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**Title:** Child’s biologic sex as a risk factor for infection with influenza virus and respiratory syncytial virus from 0-2 years in the PREVAIL Birth Cohort

**Introduction:** Biologic sex is known to moderate innate and adaptive immune response and infection risk. Adult females tend to mount stronger immune response to infectious challenge than males and thus experience lower incidence and severity of certain infections. The SARS-CoV2 pandemic has highlighted this phenomenon, as adult males are at greater risk for severe disease and mortality from COVID-19. However, the impact of biologic sex on acute respiratory infections in children under two is poorly defined. To address this gap, we have analyzed sex-specific risk of two respiratory pathogens with a high pediatric disease burden, Influenza (IV) and Respiratory Syncytial Virus (RSV).

**Methods:** The PREVAIL Cohort, a CDC-funded birth cohort conducted from 4/2017–4/2020 in Cincinnati, OH, surveilled infants from birth to 2 years of age with weekly text surveys for presence of fever and respiratory symptoms. Weekly mid-turbinate nasal swabs were tested using the Luminex Respiratory Pathogen Panel, with a viral infection defined as including all positive tests ≤14 days apart. Maternal report and medical chart abstractions identified use of primary care, emergency department, and hospital admissions. Highly adherent participants (submitted ≥70% of nasal swabs) were included in this analysis.

**Results:** PREVAIL enrolled 245 mother-infant dyads; 101 (41%) met adherence criteria, providing 178 child-years of follow up. Covariates, including demographic characteristics, breastfeeding duration, child-years of follow-up, use of out-of-home childcare or age at time of infection, did not differ by sex. Overall incidence of RSV was 0.60 infections/child-year with no significant differences by sex. Overall incidence of IV was 0.16 infections/child-year. Males were significantly more likely to have an influenza infection than females (respectively, 0.23 v. 0.08 infections/child-year; aOR:4.6 (95%CI 1.6-13.1)). Among children infected with IV or RSV, there were no significant differences in the presence or absence of symptoms or use of medical facilities.

**Conclusion:** Significant differences were found by biologic sex in incidence of IV, but not RSV, in children less than 2 years of age in the PREVAIL Cohort. Given these differences, infection risk associated with sex may be pathogen-specific. Epidemiologic studies of respiratory infection in children should be cautious to disregard null findings associated with sex when pathogen-specific analyses are not available.