

Severe RSV Disease in Preterm Infants Born at 29 to 35 Weeks' Gestation in the United States

The Committee on Infectious Diseases guidance that, among preterm infants without chronic lung disease, none born at 29 to 35 weeks' gestational age (wGA) have a substantial clinical benefit from respiratory syncytial virus (RSV) prophylaxis¹ contradicts numerous studies that demonstrate the elevated risk of severe RSV disease among this population and conclude that risk factors and young chronological age can identify higher-risk subgroups. The guidance also does not meet the Institute of Medicine's Standards for Developing Trustworthy Clinical Practice Guidelines,² because it lacks a systematic evidence review, ratings of the level of confidence in the evidence and strength of the recommendations, and descriptions of potential benefits and harms, such as the number of RSV hospitalizations and ICU admissions that will occur among the ~50 000 infants no longer recommended for RSV prophylaxis.

The guidance references several studies in an incomplete and potentially misleading manner. It states that Hall et al observed similar RSV hospitalization rates among preterm and term infants. However, Hall et al cannot be used to describe the burden of RSV in preterm infants in the absence of prophylaxis, because ~70% of eligible infants in the study population were receiving palivizumab.³ In randomized, double-blind studies, palivizumab reduced RSV hospitalizations by 78% and 82% in preterm infants without chronic lung disease. This explains why the study's supplemental data showed infants <32 wGA had lower RSV hospitalization rates at ages when palivizumab is administered.

RSV hospitalization rates are cited from Stevens et al of 7.5% and 4.4% for infants 29 to 30 wGA and 31 to 32 wGA, respectively, at 0 to 12 months without

chronic lung disease. However, these rates did not include hospitalizations in the community's regional hospitals. "To enhance the generalizability of the study findings," the authors calculated community-wide RSV hospitalization rates of 10.0% and 6.4% for these groups. Although the authors stated that these calculations could overestimate disease, it is now known they would also underestimate the true rates because of the suboptimal sensitivity of antigen detection and viral culture.

RSV hospitalization rates for 32- to 34-wGA infants from Winterstein et al (3.1% in Florida and 4.5% in Texas) are from health care insurance claims, which underestimate true incidence because of incomplete testing for RSV. In a recent study of 1642 US infants 32 to 35 wGA, only 46% of infants hospitalized with lower respiratory illness were tested for RSV during routine care.⁴ Winterstein et al also demonstrated that RSV hospitalization rates were significantly higher with younger age, supporting the 2012 American Academy of Pediatrics recommendations for use in 32- to 34-wGA infants.

Additionally, the guidance cites the "overall declining incidence of hospitalizations for bronchiolitis in the United States" from Hasegawa et al. However, Hasegawa et al reported no decrease among infants with high-risk conditions such as preterm birth.⁵ This lack of a decline is expected, given that palivizumab use was similar in 2000 and 2009, and demonstrates the continuing burden of severe RSV disease among children at high risk.

Therefore, Committee on Infectious Diseases guidance against the use of RSV prophylaxis in preterm infants 29 to 35 wGA without chronic lung disease appears to warrant additional evaluation before implementation.

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Conflict of Interest:

Christopher S. Ambrose is an employee of AstraZeneca, the parent company of MedImmune.

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Re: Technical Report

I appreciate the technical summary on palivizumab prophylaxis. However, I find the comment about vial sharing to be controversial. Even in twins, this does not seem to represent accurate billing.

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Conflict of Interest:

None declared.

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