Doctopic: Analysis and Interpretation
THELANCETID-D-25-00546
S1473-3099(25)00231-2

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Maternal vaccination to prevent severe RSV disease in infants

Respiratory syncytial virus (RSV) is a major cause of severe lower respiratory tract disease (LRTD), hospitalisation, and mortality in infants globally.[1] Annually, RSV causes over 45 000 deaths, 1·4 million admissions to hospital, and 6·6 million LRTD episodes in infants younger than 6 months, with more than 95% of deaths occurring in low-income and-middle-income countries (LMICs) and around two-thirds outside a health facility.[1] RSV is the major pathogen responsible for LRTD hospitalisation, consistently causing around a quarter to a third of LRTD hospitalisations in young children.[2] The highest rates of RSV-hospitalisation are in healthy term infants under 3 months of age.[3]

The development of effective preventive strategies for RSV disease in infants—either vaccination of pregnant women with an RSVpreF vaccine or administration of a long-acting monoclonal antibody to infants—represents remarkable progress, making this a preventable burden.[4] As a result, WHO has recommended that all countries should introduce either of these preventive interventions.[5] Many high-income countries have introduced these, but implementation in LMICs, where the burden is greatest, remains sparse. Maternal RSVpreF vaccination is most likely to be implemented in LMICs given cost considerations and prequalification of the vaccine (Abrysvo, Pfizer , New York, NY, USA) by WHO. Guidelines recommend vaccination at different windows of gestational age; WHO has recommended vaccination in the third trimester of pregnancy.[5]

The BERNI study by Gonzalo Pérez Marc and colleagues in *The Lancet Infectious Diseases*,[6] provides the first national-level, real-world effectiveness data for maternal RSVpreF vaccination from an ongoing, 3-year, hospital-based, retrospective observational study in Argentina. The authors used a test-negative, case-control design and included infants hospitalised with LRTD across 12 hospitals—covering public, private, and social security centres—in five provinces of Argentina following seasonal introduction of maternal RSVpreF vaccination during 32 weeks to less than 37 weeks of pregnancy into the national programme. The primary outcome was RSV-associated LRTD hospitalisation, with a secondary outcome of severe RSV-associated LRTD hospitalisation. Data were collected through the RSV season from medical records, epidemiological surveillance, and hospital statistics and hospitalisations are reported for the first season. The study from April 1 to Sept 30, 2024 included 505 infants aged up to 6 months hospitalised for LRTD and tested for RSV (286 with RSV-LRTD were cases; 219 with other non-RSV-LRTD were controls).

51 (18%) cases and 109 (50%) controls were born to mothers who had received RSVpreF during pregnancy, representing a vaccine effectiveness against RSV-associated LRTD hospitalisation from birth to age 3 months of 79% (95% CI 62–88) and from birth to age 6 months of 71% (53–82). Effectiveness against severe RSV-associated LRTD hospitalisation was 77% (45–90) from birth to age 6 months. Vaccine effectiveness was similar to results from the phase 3 MATISSE study done in 18 countries in which maternal RSVpreF vaccination had an efficacy of 82% and 70% in preventing severe RSV-LRTD from birth to age 3 months and 6 months, respectively, and 55% for RSV-associated hospitalisation from birth to age 6 months.[7] The BERNI study provides reassuring real-world evidence of high vaccine effectiveness, with results similar to MATISSE, despite differences in setting, population (with broader inclusion of all pregnant women in BERNI), gestational age at vaccination, and study design.

The BERNI study also suggests additional public health benefits, with higher immunisation coverage for other vaccines given in pregnancy among women who received RSVpreF (96%) compared with those who were not vaccinated with RSVpreF (77%) and less severe LRTD in infants of vaccinated women. Although infants hospitalised with RSV-associated LRTD had more severe disease than those with non-RSV LRTD, among all children hospitalised with LRTD, disease was less severe among those born to mothers who received RSVpreF compared with those born to unvaccinated mothers, with a lower proportion progressing to severe LRTD or requiring intensive care and all three RSV-associated LRTD deaths in infants whose mothers were unvaccinated.

These results show the feasibility and effectiveness of a large national maternal immunisation programme, with coverage of over 60% (representing >140 000 women) achieved in the first seasonal campaign and high vaccine effectiveness sustained to 6 months of age in infants, the highest risk period for RSV hospitalisation and severe disease. Lessons that enabled this impressive national implementation will be valuable for other countries—such success can be ascribed to several factors including well established maternal immunisation programmes, educational initiatives, ability of many health facilities to deliver maternal immunisation, and immunisation provided free of charge at routine antenatal visits.

Argentina has expanded the seasonal window for maternal immunisation with RSVpreF; as the study progresses it will be important to continue to monitor infant outcomes and other potential public health effects. The study did not evaluate the effect on less severe, non-hospitalised RSV disease, which represents a greater proportion of RSV-associated LRTD cases. Further, in MATISSE, there was a 31% reduction in all-cause LRTD hospitalisations in infants born to women vaccinated with RSVpreF, suggesting an important public health benefit;[7] this should be measured in future. Importantly, many RSV-associated deaths occur in the community in Argentina and LMICs,[8] thus, the effect on infant mortality including community deaths will be important to quantify. Additionally, as prevention of early life RSV disease occurs, it will be key to investigate potential effects on longer term outcomes associated with RSV-associated LRTD in young children, including subsequent recurrent non-RSV LRTD, recurrent wheezing, asthma, or lung function impairment.[9] Modelling data indicate that maternal preF vaccination would be cost effective at a dose of US$50 in Argentina, averting substantial numbers of deaths, hospitalisations, clinic visits, and cases;[10] evaluation of the economic impact will provide important information for other countries to support implementation.

RSV-associated LRTD, particularly severe disease, is now a preventable disease in infants. Maternal immunisation could have a major impact on child health, especially for those in LMICs with poor access to health care, given the high burden and associated mortality.[1,3] Global implementation of effective RSV preventive interventions for all infants is urgently needed, prioritising those in LMICs, to strengthen child health and reduce global inequity, as the Argentinian experience has shown to be possible.

The authors declare no competing interests[A: ok?]

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