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Progress at last against RSV

The approval of two vaccines and a monoclonal antibody that target respiratory syncytial virus could shift the tide on the prevention and treatment of infection with this virus.

A surge in respiratory syncytial virus (RSV) infections and RSV-related hospitalizations in the 2023 Southern Hemisphere winter, similar to that seen in 2022 in northern climes, has strained already fragile healthcare systems that are also coping with the influenza season and COVID-19. Taking a disproportionate toll on young children and older adults, RSV infections can cause severe lower respiratory tract disease and death. RSV has long thwarted vaccinologists, who have been cautious, given the high rate of vaccine-associated disease in infants who received a vaccine made of formalin-inactivated whole RSV particles in the 1960s[1]. Hope is on the horizon, however, with two new RSV vaccines and a monoclonal antibody now available for older adults and infants, respectively, and vaccine availability for pregnant people likely forthcoming.

In May 2023, the US Food and Drug Administration (FDA) approved RSV vaccines manufactured by GlaxoSmithKline (GSK) and Pfizer for use in adults 60 years of age or older. These vaccines were also recommended for approval by the European Medicines Agency, with additional recommendations expected globally. In randomized, placebo-controlled phase 3 trials in adults 60 years of age or older, both vaccines, which target the pre-fusion form of the RSV fusion glycoprotein, showed impressive efficacies of over 80% in preventing RSV-related lower respiratory tract disease[2,3]. On the basis of these data, the US Centers for Disease Control and Prevention (CDC) ultimately opted for a moderate recommendation in June, cautiously advised that people 60 years of age or older may — rather than should — receive these vaccines after consultation with their healthcare providers. This caution reflects concerns about the trial populations having been skewed toward healthier older adults rather than those at highest risk of RSV-related complications. As a result of this recommendation, RSV vaccine uptake in older adults is likely to be reduced, despite the promising results and general enthusiasm about the vaccines. Clarity on the effectiveness and safety profile of vaccination against RSV in this population will ultimately be borne out as health agencies collect and analyze real-world data in forthcoming RSV seasons.

Pfizer has also demonstrated efficacy of their RSV vaccine in people between 24 and 36 weeks of pregnancy[4], when antibodies can cross the placenta and provide protection to newborns. In August, the FDA approved this vaccine for use in pregnant people. Questions about safety, however, have been raised, as a small (but not statistically significant) increase in the frequency of premature births was observed in the vaccinated group versus the placebo group. GSK stopped trials of its RSV vaccine in pregnant women last year due to increases seen in preterm births. Prematurity carries considerable health risks for babies, including an increased risk of RSV-related complications, and neither Pfizer nor GSK has provided much insight into potential causes or determinants. If the Pfizer vaccine is ultimately recommended for use in pregnant people by the CDC and other public health agencies, as is now expected, post-marketing surveillance will be critical to both better characterize its safety and potentially inform guidance for patients.

Arguably, the most exciting development in the RSV-preventative landscape is not a vaccine but a monoclonal antibody, which has the advantage of providing immediate protection. Nirsevimab, an F-protein-binding monoclonal antibody manufactured by AstraZeneca and Sanofi, exhibited efficacies of over 70% in preventing medically attended RSV-associated lower respiratory tract disease in phase 2 and 3 trials conducted in preterm and healthy infants[5,6]. In July, the FDA approved nirsevimab for use in babies and vulnerable toddlers under 2 years of age. As maternal antibodies wane over the first year of life, use of this monoclonal antibody could fill an important gap in protection for young children, even if mothers are vaccinated before delivery. Although nirsevimab can be envisioned as a seasonal preventative tool, it is unclear how widely it will be used, given implementation challenges and its prohibitive cost, which may especially limit its use in low-income and middle-income countries (LMICs). In the USA, the CDC has recommended that it be included in the federally funded Vaccines for Children program, which would make it free for about 50% of US children below 2 years of age. Although this news is encouraging, in 2019 it was estimated that there were over 100,000 RSV-related deaths in children 5 years of age and younger globally, with particularly high mortality and morbidity in young infants and in LMICs[7]. It is therefore vitally important that vaccines and preventative therapies such as nirsevimab are globally accessible.

The development of these new preventative tools is exciting, but it also raises important questions. It is likely that infants will soon be able to receive protection both via maternal vaccination and via antibody injection. However, it remains unclear whether these treatment modalities will have an additive effect, or whether the RSV vaccine could affect the immunogenicity of other routine vaccines administered during pregnancy, if given at the same time. More broadly, vaccine hesitancy and anti-vaccine sentiment pose major obstacles to uptake. Tailored guidance for healthcare and community providers, as well as data collection on attitudes toward these vaccines and nirsevimab, could both aid acceptability and help to inform public health strategies to better educate at-risk populations.

The approvals of these vaccines and the blocking antibody are major steps forward for public health that are certainly worthy of celebration. The responsibility now lies with global and national health agencies to ensure fair distribution and effective, transparent messaging that encourages broad uptake, with the hope that the burden of RSV will be substantially reduced in future winters.

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