Maternal and Infant RSV Protection Program

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Department of Infectious Diseases

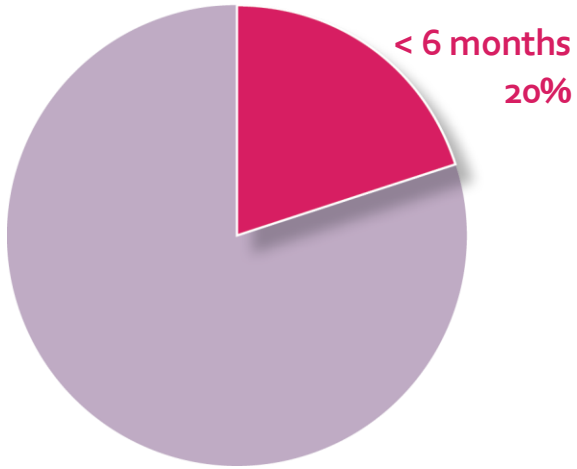
2024

A joint venture between The University of Melbourne and The Royal Melbourne Hospital

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

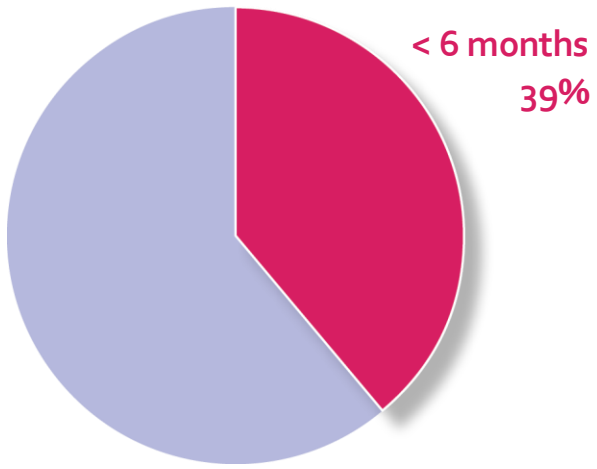
LEADING CAUSE OF SEVERE RESPIRATORY INFECTION

33,000,000
episodes



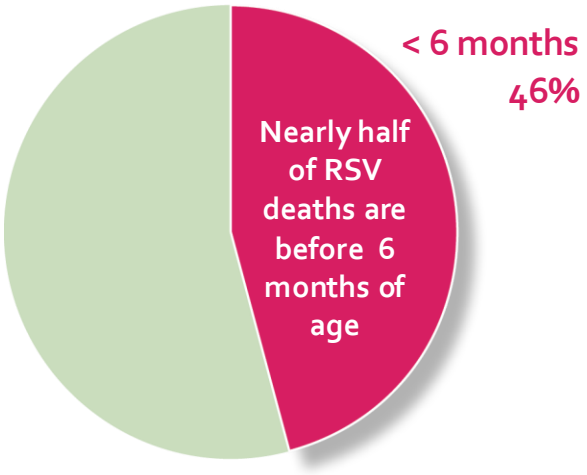
LEADING CAUSE OF PEDIATRIC HOSPITALIZATION

3.6 million
hospitalizations



IMPORTANT CAUSE OF PEDIATRIC MORTALITY

101,000
deaths



TOTAL GLOBAL CHILD MORTALITY DUE TO RSV

3.6% < 6 MONTHS

2.3% < 5 YEARS

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

Original slide developed by PATH, UMC Utrecht, and the World Health Organization. Last updated: December 2023

RSV can be deadly

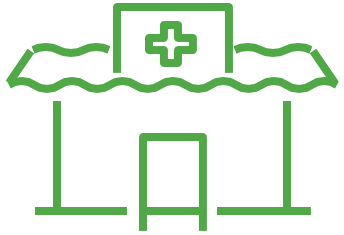
Although premature birth and underlying health issues increase risk for severe disease, risk factors for death are much broader.

In fact, most global RSV deaths occur

in infants born **full term**

before 3 months of age

in **low- and middle-income** areas



outside the healthcare system

Original slide developed by the Seattle Children's Hospital; University of Washington; PATH; WHO. Last updated: October 2023

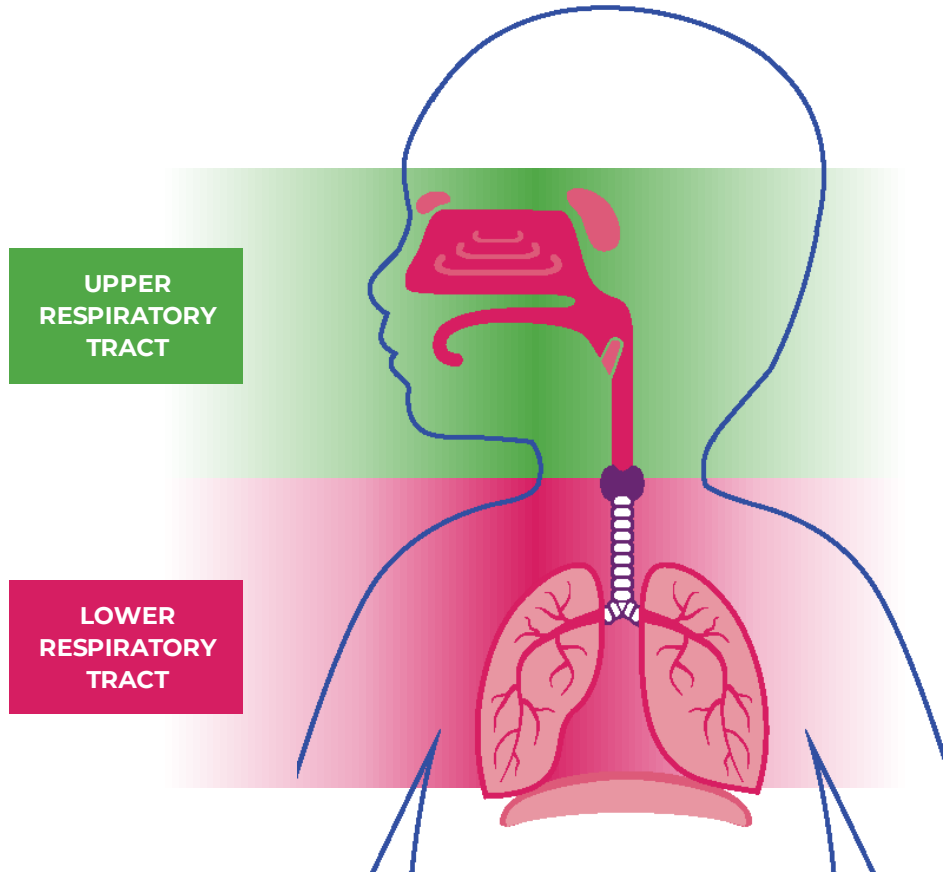
RSV affects the lungs and breathing passages

Symptoms typically occur 3-5 days after infection and can last 5-10 days

RSV infects the respiratory epithelial cells of the respiratory system and triggers a host inflammatory response.

Symptoms often start in the upper respiratory tract and are typically mild. In many cases, RSV can also infect the lower respiratory tract.

UPPER RESPIRATORY SYMPTOMS	LOWER RESPIRATORY SYMPTOMS	GENERAL SYMPTOMS
Runny nose	Coughing	Low-grade fever
Nasal congestion	Wheezing	Apnea (pause in breathing)
Earache/otitis media	Fast breathing	Poor feeding
		Dehydration



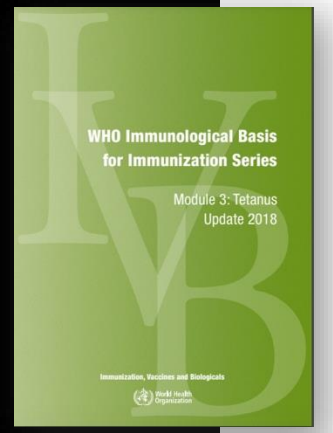
Maternal immunization is not new. We can build on experience.

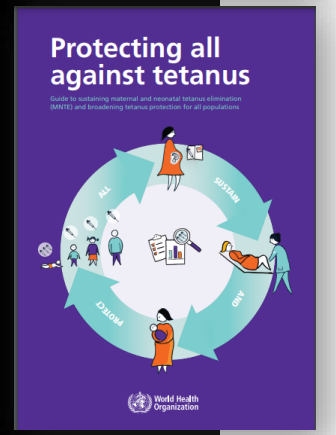
	Vaccine
Widespread/ global use	• Tetanus
Use in limited (mostly higher income) markets	• Influenza (seasonal) • COVID-19 • Pertussis
New and emerging opportunities	• **RSV** • Group B *Streptococcus* (GBS)

EXAMPLE

Maternal and neonatal tetanus (MNT) elimination

- Vaccination safely used in pregnancy since the 1960s
  - Tetanus toxoid and tetanus-diphtheria vaccines
- Maternal immunization pivotal in MNT elimination in most countries around the world
- Strong WHO guidance / widespread acceptance
- In low- and middle-income markets, delivered routinely or via campaigns & supplemental immunization activities





Maternal Immunisation for RSV prevention:

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Respiratory Syncytial Virus Vaccination during Pregnancy and Effects in Infants

S.A. Madhi, F.P. Polack, P.A. Piedra, F.M. Munoz, A.A. Trenholme, E.A.F. Simões, G.K. Swamy, S. Agrawal, K. Ahmed, A. August, A.H. Baqui, A. Calvert, J. Chen, I. Cho, M.F. Cotton, C.L. Cutland, J.A. Englund, A. Fix, B. Gonik, L. Hammitt, P.T. Heath, J.N. de Jesus, C.E. Jones, A. Khalil, D.W. Kimberlin, R. Libster, C.J. Llapur, M. Lucero, G. Pérez Marc, H.S. Marshall, M.S. Masenya, F. Martinón-Torres, J.K. Meece, T.M. Nolan, A. Osman, K.P. Perrett, J.S. Plested, P.C. Richmond, M.D. Snape, J.H. Shakib, V. Shinde, T. Stoney, D.N. Thomas, A.T. Tita, M.W. Varner, M. Vatish, K. Vrbicky, J. Wen, K. Zaman, H.J. Zar, G.M. Glenn, and L.F. Fries, for the Prepare Study Group*

- Provided proof of safety and efficacy of maternal RSV vaccination (2020)
  - Overall VE 39.4% at 90 days against MA-LRTI
  - Reduced antibiotic prescriptions by 13%
  - Larger impact in LMICs (VE 11.6% US vs 42.5% SA)
  - Novavax discontinued RSV program as VE did not meet prespecified criterion for success

GSK maternal RSV vaccine clinical trial and preterm birth

- Trial of a similar GSK maternal RSV vaccine (stabilized prefusion F protein vaccine without an adjuvant) was halted due to an imbalance of preterm births with higher numbers in the vaccine vs placebo group

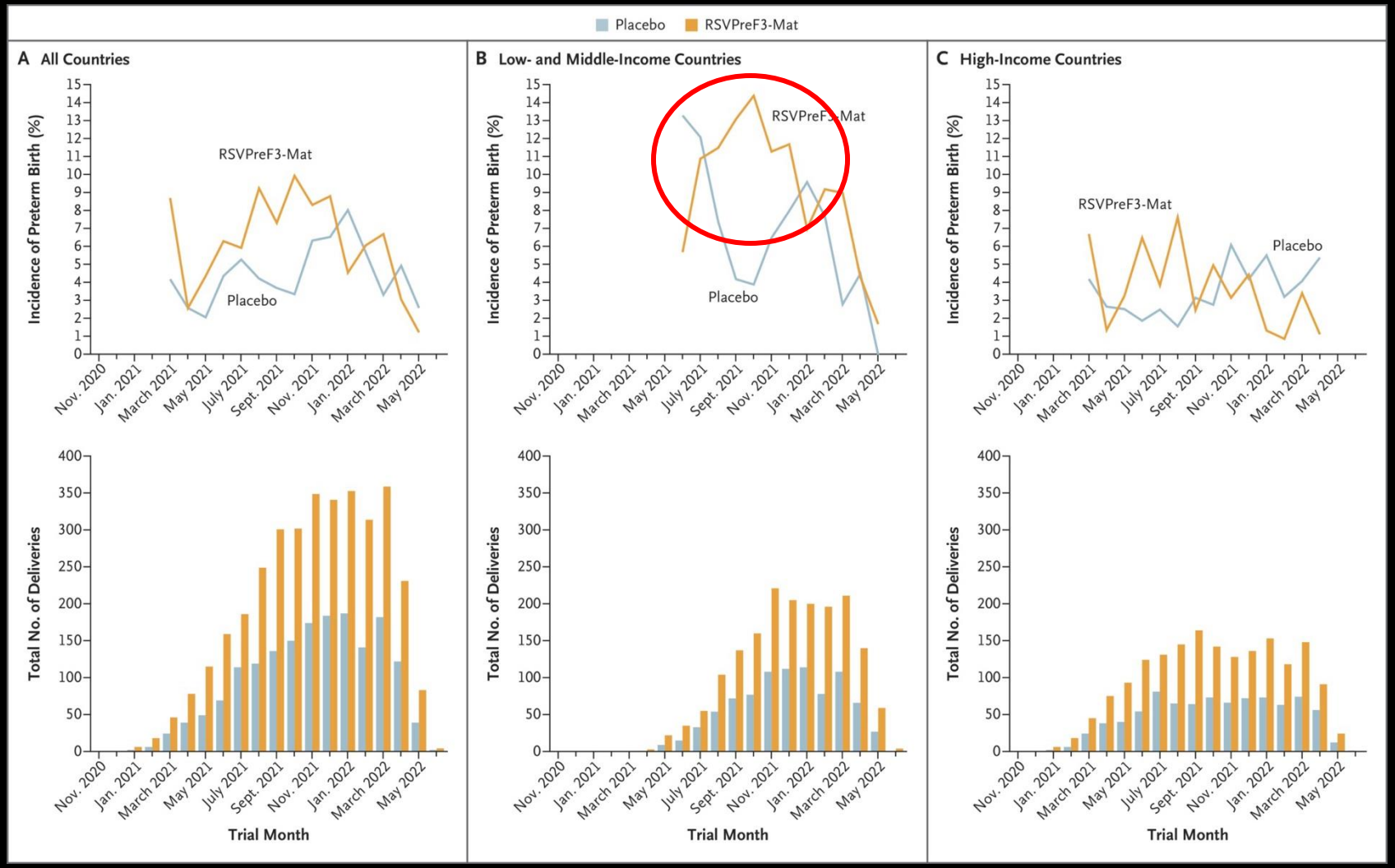
Outcome	Vaccine group, n (%) N=3,496	Placebo group, n (%) N=1,739	Relative Risk (95% CI)
Preterm birth (<37 weeks gestation)	238 (6.81%)	86 (4.95%)	1.38 (1.08, 1.75)
Neonatal death	13 (0.37%)	3 (0.17%)	2.16 (0.62, 7.55)

- Imbalance of neonatal deaths was a consequence of preterm birth imbalance
- Imbalance in preterm births was seen in low and middle-income countries (RR: 1.57, 95% CI: 1.17, 2.10) but not high-income countries (RR: 1.04, 95% CI: 0.68, 1.58)
- Imbalance was observed from April–December 2021, but not consistently after December 2021
- Reason for the imbalance remains unclear

Study vaccine given at 24 0/7 to 34 0/7 weeks gestation

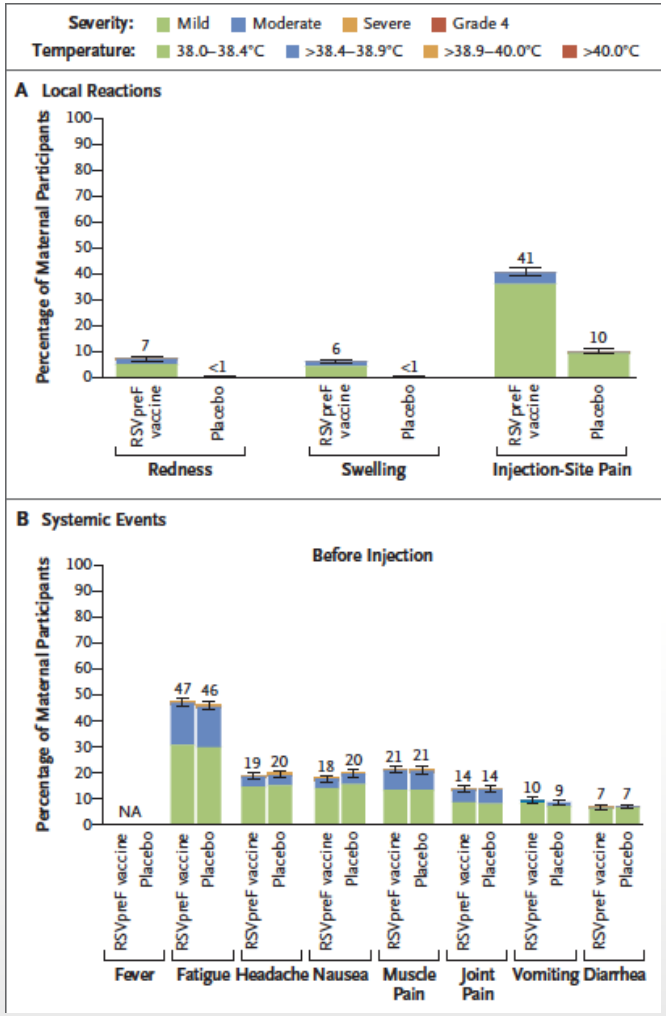
Vaccines and Related Biological Products Advisory Committee February 28 - March 1, 2023 Meeting Briefing Document- Sponsor GSK (fda.gov)

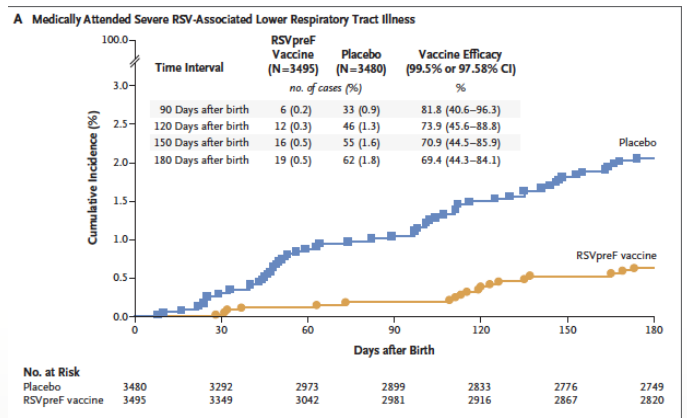
Monthly Incidence of Preterm Births and Number of Deliveries



Dieussaert I et al. N Engl J Med2024;390:1009-1021

The NEW ENGLAND JOURNAL of MEDICINE





The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group*

Phase 3 clinical study evidence

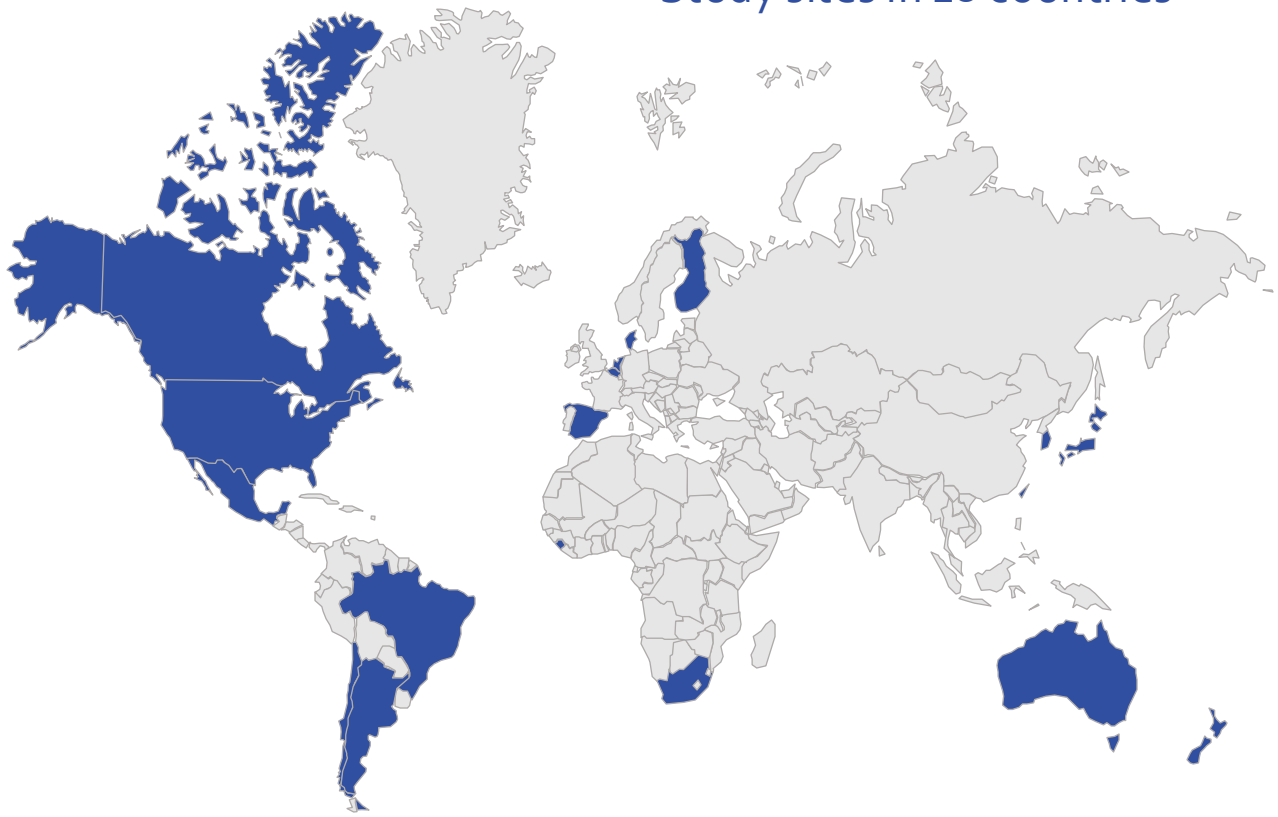
pre-F RSV maternal vaccine efficacy and safety in infants born to women vaccinated during pregnancy

Study product: Abrysvo™

7,392 pregnant participants ≤49 years between ≥ 24 and ≤ 36 weeks gestation

7,128 infants enrolled

Study sites in 18 countries



Reference: Kampmann B, et al. *New England Journal of Medicine*. 288(16):2023.

Pre-F RSV maternal vaccine efficacious against severe medically attended RSV in infants

	EFFICACY (%) FROM BIRTH THROUGH **90 DAYS** (CONFIDENCE INTERVAL)	EFFICACY (%) FROM BIRTH THROUGH **180 DAYS** (CONFIDENCE INTERVAL)
Severe medically attended RSV-LRTI	81.8% (95% CI, 40.6% to 96.3%)	69.4% (95% CI, 44.3% to 84.1%)
Medically attended RSV-LRTI	57.1%* (95% CI, 14.7 to 79.8) **did not reach pre-specified level of statistical significance*	51.3% (95% CI, 29.4% to 66.8%)

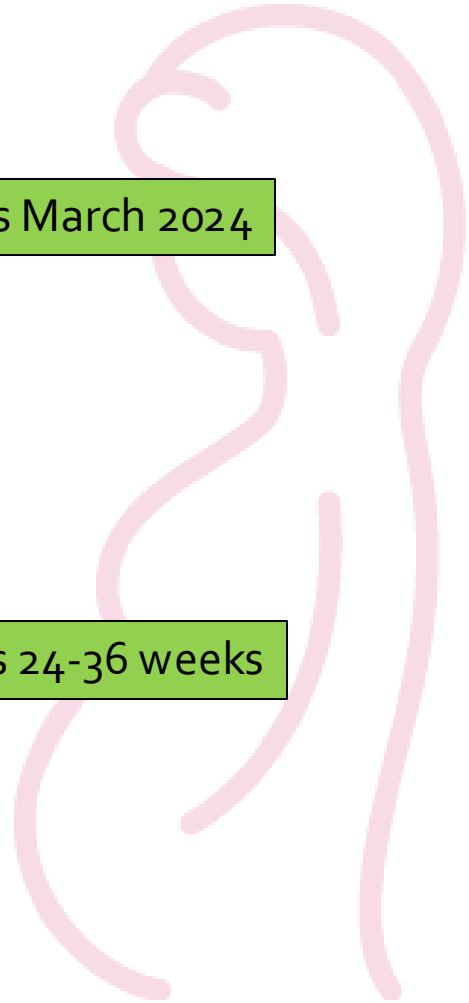
Efficacy remains high through first, most critical 6 months after birth—when infants are at greatest risk.

Reference: Kampmann B, et al. *New England Journal of Medicine*. 288(16):2023.

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

New RSV maternal vaccine licensed to protect infants

DEVELOPED BY	Pfizer, Inc. (Abrysvo™)		
APPROVAL	in Europe (August 2023)	in the US (August 2023)	In Aus March 2024
MATERNAL IMMUNIZATION INDICATION	• For immunization of pregnant individuals to help protect their infants from birth through 6 months of age from lower respiratory tract disease due to RSV • Vaccination likely needed with each pregnancy		
APPROVED GESTATIONAL AGE WINDOWS	24-36 weeks (Europe)	32-36 weeks (US)	In Aus 24-36 weeks
ABOUT THE PRODUCT	• For intramuscular injection • Uses standard cold chain • Lyophilized (freeze-dried) prefilled syringe; single-dose vial / multi-dose vial presentation in development • Can be co-administered with other maternal vaccines		



Both products protect infants via passive immunization, but have differences

	Maternal vaccine	Long-acting mAb
PROTECTION	Maternal antibodies protect infant in the first 6 months **after birth**.	mAbs protect for at least 5 months **after administration,** whenever given.
HOW IT WORKS	• Given to pregnant women • Induces antibodies against **multiple** neutralizing sites on the Fusion protein in the mother and passed to infant. • Much less likely that a virus mutation would render induced antibodies ineffective.	• Given to infants at birth or as soon as possible • Antibodies against a **single** potent neutralizing site on the Fusion protein. • A virus mutation could render the antibody ineffective.
COST	• Gavi plans to support a maternal RSV vaccine for eligible countries.* • A pricing agreement** on multidose vial can make RSV maternal vaccine more accessible for GAVI-eligible countries.	Gavi plans to support a long-acting mAb when an affordable product is available for eligible countries.*
AVAILABILITY	Earliest availability in low- and middle-income settings likely in **2025.**	Uncertain timing of availability in low- and middle-income settings due to price and supply barriers.

*Gavi, the Vaccine Alliance. Review of Decisions: Board Meeting, 28-29 November 2018. Geneva, Switzerland. Accessed at: https://www.gavi.org/sites/default/files/board/minutes/2018/Board-2018-Mtg-2-Review%20of%20Decisions.pdf

** Media center announcement accessed at: https://www.gatesfoundation.org/ideas/media-center/press-releases/2022/09/gates-foundation-announces-grants-to-reduce-infant-mortality

ATAGI Recommendations

- Pregnant women are recommended to receive a vaccine 28-36 weeks
- Abrysvo is the only RSV vaccine approved for use in pregnancy NOT Arexvy
- Reduces risk of disease by around 70% in infants <6 months of age
- Advice on repeat vaccination will be provided when data available
- Need 2 weeks post vaccination for adequate protection
- If inadvertently vaccinated <28 weeks a repeat dose not indicated