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Does augmentation or induction of labor with oxytocin increase the risk for autism?

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TO THE EDITORS

We read with great interest the editorial by Drs Vintzileos and Ananth¹ that discusses the recent article by Gregory et al² demonstrating an association between labor induction and augmentation and subsequent diagnosis of autism spectrum disorders (ASD). As obstetricians and pediatricians, we agree with both Gregory et al² and Drs Vintzileos and Ananth¹ that any suggestion that oxytocin exposure could lead to autism should be examined carefully.

However, we disagree with the criticisms made by Vintzileos and Ananth¹ and believe that they highlight issues that likely do not compromise the validity of the presented results. While the diagnostic criteria of pervasive developmental disorder-not otherwise specified (atypical autism) did change over the years of the study, this change alone is not sufficient to cause a falsely positive result. Misclassification can lead to falsely strong estimates of an association only if it is differential; in this case it would require overdiagnosis of autism to occur more often in children born following induced or augmented labor than in others and it is difficult to hypothesize that this was the case.

One way to account for the possible confounding influence of changing diagnostic criteria over time is to control for year of diagnosis. Gregory et al² did include calendar year as one of the variables in their Model 5, and the adjusted odds ratios for ASD remained statistically significant in pregnancies in which labors were induced or augmented. Vintzileos and Ananth¹ cite Table 3 but we disagree with their interpretation; like all other listed covariates in the model, the adjusted odds ratios for the years 1996 through 1998 estimate the association between birth year itself and subsequent ASD diagnosis (controlling for all other

covariates), not the association of induction and augmentation with ASD during those specific years.

We agree that there are important limitations of the Gregory et al² report that do seriously compromise its validity, including the lack of inclusion of important confounders (particularly low birthweight and gestational age < 41 weeks), lack of appropriate statistical techniques to deal with varying lengths of follow-up, and a high rate of loss to follow-up and incomplete records. We hope that future work in this area can avoid or address these methodological limitations.

REFERENCES

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