# Perinatal and Neonatal Risk Factors for Autism: A Comprehensive Meta-analysis

**WHAT'S KNOWN ON THIS SUBJECT:** Autism etiology is unknown, although perinatal and neonatal exposures have been the focus of epidemiologic research for more than 40 years. Although studies show that obstetrical and neonatal complications may increase autism risk, the specific complications and magnitude of effect have been inconsistent.

**WHAT THIS STUDY ADDS:** Our study provides the first review and meta-analysis of all 64 studies of perinatal and neonatal risk factors for autism published through March 2007.

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## abstract

**BACKGROUND:** The etiology of autism is unknown, although perinatal and neonatal exposures have been the focus of epidemiologic research for over 40 years.

**OBJECTIVE:** To provide the first review and meta-analysis of the association between perinatal and neonatal factors and autism risk.

**METHODS:** PubMed, Embase, and PsycInfo databases were searched for studies that examined the association between perinatal and neonatal factors and autism through March 2007. Forty studies were eligible for the meta-analysis. For each exposure, a summary effect estimate was calculated using a random-effects model. Heterogeneity in effect estimates across studies was examined, and, if found, a meta-regression was conducted to identify measured methodological factors that could explain between-study variability.

**RESULTS:** Over 60 perinatal and neonatal factors were examined. Factors associated with autism risk in the meta-analysis were abnormal presentation, umbilical-cord complications, fetal distress, birth injury or trauma, multiple birth, maternal hemorrhage, summer birth, low birth weight, small for gestational age, congenital malformation, low 5-minute Apgar score, feeding difficulties, meconium aspiration, neonatal anemia, ABO or Rh incompatibility, and hyperbilirubinemia. Factors not associated with autism risk included anesthesia, assisted vaginal delivery, postterm birth, high birth weight, and head circumference.

**CONCLUSIONS:** There is insufficient evidence to implicate any 1 perinatal or neonatal factor in autism etiology, although there is some evidence to suggest that exposure to a broad class of conditions reflecting general compromises to perinatal and neonatal health may increase the risk. Methodological variations were likely sources of heterogeneity of risk factor effects across studies. *Pediatrics* 2011;128:344–355