

National Center on Birth Defects and Developmental Disabilities



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

LA Schieve, LH Tian, C Drews-Botsch, GC Windham, C
Newschaffer, JL Daniels, LC Lee, LA Croen, MD Fallin

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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

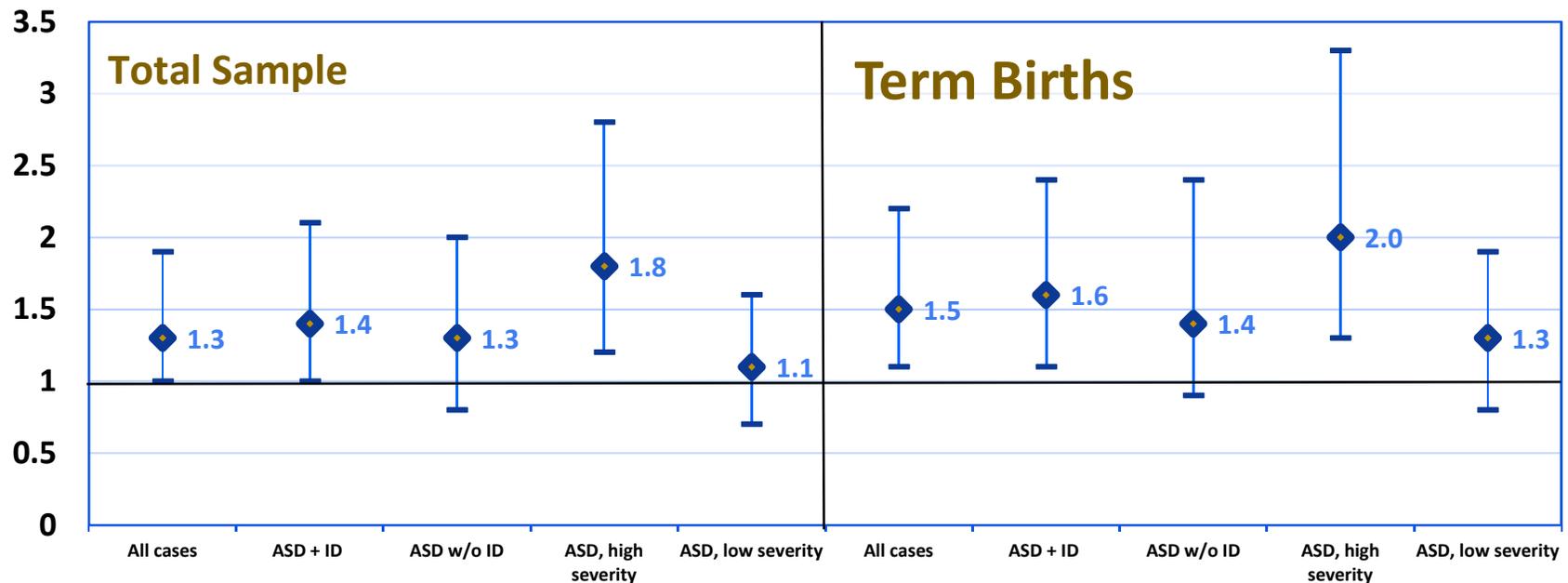
Methods

- 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 \geq 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

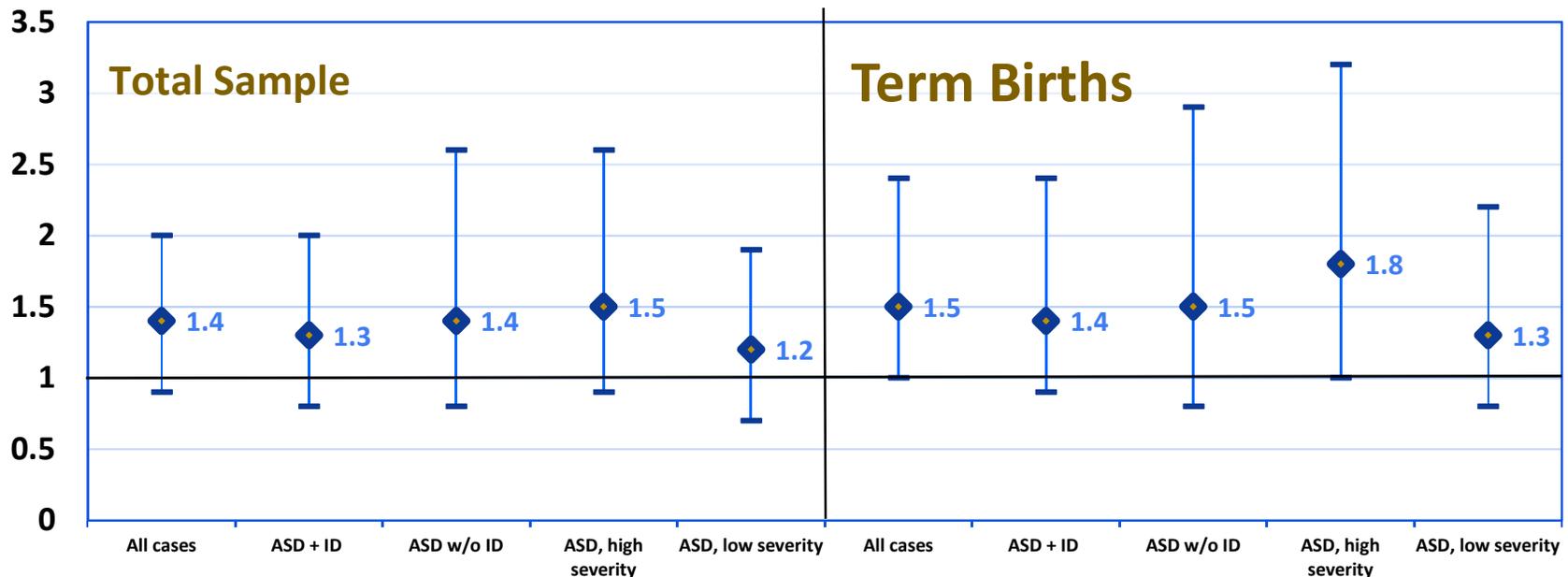
- Odds ratios derived from multivariable logistic regression
 - adjusted for child sex, maternal age, education, race-ethnicity
- Analyses run for total sample and sample limited to children born at term (37 or more weeks gestation) to eliminate competing risks caused by preterm birth
- Several factors possibly related to the underlying mechanism also assessed

Adjusted odds ratios and 95% confidence intervals: *Association between ASD and inter-pregnancy interval <18 months*



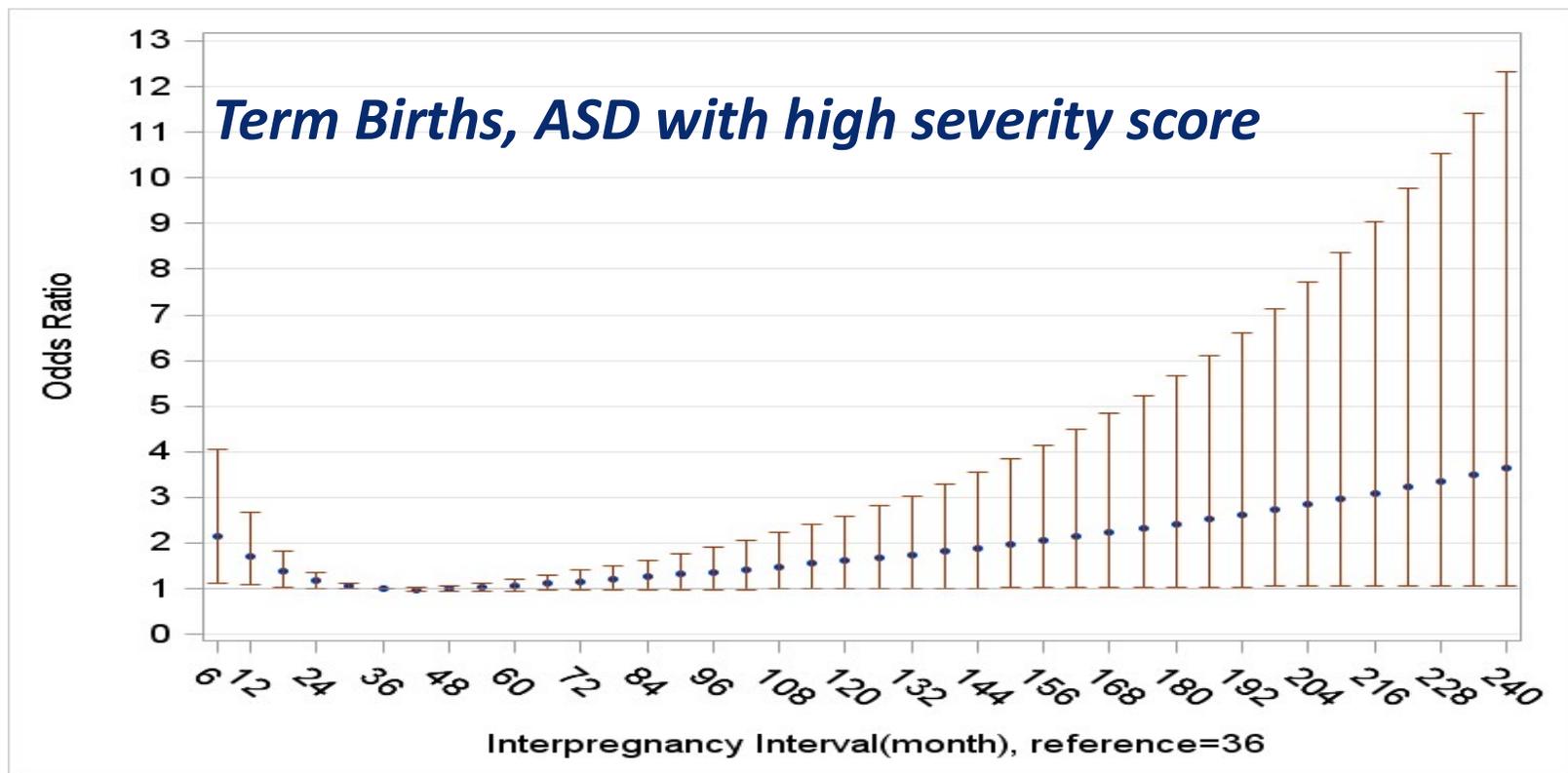
- Modest association between ASD and short birth spacing
- Slightly more pronounced among term births
- Much more pronounced among ASD cases with high ASD symptom severity

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

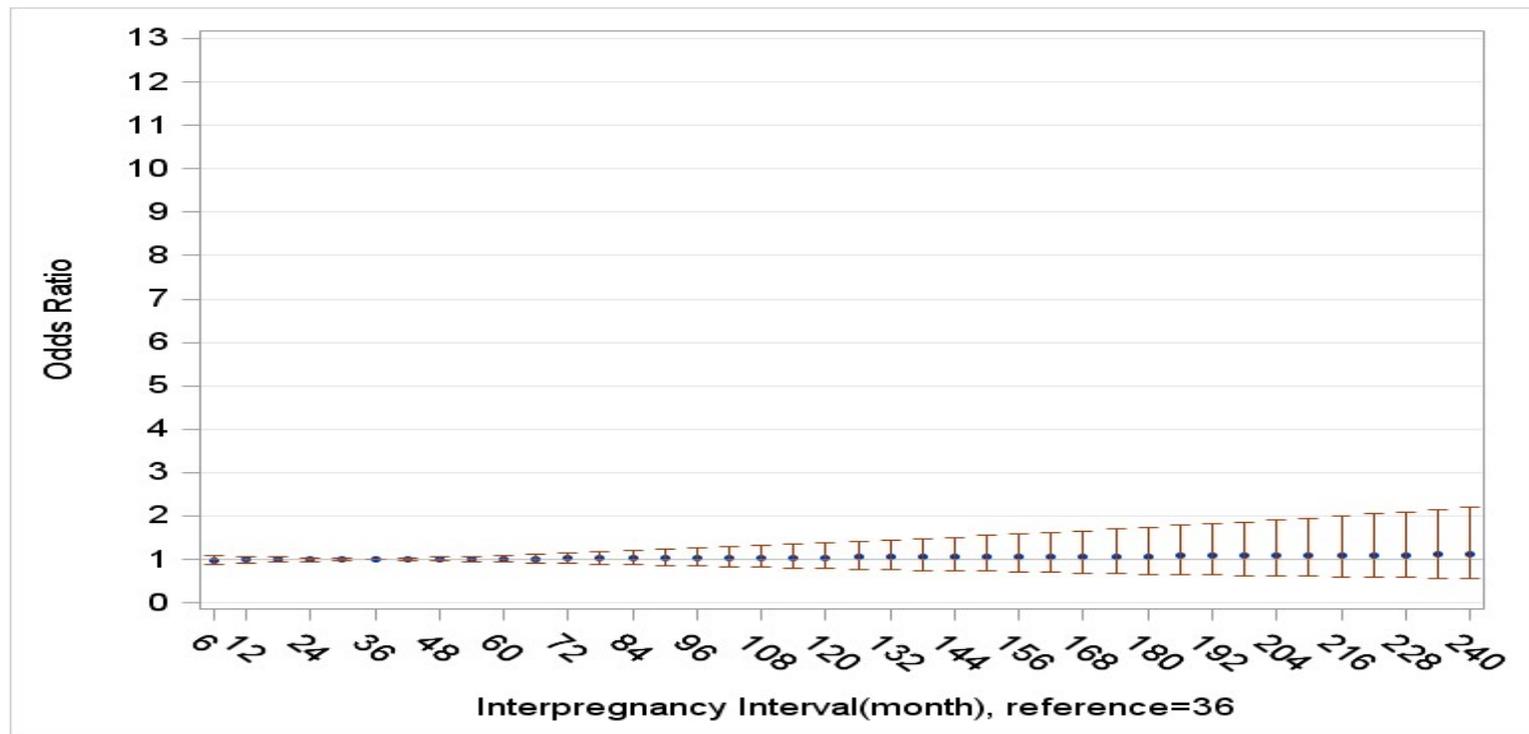
Cubic spline analysis demonstrating a U-shaped association between **ASD** and inter-pregnancy interval



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



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

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**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.