

Are Autism and Prematurity Related?

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In a recently released study in *Pediatrics* ([10.1542/peds.2020-032300](https://doi.org/10.1542/peds.2020-032300)), Dr. Casey Crump and colleagues determined associations between preterm and early term birth and risk for autism (autism spectrum disorder or ASD), examining sex-specific differences and potential causality in a very large birth cohort.

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born during 1973-2013 who survived through age 1 year of life were included. This amazingly large cohort of more than 4 million children was followed through December 31, 2015 (median age of 21.5 years at last follow up). The diagnosis of autism was ascertained based on at least one diagnosis and using comprehensive national registries: The Hospital Register (>99% national coverage by 1987), The Outpatient Register (started in 2001 and includes all specialty clinics nationwide) and The Primary Care Registry (covered >90% of the population by 2018). The diagnosis of ASD in Sweden was previously validated with a positive predictive value of 96%. Multiple covariates including biological and demographic factors were included. The word “comprehensive” hardly begins to describe this remarkable and scientifically solid study.

In this cohort, ASD was identified in 58,404 individuals (1.4%). Even the briefest glance at the study abstract alerts you that the authors found a clear inverse association between risk of autism diagnosis and gestational age at birth, and this association extends from the extremely preterm group (22-27 weeks gestational age) to early term birth (gestational ages 37-38 weeks). A 5% lower prevalence of ASD, on average, was associated with each added week of gestation. Additional analyses, including sex-specific rates, risk associated with being small for gestational age as compared to average for gestational age, and comparison of medically indicated versus spontaneous preterm birth, are fascinating and well explained.

Although the association between prematurity and autism is not new, this comprehensive population-based study extends this link and provides highly granular information not previously available. A commentary by

Drs. Elizabeth McGowan and Stephen Sheinkopf ([10.1542/peds.2021-051978](#)) extends our understanding of this work by considering and discussing mechanisms underlying the prematurity-autism relationship. Is neuronal injury involved? Do inflammatory cytokines play a role? Whether the relationship between prematurity and autism is causal or relates to shared etiologies, this intriguing link may ultimately serve as a portal to begin unravelling the still largely unknown causes of both prematurity and ASD.

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