Indian Academy of Pediatrics (IAP)

# nRICH

**N**ewer **R**esearch and recommendations **I**n **C**hild **H**ealth


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## UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023


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**Dear fellow IAPans,**

**nRICH**

**N**ewer **R**esearch and recommendations **I**n **C**hild **H**ealth-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialities of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology,vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

*Upendra Kinjawadekar*
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# Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV

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## BASED ON ARTICLE

Beate Kampmann, Shabir A. Madhi, Iona Munjal, et al

**Background**: Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections in young children and is responsible for an estimated 160,000 deaths annually worldwide. For patients with bronchiolitis and pneumonia, RSV has been identified as the etiologic agent in as many as 90 and 50% of cases, respectively. Contrary to the belief, 78% of RSV hospitalizations happen in otherwise healthy full-term children. 50% of RSV hospitalizations happen during RSV season, whereas 50% happen outside the season. RSV season happens during winter season in the West and in the months of June through October in India with a small peak during winter season.

Respiratory syncytial virus vaccine development has progressed for a half century, yielding an extraordinary number of vaccine candidates. Products include killed virus, purified RSV proteins, attenuated RSV, nanoparticles, virus-like particles (VLPs; particles that mimic native virus conformation but lack genetic material), virosomes (vesicular membranes carrying virus-derived proteins without nucleocapsids or genetic material), replication-competent vectors carrying RSV genes, and replication-deficient vectors carrying RSV genes. However, none of the vaccines have been found useful when given to children directly. RSV specific monoclonal antibodies have been recently licensed aborad to prevent severe RSV infections in children more than 6 months of age. However, that leaves children < 6 months of age vulnerable to severe RSV infection. In fact, 50% of hospitalizations in infants happen in children below 3 months of age. One way to protect these infants < 6 months of age will be to vaccinate pregnant ladies in late 2 nd or 3rd trimester with RSV vaccine and depend on transplacental antibodies to protect the babies.

G and F proteins comprise the major glycoprotein spikes on the viral membrane and are major targets of neutralizing antibodies. SH is a third integral membrane protein, but is not required for efficient viral growth in vitro or in vivo. There have been numerous attempts to formulate F protein vaccines with adjuvants or as a chimeric protein with RSV G. Combinations of RSV F, G and M proteins have also been clinically tested.

**Methods**: In this phase 3, double-blind efficacy and safety trial conducted in 18 countries, pregnant women < 49 years of age and at 24 through 36 weeks' gestation, were randomly assigned, in a 1:1 ratio to receive a single intramuscular injection of 120 µg of a bivalent RSV prefusion F protein–based (RSVpreF) vaccine (60 ug each of the stabilized preF glycoproteins from the two main cocirculating

antigenic subgroups RSV A and RSV B) or placebo. The two primary efficacy end points were medically attended severe RSV-associated lower respiratory tract illness and medically attended any severity RSV-associated lower respiratory tract illness in infants within 90, 120, 150-, and 180bdays after birth. A lower boundary of the confidence interval for vaccine efficacy (99.5% confidence interval [CI] at 90 days; 97.58% CI at later intervals) greater than 20% was considered to meet the success criterion for vaccine efficacy with respect to the primary end points. From June 17, 2020, through October 2, 2022, a total of 7392 women underwent randomization and 7358 received either RSVpreF vaccine (3682 participants) or placebo (3676 participants).

**Results**: At this prespecified interim analysis, the success criterion for vaccine efficacy was met with respect to one primary end point. Overall, 3570 infants born to mothersbbwho had received RSVpreF vaccine and 3558 born to those who had received placebo were evaluated. Medically attended severe lower respiratory tract illness occurred within 90 days after birth in 6 infants of women in the vaccine group and 33 infants of women in the placebo group (vaccine efficacy, 81.8%; 99.5% CI, 40.6 to 96.3); 19 cases and 62 cases, respectively, occurred within 180 days after birth (vaccine efficacy, 69.4%; 97.58% CI, 44.3 to 84.1). Medically attended RSV associated lower respiratory tract illness occurred within 90 days after birth in 24 infants of women in the vaccine group and 56 infants of women in the placebo group (vaccine efficacy, 57.1%; 99.5% CI, 14.7 to 79.8). No safety signals were detected in maternal participants or in infants and toddlers up to 24 months of age. The incidences of adverse events reported within 1 month after injection or within 1 month a-er birth were similar in the vaccine group (13.8% of women and 37.1% of infants) and the placebo group (13.1% and 34.5%, respectively).

**Conclusions**: It was concluded that RSVpreF vaccine administered during pregnancy was protective against medically attended severe RSV-associated lower respiratory tract illness in infants, and no safety concerns were identified.

**Commentary**: One of the difficulties of advancing any RSV vaccine candidate is that infants comprise an important target population, and the dire consequences of testing an ineffective RSV vaccine in infants is realized. Vaccine opponents argue that infants usually recover from RSV infection and that the risk of vaccine development is too high. Another concern relates to maternal antibodies which may impede vaccination in the new-born. However, maternal antibodies fall substantially by 2 months after birth and these infants have the greatest vulnerability to RSV infection. Thus, either a vaccine is given to the new-born before this vulnerable period, or a vaccine is given to mothers which induces high titres enough to protect the infant. Soon, RSV monoclonal antibody preparations are likely to be introduced in India. At present there are two RSV monocolonal antibodies tried in babies, Palivizumab and Nirsevimab. Palivizumab is indicated in Preterm babies with BPD or without BPD and other griups at risk for severe RSV infections. However, Palivizumab needs monthly injections as it has short half life. Nirsevimab has longer half life abd hence works for 6 months after one injection and is likely to be indicated for otherwise healthy late preterm and full term babies >29 weeks of gestation to prevent RSV infection. A successful RSV vaccine may well be developed within the next 5–10 years if preclinical and clinical trials progress efficiently and if many candidate vaccines are tested in parallel.

## REFERENCES

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