

Association Between Influenza Infection and Vaccination During Pregnancy and Risk of Autism Spectrum Disorder

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 Supplemental content

IMPORTANCE Maternal infections and fever during pregnancy are associated with increased risk for autism spectrum disorders (ASDs). To our knowledge, no study has investigated the association between influenza vaccination during pregnancy and ASD.

OBJECTIVE To investigate the association between influenza infection and vaccination during pregnancy and ASD risk.

DESIGN, SETTING, AND PARTICIPANTS This cohort study included 196 929 children born at Kaiser Permanente Northern California from January 1, 2000 to December 31, 2010, at a gestational age of at least 24 weeks.

EXPOSURES Data on maternal influenza infection and vaccination from conception date to delivery date, obtained from Kaiser Permanente Northern California inpatient and outpatient databases. Influenza infection was defined by the *International Classification of Diseases, Ninth Revision, Clinical Modification* codes or positive influenza laboratory test results.

MAIN OUTCOMES AND MEASURES Clinical diagnoses of ASDs identified by *International Classification of Diseases, Ninth Revision, Clinical Modification* codes 299.0, 299.8, or 299.9 recorded in Kaiser Permanente Northern California electronic medical records on at least 2 occasions any time from birth through June 2015.

RESULTS Within this cohort of 196 929 children, influenza was diagnosed in 1400 (0.7%) mothers and 45 231 (23%) received an influenza vaccination during pregnancy. The mean (SD) ages of vaccinated and unvaccinated women were 31.6 (5.2) and 30.4 (5.6) years, respectively. A total number of 3101 (1.6%) children were diagnosed with ASD. After adjusting for covariates, we found that maternal influenza infection (adjusted hazard ratio, 1.04; 95% CI, 0.68-1.58) or influenza vaccination (adjusted hazard ratio, 1.10; 95% CI, 1.00-1.21) anytime during pregnancy was not associated with increased ASD risk. In trimester-specific analyses, first-trimester influenza vaccination was the only period associated with increased ASD risk (adjusted hazard ratio, 1.20; 95% CI, 1.04-1.39). However, this association could be due to chance ($P = 0.1$) if Bonferroni corrected for the multiplicity of hypotheses tested ($n = 8$). Maternal influenza vaccination in the second or third trimester was not associated with increased ASD risk.

CONCLUSIONS AND RELEVANCE There was no association between maternal influenza infection anytime during pregnancy and increased ASD risk. There was a suggestion of increased ASD risk among children whose mothers received an influenza vaccination in their first trimester, but the association was not statistically significant after adjusting for multiple comparisons, indicating that the finding could be due to chance. These findings do not call for changes in vaccine policy or practice, but do suggest the need for additional studies on maternal influenza vaccination and autism.

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