR, and the other way around. In perinatology, this type of bias is also illustrated by the birthweight paradox, which describes a lower birthweight-specific mortality in neonates of women who smoked than in neonates of women who do not smoke (Figure 2).3

We think that the associations described in this study are subject to significant bias. Therefore, the findings of this study did not enable clinicians to say anything about the suspected neurodevelopmental outcome of viable preterm neonates with IUGR and placental fetal vascular lesions.

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