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Respiratory Syncytial Virus: Priorities and Opportunities for Prevention

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BMGF RESPIRATORY SYNCYTIAL VIRUS (RSV) STRATEGY

GOAL: *Significantly reduce RSV mortality in the first 6 months of life through maternal and neonatal immunization*

Evidence Generation	Product Development		Product Delivery
Estimate the burden of RSV mortality in LMICs	Develop RSV vaccine for maternal immunization	Develop affordable RSV mAb for birth dose administration	Enable RSV product introduction and access

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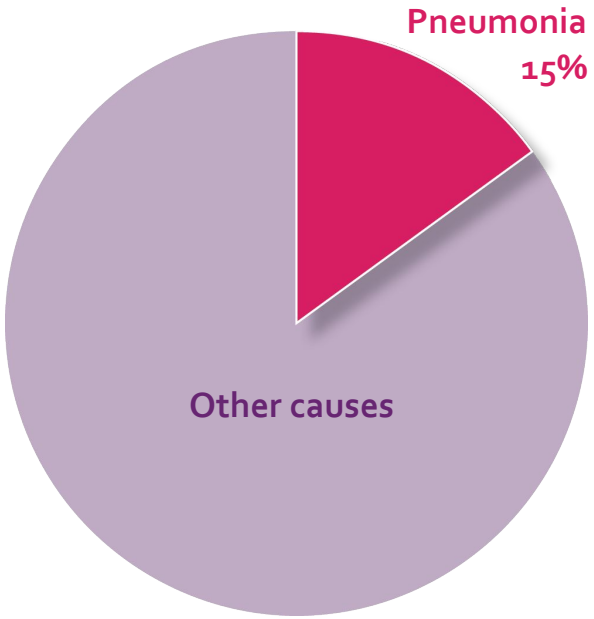
Pneumonia is the #1 cause of child mortality worldwide

Killing more children than malaria, measles, and diarrhea combined.

PNEUMONIA IS RESPONSIBLE FOR 15% OF ALL-CAUSE <5 MORTALITY

(> 700,000 deaths per year)[1]



Controlling RSV is critical in the larger pneumonia fight because it

- is the most common cause of infant pneumonia and bronchiolitis
- is a leading cause of pneumonia deaths in the first 6 months of life
- causes up to **40%** of severe pneumonia cases before 1 year of age[2]
- increases vulnerability to pneumonia caused by other viruses and bacteria

[1] Interim WHO-MCEE cause of death for children under-5 years (September 2019) updated using cause fractions from 2017 and applying them to UN-IGME estimates for 2018. [2] Pneumonia Etiology Research for Child Health (PERCH) Study Group. *Lancet*. 2019.

What is RSV?

RSV is so widespread that almost all children contract the virus before 2 years of age.

PRESENTATION

Often mild, like a cold, but can be severe (or deadly) for infants.

TRANSMISSION

Sneezing, coughing, quiet breathing, touching contaminated surface and then eyes, nose, or mouth

PARTIAL IMMUNITY

- Infection-induced immunity not fully protective
- Repeated lifelong infections

PEDIATRIC POPULATIONS AT HIGH RISK OF SEVERE DISEASE

Any child can get severely ill and be hospitalized.

- Most with severe disease are born full term and have no underlying health conditions

Additional factors that increase risk:

- Premature birth
- Comorbidities (e.g., prematurity, underlying heart/ lung disease)
- Living in socioeconomically disadvantaged areas

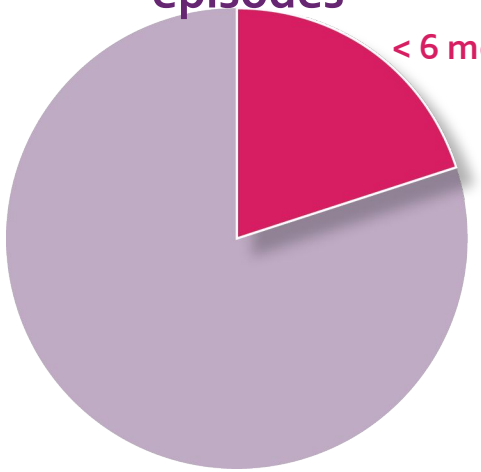
Original slide developed by the World Health Organization and PATH. Last updated: February 2024

Annual global pediatric RSV disease burden (< 5 years of age)

LEADING CAUSE OF SEVERE RESPIRATORY INFECTION

33,000,000

episodes

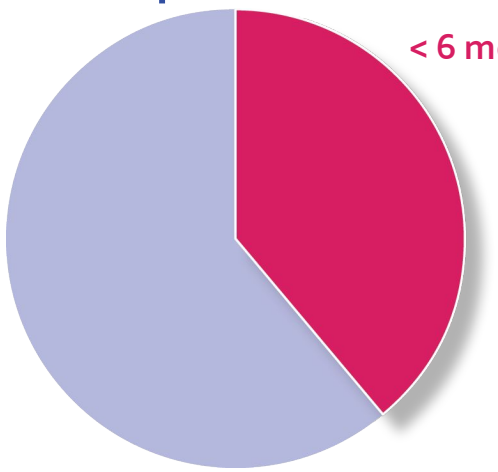


6 months to 5 years
80%

LEADING CAUSE OF PEDIATRIC HOSPITALIZATION

3.6 million

hospitalizations

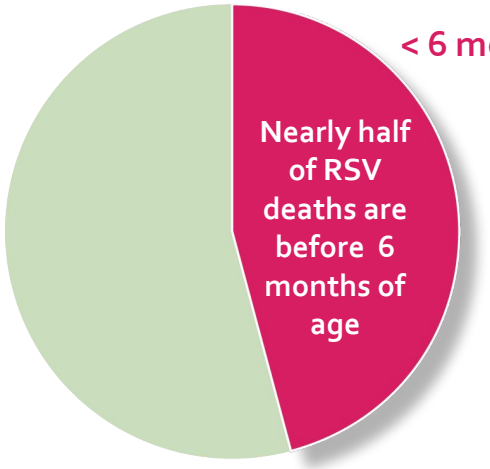


6 months to 5 years
61%

IMPORTANT CAUSE OF PEDIATRIC MORTALITY

101,000

deaths



6 months to 5 years
54%

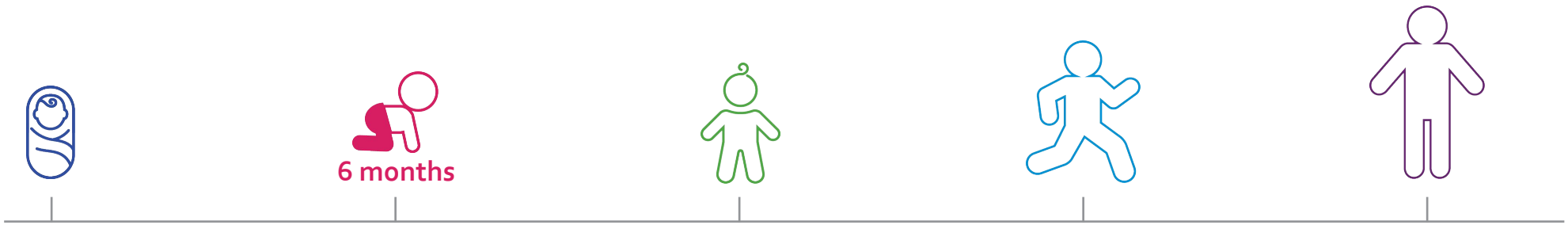
TOTAL GLOBAL CHILD MORTALITY DUE TO RSV

3.6% < 6 MONTHS

2.3% < 5 YEARS

Reference: Li Y, et al. *Lancet* 2022.

RSV's biggest risks are in the youngest children



1 IN EVERY 28 DEATHS

before 6 months of age globally is due to RSV[1]

Most severe in first few months of life due to easily blocked small airways.

Reference: PERCH Study Group. *Lancet*. 2019.

Original slide developed by the World Health Organization and PATH. Last updated: February 2024

98% of pediatric RSV mortality occurs in low- and middle-income economies[1]

In children < 6 months of age, RSV is responsible for:

Many children in low-income economies never make it to a hospital.[2]

4X

as many children die from RSV in the community than in the hospital

The disparity in RSV mortality between low- and high-income contexts is substantial.

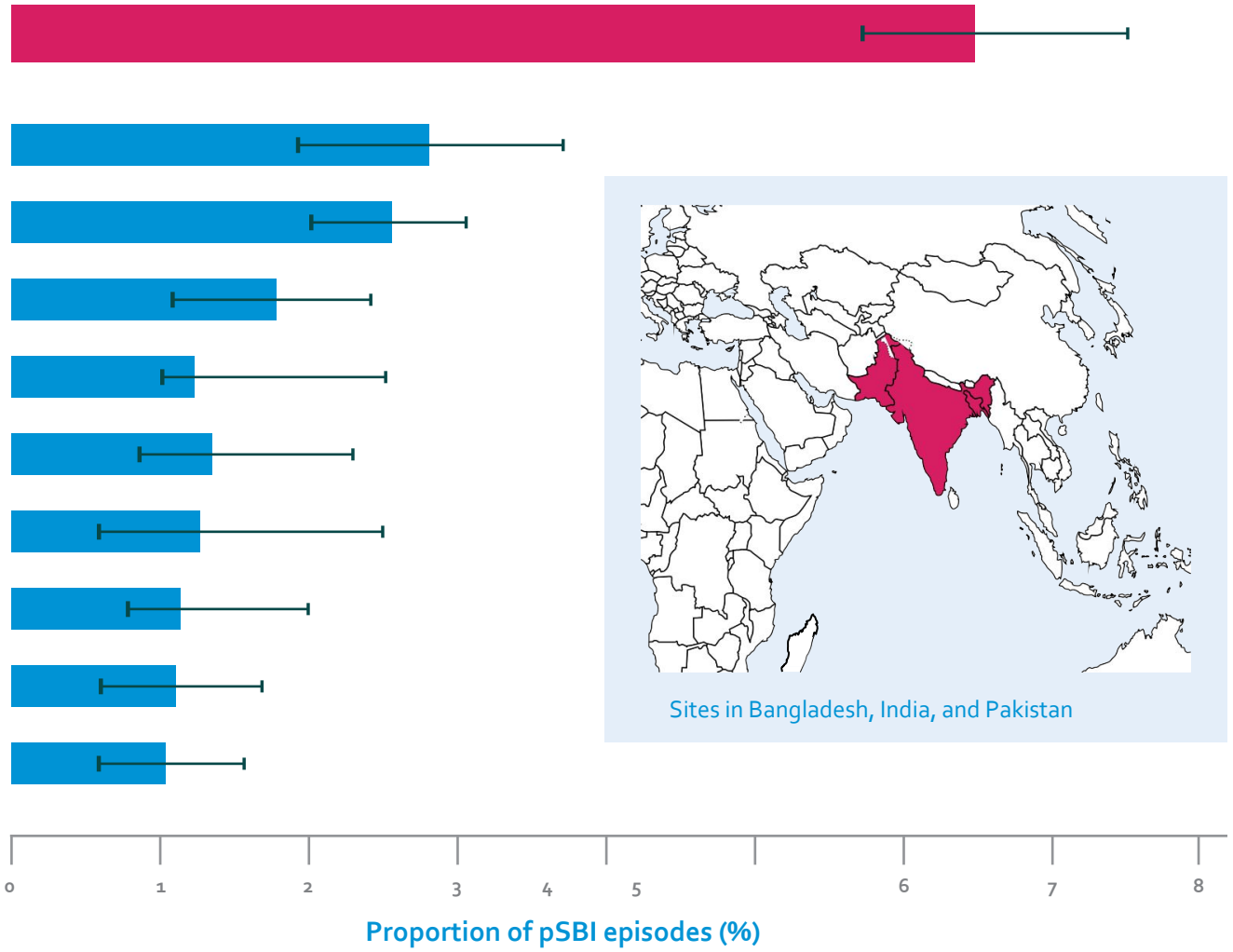
[1] Li Y, et al. *Lancet*. 2022; [2] Srikantiah P, et al. *Clin Infect Dis*. 2021.

Aetiology of Neonatal Infections in South Asia (ANISA) study

Top 10 causes of community-acquired serious infections in neonates in 3 countries in South Asia

RSV	**6.48%** (5.81-7.59)
Ureaplasma spp	2.82 (1.93-3.77)
Other blood culture	2.57 (2.05-3.11)
Klebsiella pneumonaiae	1.79 (1.17-2.49)
Escherichia coli	1.71 (1.05-2.62)
Enterovirus or rhinovirus	1.36 (0.83-2.37)
Salmonella spp	1.28 (0.53-2.52)
Streptococcus pneumoniae	1.15 (0.70-1.98)
Group B *Streptococcus*	1.12 (0.65-1.71)
Staphyloccocus aureus	1.05 (0.63-1.68)

Reference: Saha, S. et al. *Lancet,* 2018.



Sites in Bangladesh, India, and Pakistan

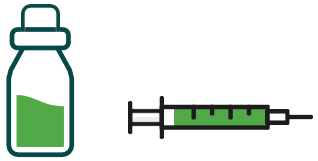
Available treatment and prevention for young infants prior to 2023

TREATMENT/MANAGEMENT

SUPPORTIVE CARE
(e.g., hydration, nutritional support, oxygen, and ventilation)

No licensed antivirals for RSV

Inappropriate antibiotic use poses antimicrobial resistance threat



MONOCLONAL ANTIBODY (MAB) PREVENTION

PALIVIZUMAB (EXISTING)
Short-lasting mAb that can prevent severe RSV in high-risk infants

Use is limited to very premature infants in high-income countries

Requires up to 5 monthly doses

Prohibitively expensive

New products emerging for RSV prevention in early life

	Maternal vaccine	
RATIONALE	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.
HOW IT WORKS	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.
TIMING	Vaccination in late 2nd or 3rd trimester of pregnancy to optimize transfer of antibodies to infant. (Currently approved gestational age windows: 24-36 weeks in Europe and 32-36 weeks in the United States.)	At birth with other birth dose vaccinations (e.g., hepatitis B; BCG, OPV) or at first Expanded Program on Immunization (EPI) visit.
PRODUCT CHARACTERISTICS	• Given in one dose • At least 5-6 months protection after birth	• Given in one dose • At least 5-6 months protection after administration (longer lasting than palivizumab)

Leading product progress for RSV prevention in early life

PRODUCT / DEVELOPER	PHASE 3 EFFICACY (%) (CONFIDENCE INTERVAL)	OUTCOME MEASURED	COMMENTS
Pre-fusion F maternal vaccine[1] Pfizer	(95% CI, 40.6% to 96.3%) **81.8%** *birth through 90 days* **69.4%** *birth through 180 days* (95% CI, 44.3% to 84.1%)	Severe medically attended RSV-LRTI	• Approved in US and Europe • Anticipate access of MDV in LMICs by mid 2026
Nirsevimab (mAb)[2] AstraZeneca / Sanofi Pasteur	**78.6%** *through 150 days* (95% CI, 48.8 to 91.0)	Very severe medically attended RSV-associated LRTI	• Approved in US and Europe • Unclear timeline for access in LMICs
	76.8% *through 150 days* (95% CI, 49.4 to 89.4)	RSV-LRTI with hospitalization	

LRTI = lower respiratory tract infection
MDV= multi-dose vial

Additional long-acting mAbs for delivery to neonates are in development and have potential for LMICs.

- Merck (Phase 2b/3)
- The Bill & Melinda Gates Medical Research Institute (Phase 1)

[1] Kampmann B, et al. *New England Journal of Medicine*. 288(16):2023. [2] Muller WJ, et al. *NEJM*. 2023. .

Getting to public health impact

GOAL What success could look like	**Improved infant health and survival through introduction and wide-scale use of RSV prevention tools (mAb and/or maternal immunization)**	
OBJECTIVES What's needed to reach the goal	**Evidence-based decisions support RSV prioritization and product adoption**	**Health systems & services deliver RSV prevention product(s) routinely, efficiently, and equitably**
OUTCOMES Elements for achieving objectives	• Evidence supports case for vaccine adoption • Increased stakeholder awareness of RSV disease and forthcoming products • Supportive policies and financing are in place	• Coordination established between EPI and ANC programs around RSV prevention • Operations and logistics in place to procure and deliver prevention product(s) as well as monitor implementation • Implementers empowered to deliver prevention product(s) • Capacity building underway to track vaccine safety and impact

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Evidence Generation

Estimate the burden of RSV mortality in LMICs

- Ensure global RSV estimates reflect full mortality burden
- Articulate full public health value of RSV prevention

Product Development

Develop RSV vaccine for maternal immunization

- Support development of low-cost highly efficacious maternal vaccine targeting the pre-fusion form of the RSV surface fusion glycoprotein (F protein)
- Vaccine approaches:
  - Protein-subunit
  - mRNA

Develop affordable RSV mAb for birth dose administration

- Support development of low-cost long-acting intramuscular RSV mAb targeting select pre-fusion F protein epitopes for infant birth dose administration

Product Delivery

Enable RSV product introduction and access

- Deep engagement with WHO, Gavi, SAGE to support policy recommendations for RSV production introduction in LMICs
- RSV health impact and cost-effectiveness analyses in LMICs

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