Autism Spectrum Disorder and Birth Spacing: Findings from the Study to Explore Early Development

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Background and Study Objective

- Previous studies reported associations between ASD and birth spacing. But they had some limitations
  - Case definitions based on non-standardized diagnostic coding
  - Limited assessment of phenotypic case subtypes
  - No assessment of other (non-ASD) developmental disabilities
  - Little examination of possible underlying mechanisms for associations

- SEED was able to address these limitations
  - Rigorous case classification based on gold standard instruments
  - Extensive developmental data to characterize phenotypic subtypes
  - Second non-ASD DD case group enrolled
  - Detailed maternal health data allowed exploration of possible mechanisms
Methods

- Analysis sample: children who were 2nd or later births

- Inter-pregnancy interval (IPI) -- time between mother’s previous birth and conception of the study child’s birth
  - Short birth spacing: IPI <18 months (16% POP controls)
  - Long birth spacing: IPI >60 months (33% POP controls)

- Case groups compared to POP controls
  - ASD (total)
  - ASD + intellectual disability (ID) vs ASD w/out ID
  - ASD with high symptom severity score vs ASD w/ lower symptom severity score (measured on ADOS)
  - DD (total)
  - DD + ID vs DD w/out ID
  - DD with ASD features vs DD without ASD features (measured on SCQ)
Methods

- Odds ratios derived from multivariable logistic regression
  - adjusted for child sex, maternal age, education, race-ethnicity

- Analyses run for total sample and sample limited to children born at term (37 or more weeks gestation) to eliminate competing risks caused by preterm birth

- Several factors possibly related to the underlying mechanism also assessed
Adjusted odds ratios and 95% confidence intervals: 
Association between ASD and inter-pregnancy interval <18 months

- Modest association between ASD and short birth spacing
- Slightly more pronounced among term births
- Much more pronounced among ASD cases with high ASD symptom severity
Adjusted odds ratios and 95% confidence intervals:

*Association between ASD and inter-pregnancy interval >60 months*

- Modest association between ASD and long birth spacing
- Slightly more pronounced among term births
- Much more pronounced among ASD cases with high ASD symptom severity
Cubic spline analysis demonstrating a U-shaped association between ASD and inter-pregnancy interval

*Term Births, ASD with high severity score*
Further analyses indicated associations were NOT explained by:

- Unplanned pregnancy
- Maternal infertility disorders
- Maternal complications during pregnancy – hypertension, diabetes
Cubic spline analysis demonstrating no association between other DDs and inter-pregnancy interval

Interpregnancy Interval(month), reference=36
Conclusion

- ASD is associated with both short and long birth spacing, particularly ASD with the highest symptom severity.
- Association not explained by unplanned pregnancy, mother’s underlying infertility disorders, or hypertension or diabetes during pregnancy.
- Two areas to investigate further are maternal nutrition and inflammation.
Many thanks to all the families who participated in SEED and made this work possible!

The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.