

## 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**

**Newer Research and recommendations In Child Health**-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 subspecialties 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*  
*National President 2023*  
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# Does respiratory syncytial virus lower respiratory illness in early life cause recurrent wheeze of early childhood and asthma? Critical review of the evidence and guidance for future studies from a World Health Organization-sponsored meeting.

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## BASED ON ARTICLE

Vaccine. 2020 Mar 4;38(11):2435-2448. doi: 10.1016/j.vaccine.2020.01.020.Epub 2020 Jan 20. PMID: 31974017; PMCID: PMC7049900. Driscoll AJ, Arshad SH, Bont L, Brunwasser SM, Cherian T, Englund JA, Fell DB, Hammitt LL, Hartert TV, Innis BL, Karron RA, Langley GE, Mulholland EK, Munywoki PK, Nair H, Ortiz JR, Savitz DA, Scheltema NM, Simões EAF, Smith PG, Were F, Zar HJ, Feikin DR.

## SUMMARY

Respiratory syncytial virus (RSV) is a leading cause of LRTI and hospitalization in infants and children globally causing an estimated 33.1 million LRTI episodes, 3.2 million hospitalizations, and 118,000 deaths annually (2015 data).

45% of all hospitalizations and deaths are in infants below 6 months of age, and 99% of global RSV mortality occurs in low and middle income group countries.

Babies born preterm, those with low birth weight, chronic lung disease, congenital heart disease, or immunosuppression do have increased risk of severe disease, but severe RSV LRTI also commonly occurs in children born full-term with no underlying illnesses. This clinically presents as bronchiolitis or pneumonia.

A long-standing question is whether RSV LRTI in early life causes subsequent recurrent wheeze of early childhood (RWEC) and asthma. The current evidence supporting a causal association between RSV and RWEC/asthma is mixed.

The WHO convened a meeting of experts to clarify this issue. They approached this question from two angles:

Firstly, to ask what impact would preventing RSV infection (by vaccines or Monoclonal antibody) have on the subsequent development of RWEC in RCTs and to work out the sample size needed for this.

Secondly, to assess the strength of the available evidence for a cause effect relationship between early life LRTI and subsequent RWEC/Asthma.

Large numbers of under five children experience Viral triggered wheeze, and only a small proportion of these wheezers have asthma- a disease with multiple phenotypes. Asthma is believed to be caused by complex interactions between genes and the environment. Numerous markers of asthma risk have been identified, one of which may be RSV infection in infancy.

Are there any biological clues to connect early life RSV and later RWEC/Asthma?

For one, mice infected with RSV have sustained airway hyperreactivity and histologic changes characteristic of human asthma that persist after clearance of the virus.

In one infant cohort, a distinct nasal immune response pattern to acute RSV illness was associated with increased risk of subsequent wheeze.

However it is still unclear why some otherwise healthy infants develop severe LRTI with RSV. The possible causes are infection with a more virulent RSV strain, or genetic/environmental factors that increase their vulnerability. But these same factors could also be enhancing the chances of getting RWEC/Asthma later, not related to prior RSV infection. Some studies of Pulmonary function done prior to any LRTI event, do reveal lower lung compliance in the cohort that later suffered from severe RSV disease or recurrent wheeze.

Evidence for an association between early life RSV LRTI and RWEC/asthma comes from observational studies, two of which have been conducted in LMICs. These studies compare this exposed group to those without RSV LRTI, and to individuals hospitalized for a non-respiratory condition. Many find a positive association between RSV LRTI and subsequent RWEC.

Conversely, two randomized placebo-controlled trials of efficacious anti-RSV monoclonal antibodies (mAbs) in heterogeneous infant populations have found no difference in physician-diagnosed RWEC or asthma by treatment group in the cohort of medically attended wheezing children between one and three years of age.

This report summarizes many of the methodologic challenges faced by studies that aim to assess (1) whether there is a causal association between early life RSV LRTI and subsequent RWEC and asthma, or (2) whether an effective RSV preventive product could be expected to reduce the risk of subsequent RWEC/asthma.

Notwithstanding the above issues, prevention of severe, acute RSV disease in young children, a well-established, substantial public health burden, should continue to be the highest priority for policy-setting bodies deliberating on RSV.