Optimizing the sensitivity of detection of respiratory syncytial virus infections in longitudinal studies using the combination of weekly sample testing and biannual serology

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Background: Cohort studies with frequent sampling and testing can improve the full capture of infections and disease burden but are often challenged by incomplete adherence to sampling regimens. We describe the detection sensitivity of respiratory syncytial virus (RSV) infection achieved in a birth cohort using a combination of weekly nasal sample testing and serology.

Methods: The PREVAIL Cohort (2017-2020 Cincinnati, OH) followed mothers and their healthy babies from birth to age two. Mothers collected mid-turbinate nasal swabs weekly which were tested for RSV using real-time polymerase chain reaction (RT-qPCR). Serum was collected at age 6 weeks and biannually from 6-24 months and tested for RSV pre-fusion F IgG and IgA antibody. Mixed effects classification and regression trees (CART) identified IgG and IgA thresholds consistent with a RT-qPCR-identified RSV infection using a subset of participants having ≥90% weekly sample adherence. Resulting thresholds were applied to participants with ≥18 months of follow-up who provided either ≥70% of weekly samples or serum at age 18 to 24 months. Incidence rates were compared using Fisher's exact test.

Results: Of 245 enrolled participants, 194 (79%) met analysis inclusion criteria. CART identified a $\log_{10}$ change in IgG>0.32 or IgA>0.20, providing 95% sensitivity and 100% specificity for identifying RSV seropositivity. Comparing RT-qPCR-only to a combination of RT-qPCR and serology, RSV cumulative incidence (49% *vs* 75%, $p<0.001$) and incidence density increased (0.33 *vs* 0.71 infections/child-year, $p<0.001$).

Conclusion: CART-identified thresholds in serum antibody accurately identified incident RSV infections, capturing a more robust estimate of disease burden.

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