

# On the verge of RESPIRATORY SYNCYTIAL VIRUS disease prevention

New immunization tools to protect in early life

**Respiratory syncytial virus (RSV) is a major, under-recognized public health problem causing more severe respiratory infections and hospitalizations in infants and young children each year than any other pathogen. Now, new tools for early RSV prevention have achieved licensure—and the chance to address this pervasive virus has never been better.**

## What is RSV and its disease burden?

Virtually everyone gets RSV, usually by age 2. RSV disease is often mild, like a cold, but can be severe (or deadly) for young children. Though any child can get severely ill or hospitalized due to RSV, infants are the most vulnerable due to easily blocked small airways. Serious complications include bronchiolitis and pneumonia and can harm lung health long term. RSV can occur seasonally in many areas and year-round in others.

In 2019, RSV led to an estimated 33 million severe respiratory infections, 3.5 million hospitalizations, and 101,000 deaths before 5 years of age worldwide—with nearly half of RSV deaths before 6 months of age.<sup>1</sup> RSV causes up to 40% of all pneumonia cases before 1 year of age and is the world's leading cause of pneumonia deaths under 6 months old.<sup>2</sup>

RSV is just as common in low- and middle-income areas of the world as in high-income ones. Despite RSV's global reach, however, over 98% of pediatric RSV deaths occur in low- and middle-income economies where many children never make it to hospital.<sup>3</sup> In fact, RSV deaths before 6 months of age in low-income areas are 4 times likelier to occur in the community than in the hospital.<sup>3</sup> Available data in these regions also show substantial burden on health systems and livelihoods.

## New interventions to prevent infant RSV

Until recently, the only preventive agent for RSV has been a monoclonal antibody (mAb) recommended for the highest-risk infants (palivizumab). It requires a multi-dose schedule unaffordable and impractical for most countries. Now, promising prevention products are licensed that use breakthrough technology that neutralizes the virus' pre-fusion (F) protein responsible for fusing to and infecting host cells. Products could start becoming globally available as early as 2024, underscoring the need to prepare for implementation now.

- » **A vaccine given in pregnancy**—An RSV maternal vaccine by Pfizer, Inc. is licensed in the US and Europe. World Health Organization prequalification could be possible as early as 2024.
- » **New mAbs for delivery to newborns**—A long-acting, one-dose mAb (nirsevimab) by AstraZeneca/Sanofi is now approved in Europe and the US and other promising mAbs for low-income contexts are also in various stages of development. Though price and supply are expected to be early barriers to access, nirsevimab is paving the way for long-acting mAbs as a wave of the future.

A communications toolkit is available to help you learn more about RSV prevention and spread the word.  
[bit.ly/RSVInfoToolkit](https://bit.ly/RSVInfoToolkit)



## Why focus on RSV? And why now?



**New, game-changing tools for preventing RSV in early life are now licensed.**

- vaccine given in pregnancy
- long-acting monoclonal antibodies given to newborns

**A chance to make headway against a huge annual disease burden before age 5.**

- 33M severe respiratory infections
- 3.5M hospitalizations
- 101K deaths (46% before 6 months old)
- strain on health systems and livelihoods



**Adding RSV to the immunization toolkit could**

- keep children out of the hospital
- save many young lives
- free up resources for other health priorities

<sup>1</sup> Li Y, et al. *Lancet* 2022; <sup>2</sup> PERCH Study Group. *Lancet*. 2019; <sup>3</sup> Srikantiah P, et al. *Clin Infect Dis*. 2021.



## Maternal vaccine



## Monoclonal antibody

<b>RATIONALE</b>	Vaccination in pregnancy can directly enhance the pregnant vaccinee's immunity and increase natural antibody transfer to baby across the placenta for protection in early life.	Directly immunizing neonates soon after birth provides antibodies for critical protection in early life.
<b>HOW IT WORKS</b>	Pre-F protein in the vaccine induces antibodies that neutralize the virus.	mAbs are manufactured antibodies to the RSV pre-F protein that neutralize the virus.
<b>TIMING</b>	Vaccination in late 2nd or 3rd trimester of pregnancy to optimize transfer of antibodies to infant. (Specific timing windows vary by country of license.)	At birth with other birth dose vaccinations (e.g., hepatitis B; BCG, OPV) or at first Expanded Program on Immunization (EPI) visit.
<b>PRODUCT CHARACTERISTICS</b>	<ul style="list-style-type: none"> <li>Given in one dose</li> <li>At least 5-6 months protection after birth</li> </ul>	<ul style="list-style-type: none"> <li>Given in one dose</li> <li>At least 5-6 months protection after administration (longer lasting than palivizumab)</li> </ul>

### A need for cross-program coordination

While maternal RSV vaccines and mAbs both offer protection for young infants, their target populations for administration differ and, therefore, will require different strategies for delivery—likely via two platforms: 1) **maternal and child health (MCH) programs** for maternal vaccine through **antenatal care (ANC) services** and 2) **Expanded Program on Immunization (EPI)** for mAbs. Both programs will likely intersect at least to some degree for either product. Since both RSV preventive products require strategies that do not fit with the most familiar EPI schedule targeting young children, countries will need to undertake strengthening of ANC and/or newborn delivery platforms for their introduction. The path to country introduction for either intervention will vary widely based on the choice of product, delivery platform selected, hierarchy of care, RSV seasonality, and other factors. Several potential advantages and challenges are important considerations.

	Likely advantages	Possible challenges
<b>Maternal vaccine</b>	<ul style="list-style-type: none"> <li>Existing tetanus, COVID-19, and other maternal immunization programs may be leveraged</li> <li>Offering RSV vaccine during ANC may also benefit ANC coverage, uptake, and perceived quality of care</li> <li>Vaccine safety monitoring systems could also track pregnancy and other maternal/child health outcomes</li> </ul>	<ul style="list-style-type: none"> <li>ANC/EPI coordination and readiness needs may be uncharted in some countries</li> <li>Reaching pregnant patients in key gestational age window and missing preterm infants born before the window</li> <li>Expanding pregnancy registry surveillance/linking mother-infant records</li> </ul>
<b>Long acting mAbs</b>	<ul style="list-style-type: none"> <li>Delivered similarly to BCG, hepatitis B, OPV birth doses</li> <li>Intramuscular injection, like many vaccines</li> <li>Robust immunization infrastructure/systems in place</li> <li>Skilled workforce familiar with nuances of immunization</li> </ul>	<ul style="list-style-type: none"> <li>Identifying and reaching infants born outside formal healthcare settings</li> <li>mAbs may be new policy and regulatory territory for some</li> <li>Cost and supply barriers to access</li> <li>Although designed to require only one dose, two doses may be needed based on weight</li> </ul>
<b>Common across products</b>	<ul style="list-style-type: none"> <li>Both products will protect babies during the most critical first six months of life</li> <li>Provide passive protection against RSV</li> <li>Only one dose needed, which simplifies delivery</li> <li>Potential to be cost-effective in low- and middle-income economies (context dependent)</li> </ul>	<ul style="list-style-type: none"> <li>Awareness gaps or reluctance/hesitancy may affect demand/acceptability/uptake</li> <li>Additional services may strain health system components</li> <li>Seasonal dosing could be logistically challenging</li> <li>Competing immunization and MCH program priorities</li> </ul>

### The takeaway

With new products near, **now is the time to raise awareness and support global, regional, and country decision-making** around RSV prevention, policy, and implementation preparedness. Domains and activities to think about as countries start to consider RSV prevention include **1) the case for prioritizing RSV; 2) product choice; 3) delivery platform(s); 4) awareness/acceptance/demand; 5) disease surveillance/safety monitoring; 6) workforce readiness; 7) financing; and 8) global/country policy.**

