Vacunación materna para la prevención de enfermedad asociada a virus respiratorio sincitial en lactantes

Maternal vaccination for preventing respiratory syncytial virus-associated disease in infants

Vacinação de gestantes para prevenir doenças associadas ao vírus sincicial respiratório em lactentes

ALGUNAS CONSIDERACIONES

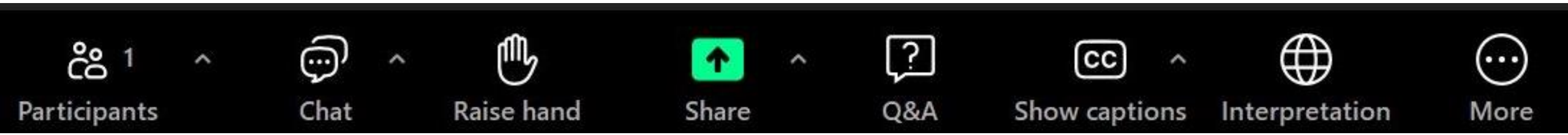
- Hay **interpretación** en español, inglés y portugués disponible. Puede elegir en idioma en el **ícono del globo** en el menú de abajo.
- Está habilitada la opción de preguntas y respuestas (**Q&A**).

SOME CONSIDERATIONS

- **Interpretation** in Spanish, English and Portuguese is available. You can choose the language from the **globe icon** in the menu below.
- The question and answer (**Q&A**) option is enabled.

ALGUMAS CONSIDERAÇÕES

- Está disponível **interpretação** em espanhol, inglês e português. Você pode escolher o idioma no **ícone do globo** no menu abaixo.
- A opção de perguntas e respostas (**Q&A**) está habilitada.



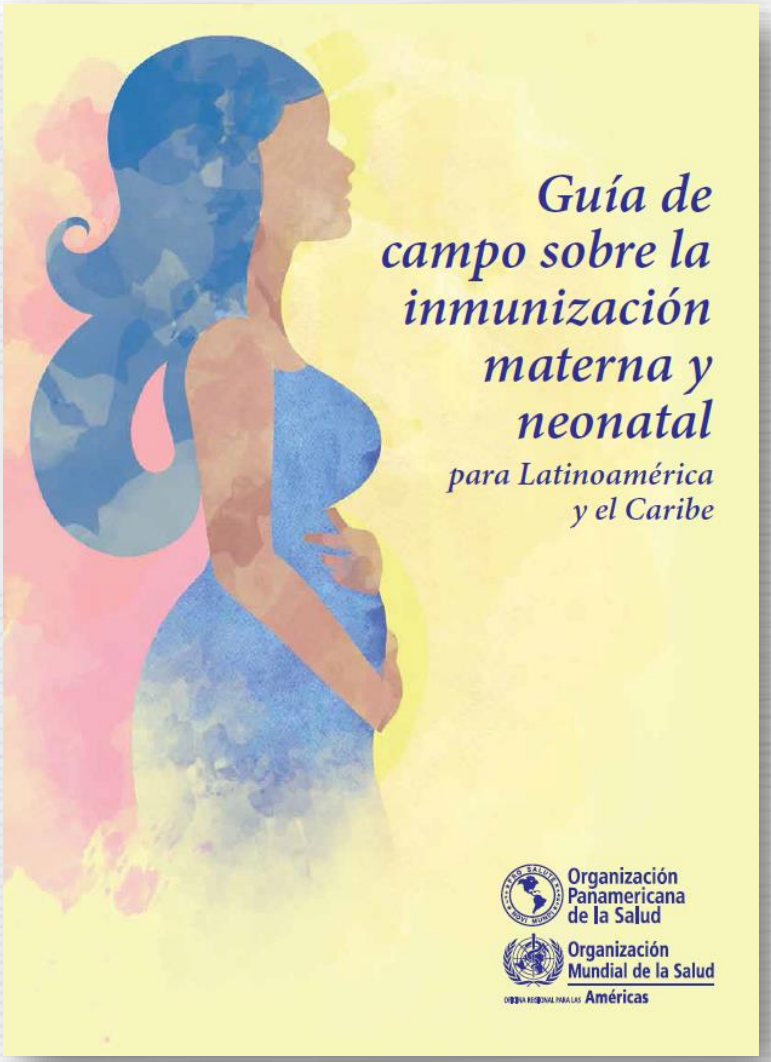
Introducción a la “Guía de campo sobre la inmunización materna y neonatal para Latinoamérica y el Caribe y el Anexo sobre la vacuna maternal contra el virus respiratorio sincitial”

Bremen de Mucio

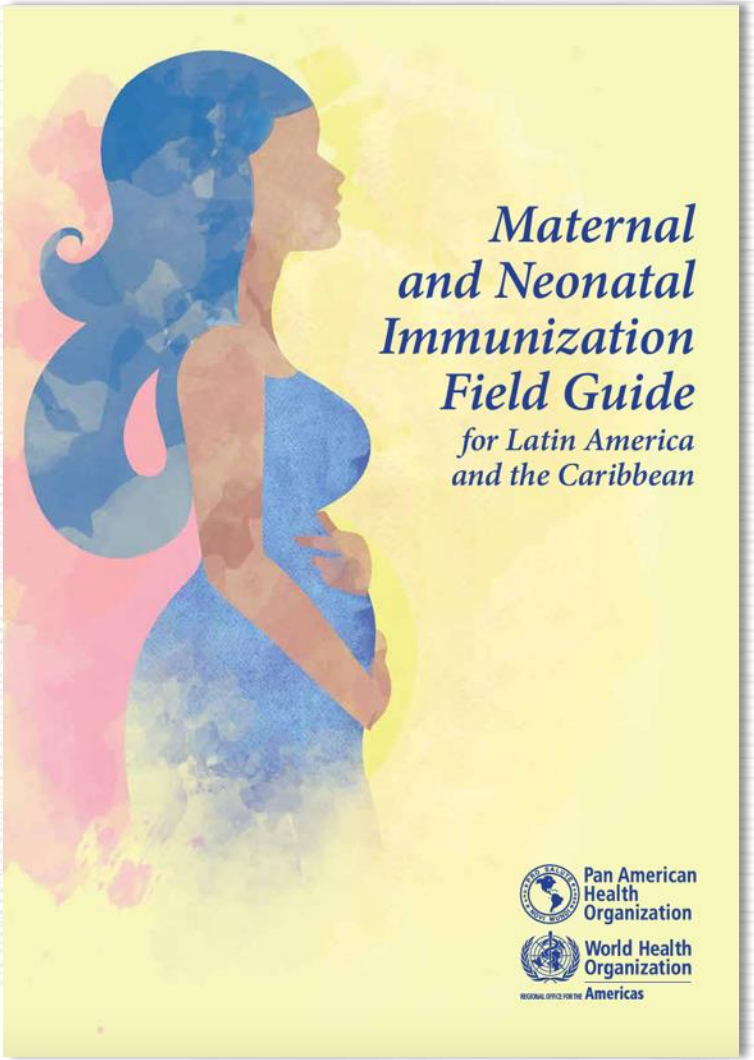
Asesor regional en salud materna

CLAP/SMR HSS OPS/OMS

OPS Organización Panamericana de la Salud
Organización Mundial de la Salud
Oficina Regional para las Américas



https://iris.paho.org/handle/10665.2/34149



https://iris.paho.org/handle/10665.2/34150

OBJECTIVE

The Pan American Health Organization's *Maternal and Neonatal Immunization Field Guide* aims to provide a practical road map of maternal and neonatal immunization to healthcare workers at all levels of the health system, integrating immunization programs and maternal and child health services. The guide might also be of use for health education programs.

AUDIENCES

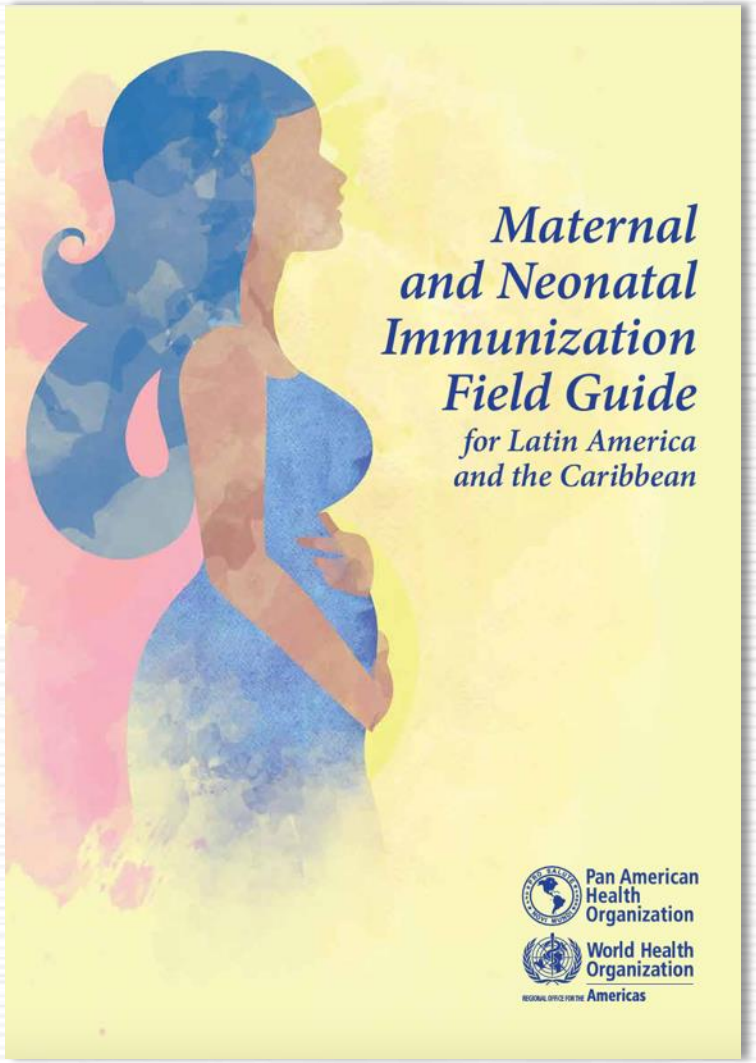
The intended audiences for the various sections of this Field Guide are:

Section I

- Managers of maternal and child health services including immunization program managers and personnel.

Section II

- Immunization program personnel.
- Personnel working with immunization, including maternal and neonatal immunizations (during pregnancy and post-partum for the mother and newborn).
- Healthcare providers: obstetricians, pediatricians, midwives, nurses, and any healthcare team members who provide care to women of childbearing age, including pregnant women or women in the post-partum period.
- Women of childbearing age.
- The media.



SECTION I. CONTEXT OF MATERNAL AND NEONATAL IMMUNIZATION

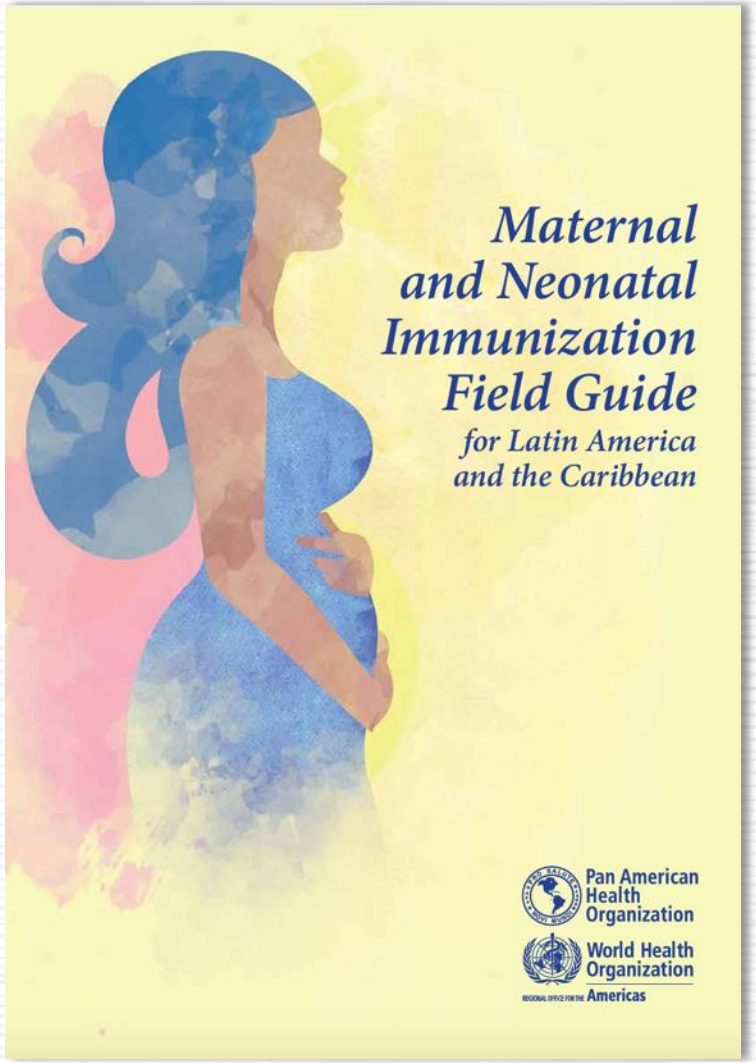
I.I Introduction to maternal and neonatal immunization

I.2. Background and rationale for maternal and neonatal immunization

I.3. Integration of programs and services

I.4. Vaccine safety and regulatory considerations

I.5. Introducing or expanding the use of maternal and neonatal vaccines



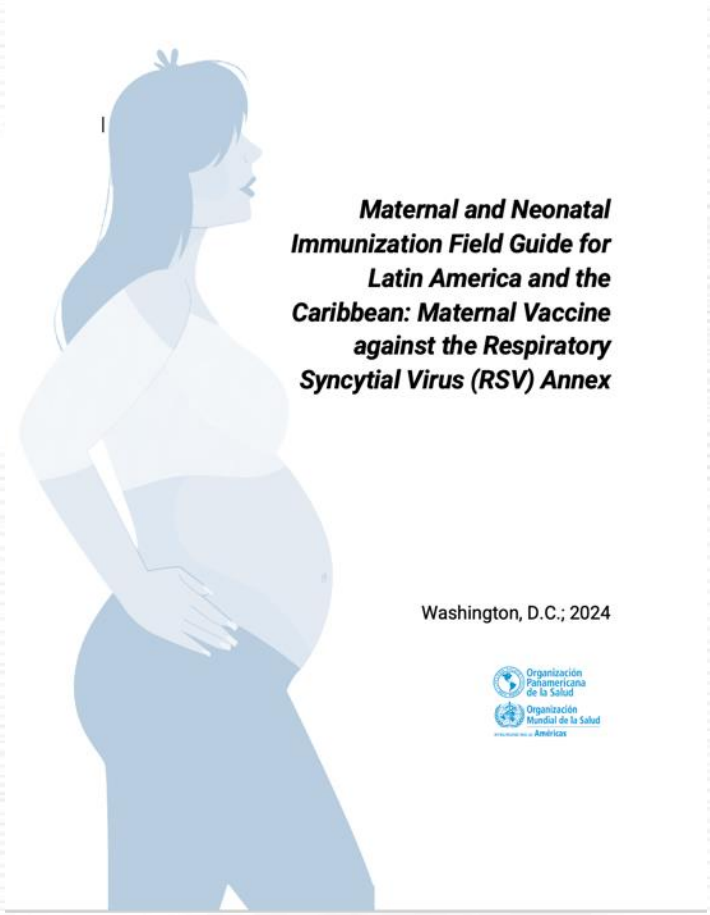
SECTION I. CONTEXT OF MATERNAL AND NEONATAL IMMUNIZATION

I.6. Regional, maternal, and neonatal immunization schedule and vaccination strategies

I.7. Information systems who/unicef

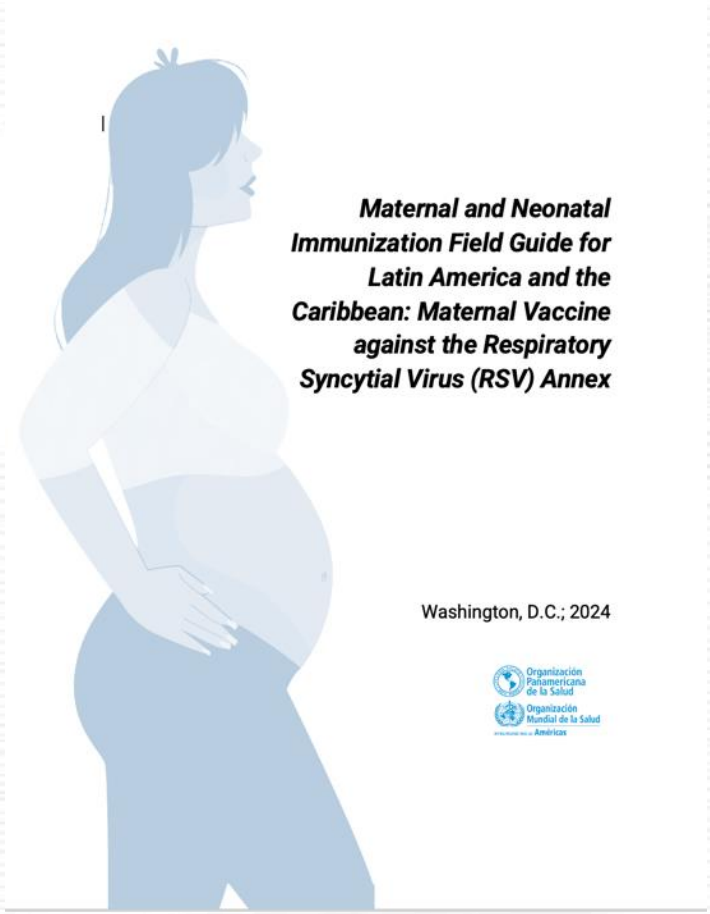
I.8. Social communication and vaccine acceptance

Maternal Vaccine against the Respiratory Syncytial Virus Annex



- Provide specific orientation on the use of maternal RSV vaccine for the prevention of LRTD in infants and young children..
- Available in Spanish https://iris.paho.org/handle/10665.2/62361

Maternal Vaccine against the Respiratory Syncytial Virus Annex



- RSV disease burden and risk factors
- Vaccine type and other vaccine candidates
- Immunogenicity, efficacy and safety
- Vaccination schedule and schedule of vaccination
- Concomitant administration with other vaccines
- Implementation considerations
- Includes maternal vaccination with passive immunization of infants with monoclonal antibodies.

Muchas gracias

OPS Organización Panamericana de la Salud
Organización Mundial de la Salud
OFICINA REGIONAL PARA LAS Américas

Enfermedad por virus respiratorio sincitial (VRS) y medidas de prevención

Webinar sobre laVacunación materna para la prevención de enfermedad asociada a VRS en lactantes

17 diciembre 2024

Francisco Nogareda
Programa Especial de Inmunización Integral
OPS/OMS

PAHO

Virus Respiratorio Sincitial (VRS)

- Virus ARN - familia de los Paramixovirus (sarampión y parotiditis)
- Tiene dos proteínas de superficie denominadas F y G: características antigénicas induciendo la síntesis de anticuerpos neutralizantes
- La proteína F (fusión) es responsable de la penetración del VRS en la células huésped y de la formación de sincitios
- Dos grupos principales: VRS-A y VRS-B. Sin diferencias clínicas ni epidemiológicas

Transmisión y presentación clínica

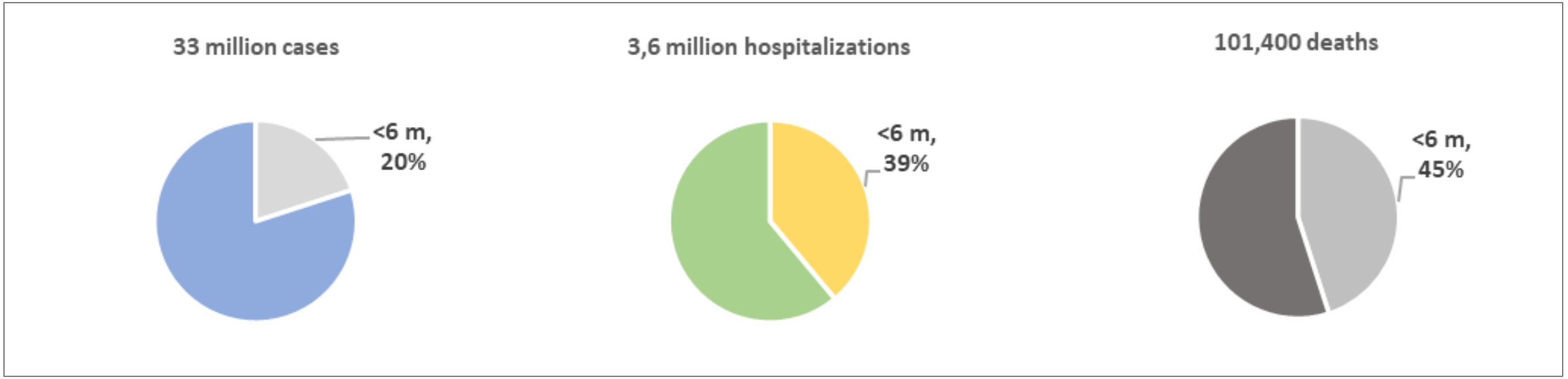
- Se transmite a través de secreciones nasofaríngeas de personas infectadas
- Periodo de incubación: 4-6 días
- Periodo de transmisibilidad: -2 a 8 días de inicio de síntomas
- En niños mayores y adultos sanos la infección suele ser asintomática o presentarse como un resfriado común
- En recién nacidos y personas con enfermedades crónicas puede provocar enfermedad grave: neumonía y bronquiolitis

Carga de enfermedad VRS

- A nivel global, VRS es la causa más frecuente de neumonía y broquiolitis en niños
- Primera causa de hospitalización y muerte en niños < 6 meses
- Más de 97% of muertes asociadas a VRS son en paises LMIC
- En LMIC, 80% de esas muertes occurren en la comunidad
- En la Región de las Américas, la mayoría de hospitalizaciones asociadas a VRS son en niños <5 años, particularlmente <6 meses

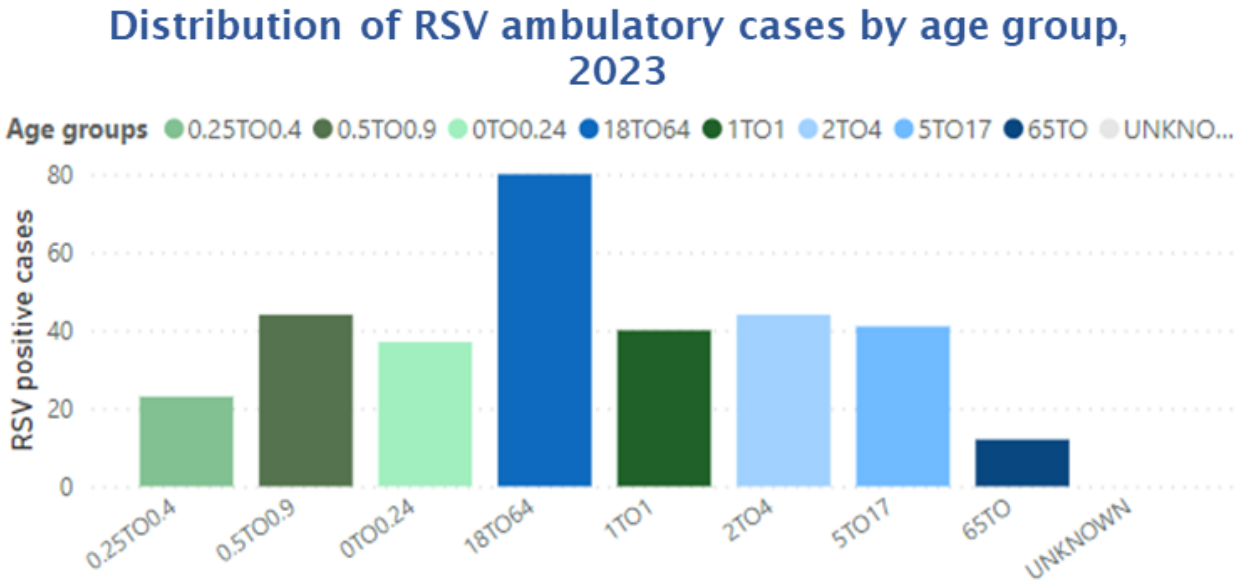
Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. The Lancet, May 2022. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00478-0/fulltext

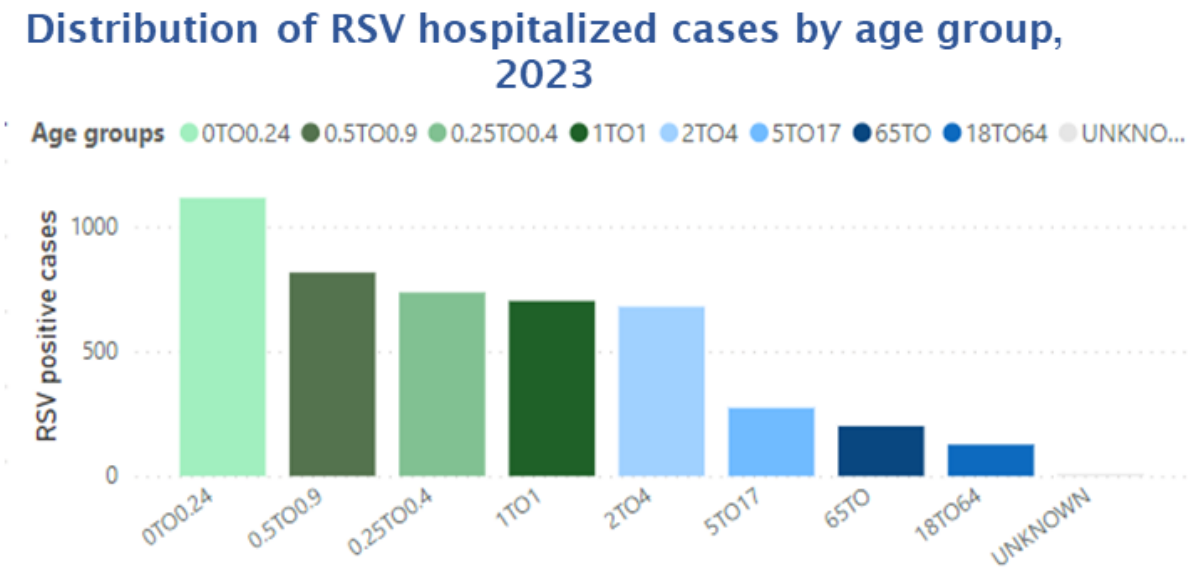
Carga de enfermedad - mundial



Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. The Lancet, May 2022. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00478-0/fulltext

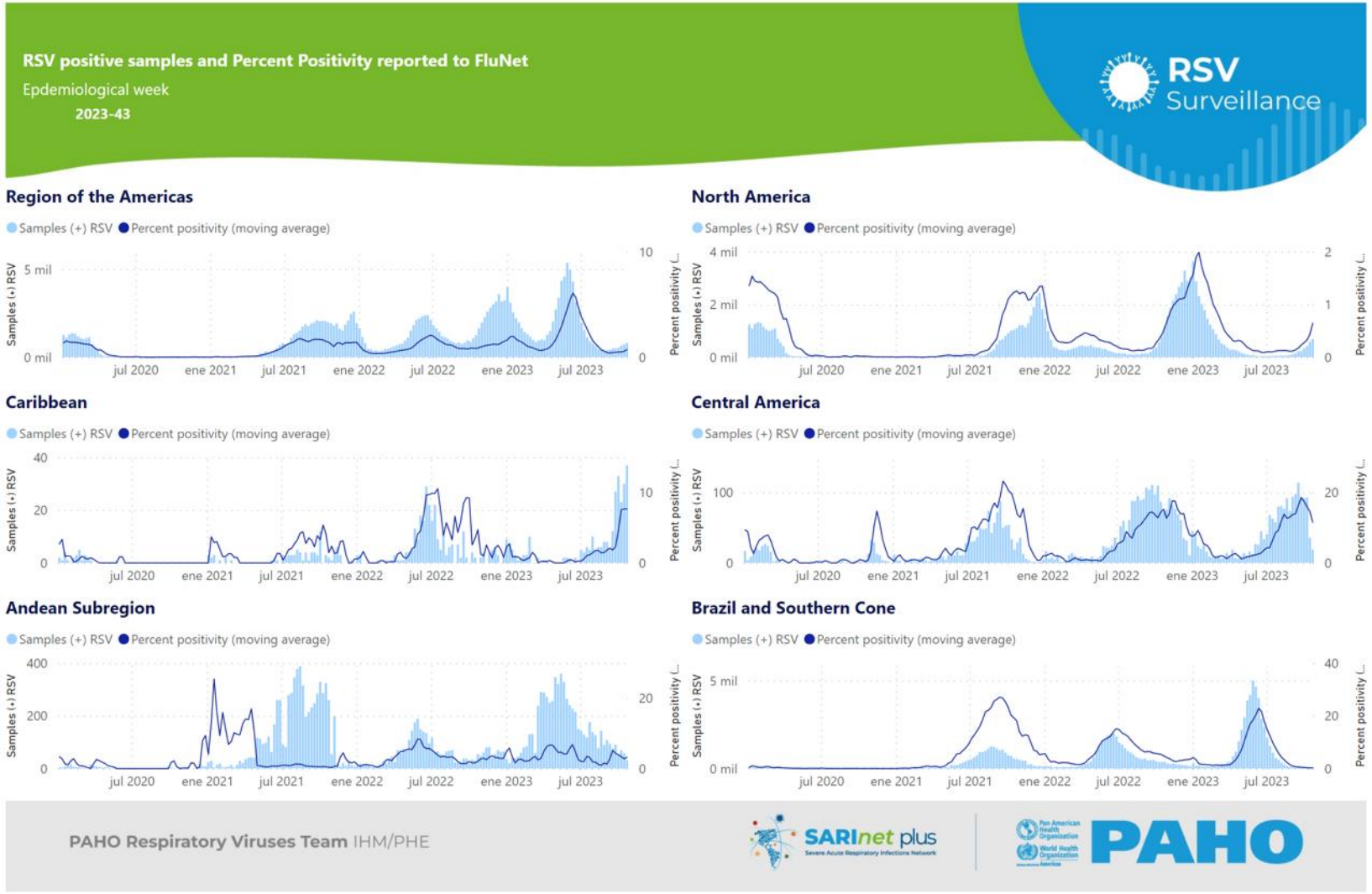
Casos y hospitalizaciones por grupo de edad en la Región de las Américas





Fuente: PAHO/WHO FluID and FluNet Platforms

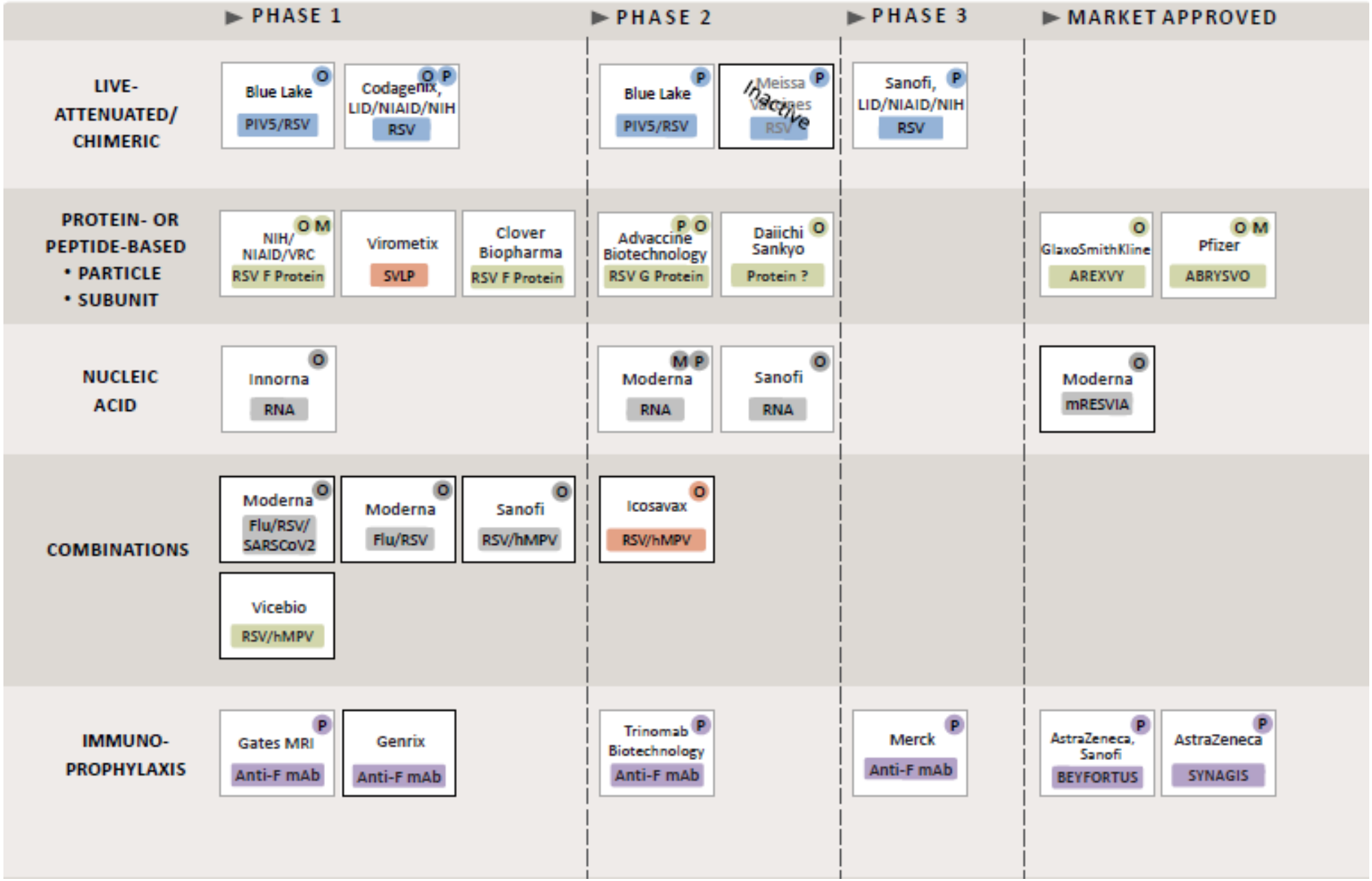
Estacionalidad



Fuente: PAHO/WHO FluID and FluNet Platforms

Grupos de riesgo

Grupos de riesgo	Factores de riesgo
Recién nacidos y niños <5 años	• Edad <6 meses • Prematuridad • Enfermedad pulmonar crónica • Enfermedad congénita cardiaca • Síndrome de Down • Inmunocomprometidos (<18 años)
Adultos mayores y personas con enfermedades crónicas	• Edad ≥65 años • Adultos con enfermedad crónica pulmonar y cardiaca • Adultos inmunocomprometidos



https://www.path.org/our-impact/resources/rsv-vaccine-and-mab-snapshot/

Prevención de VRS en lactantes

	Vacuna RSV PreF	Niservimab
Nombre	Abrysvo® (Pfizer)	Beyfortus® (Sanofi/AstraZeneca)
Indicación	Mujeres embarazadas 24-36 semanas de gestación para la prevención de enfermedad por VRS en niños hasta 6 meses.	Recién nacidos y lactantes menores de 1 año Niños hasta 24 meses con riesgo elevado de enfermedad grave en su segunda temporada
Composición	Vacuna inactivada bivalente - dos antígenos de la proteína F de prefusión para los grupos RSV-A y RSV-B	Anticuerpo neutralizante IgG1κ de larga duración sobre la proteína F de prefusión de VRS
Mecanismo de acción	Transferencia transplacentaria de anticuerpos neutralizantes	Inmunización pasiva de anticuerpos neutralizantes
Administración	Dosis única mediante inyección intramuscular	Dosis única mediante inyección intramuscular 50 mg para niños <5 kg y 100 mg para ≥5 kg. 200mg para niños en segunda temporada
Disponibilidad	Fondo Rotatorio de Vacuna de la OPS	Fondo Estratégico de la OPS
Información técnica	Abrysvo package insert. https://www.fda.gov/media/168889/download	Beyfortus Package insert. https://pdf.hres.ca/dpd_pm/00070439.PDF

Conclusiones

- Enfermedad por VRS es considerada como un problema mayor de salud pública con elevada carga de enfermedad, especialmente en <6 meses
- Actualmente existen dos productos autorizados que han demostrado su eficacia en prevenir enfermedad grave asociada a VRS en lactantes
- Tanto la vacunación materna como la administración de anticuerpo monoclonal confieren protección al recién nacido durante los primeros meses de vida
- Estrategias que combinen el uso de la vacuna materna durante el embarazo y de anticuerpos monoclonales en lactantes

GRACIAS

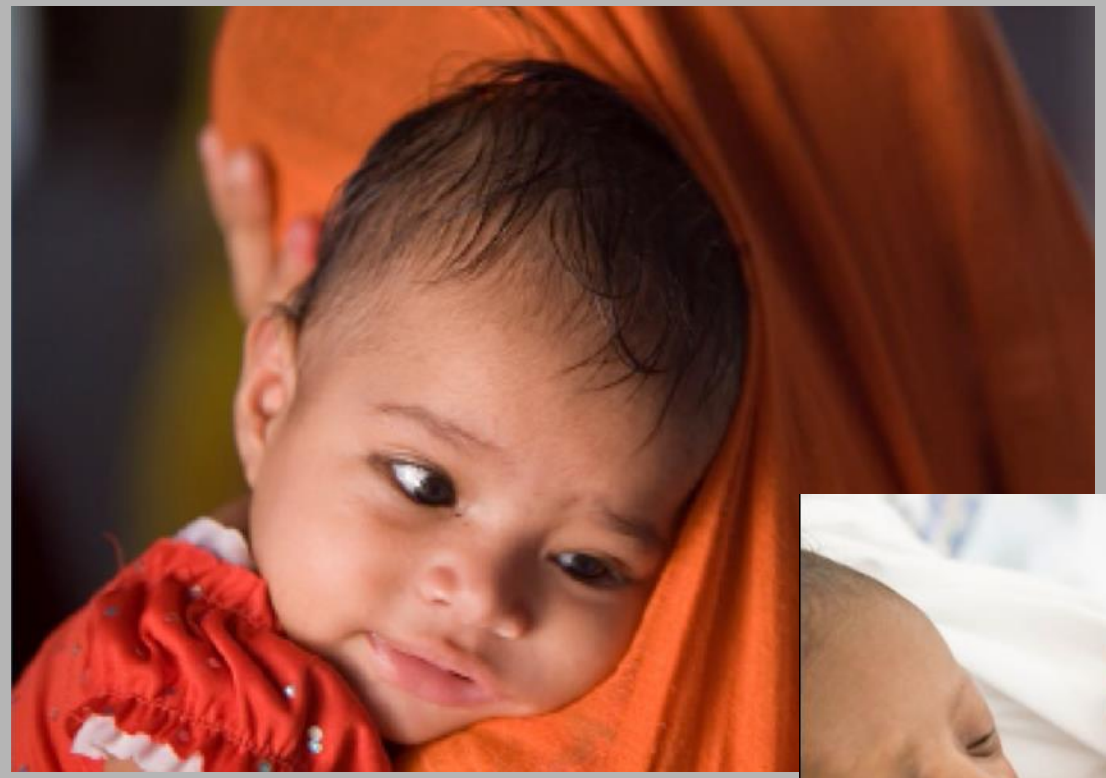
RSV Maternal vaccine (Abrysvo): Efficacy and Safety

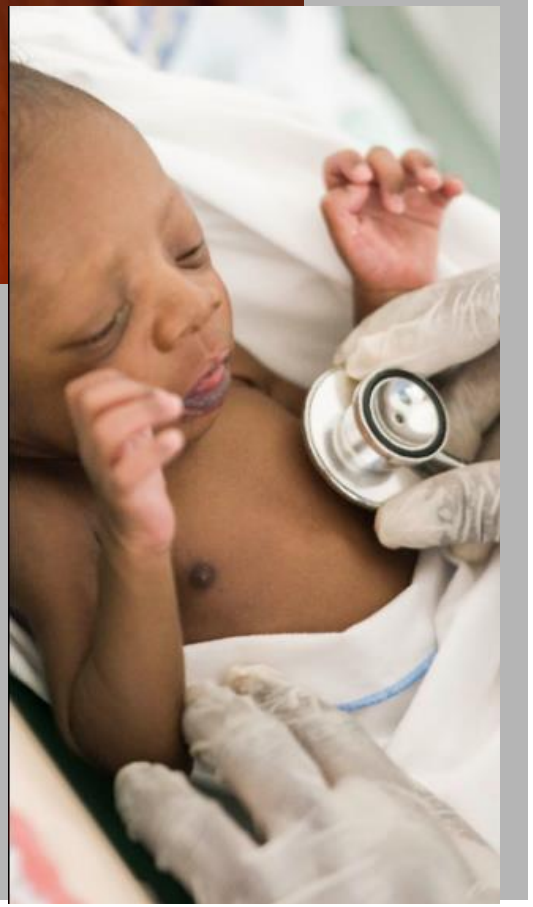
PAHO Webinar.

December 17, 2024

Daniel Feikin, MD

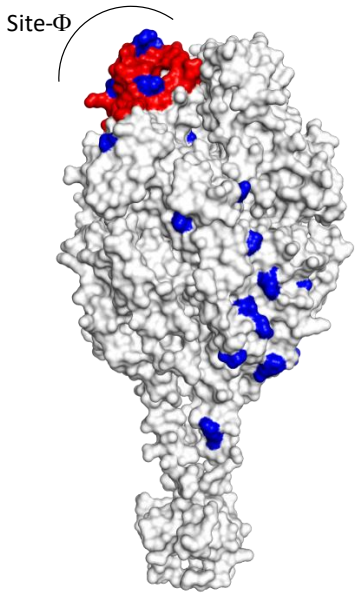
World Health Organization | IVB





Rationale for Bivalent Stabilized RSV Prefusion F Vaccine

RSV F subgroup A and B amino acid sequence differences (shown in blue) cluster in prefusion-specific sites



Balanced neutralizing responses against both RSV A and RSV B observed with bivalent prefusion F-based vaccine in contrast with other monovalent investigational RSV prefusion F-based vaccines

Ontario (RSV A) and Buenos Aires (RSV B) remain dominant genotypes and are the basis of Pfizer's RSVpreF bivalent vaccine

RSV subgroup dominance can vary over time

Both subgroup viruses are associated with severe disease

Slide content provided by Pfizer

Crank et al, Science 2019, 365:505-9; Hall et al,. J Infect Dis 1990; 162:1283-90 Langedijk et al., Rev Med Virol. 2021;e2284. https://doi.org/10.1002/rmv.2284

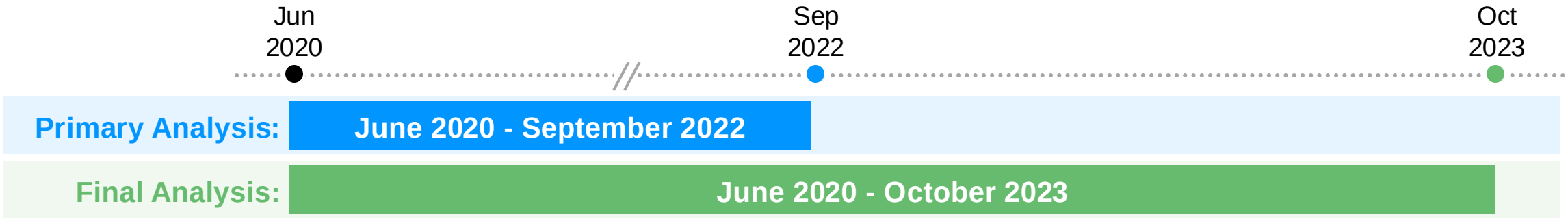
MATISSE: Phase 3 trial of Maternal Vaccination with RSV PreF / Abrysvo

Pregnant participants ≤49 years

Between ≥24 and ≤36 weeks gestation

1:1

- **RSVpreF 120 µg**
- **Placebo**



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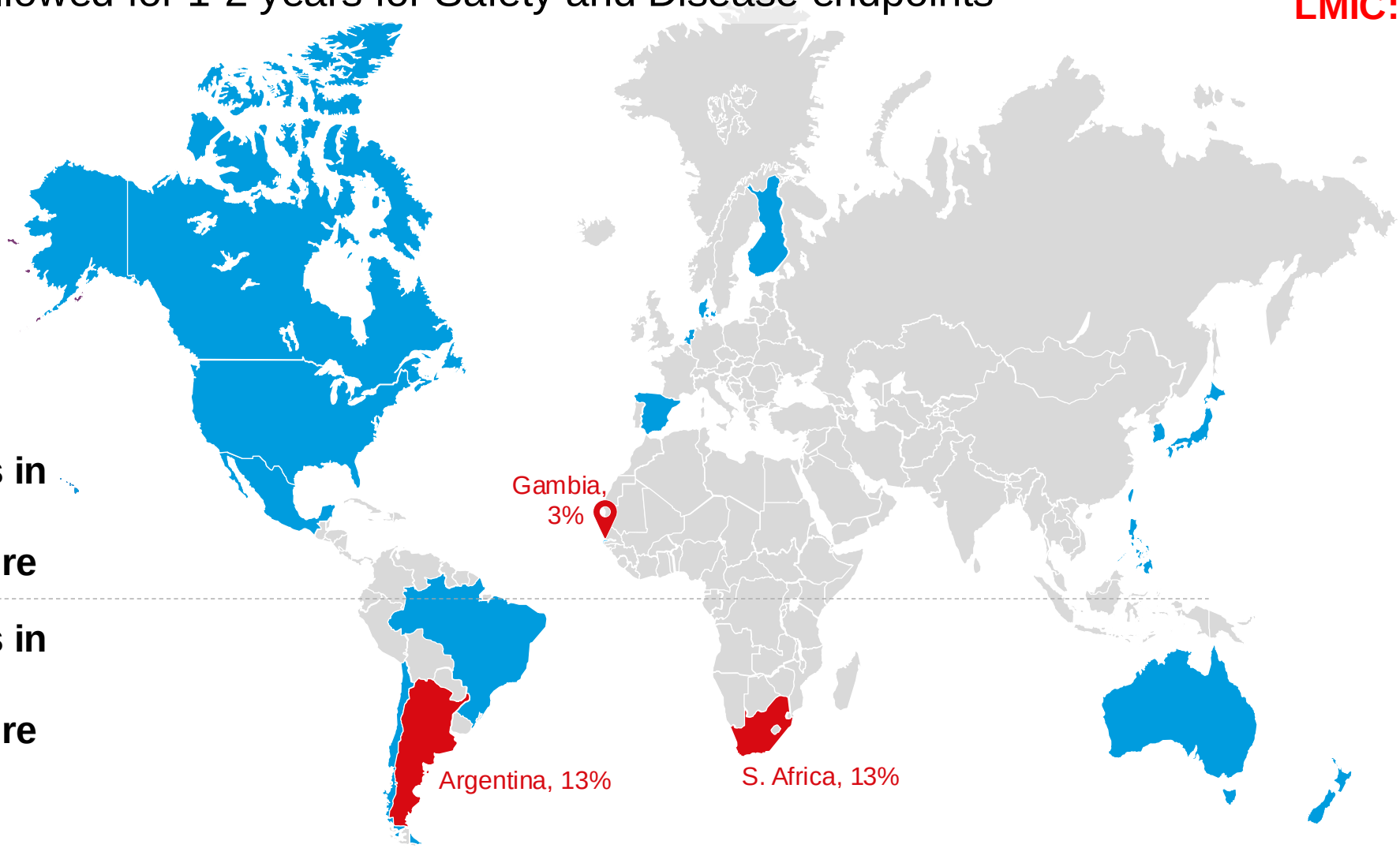
MATISSE: Phase 3 Pivotal Maternal Vaccination Trial

18 countries. **7,420** maternal participants/**7,307** infants enrolled

Infants followed for 1-2 years for Safety and Disease endpoints

LMIC: 31%



2 seasons in Northern Hemisphere

2 seasons in Southern Hemisphere

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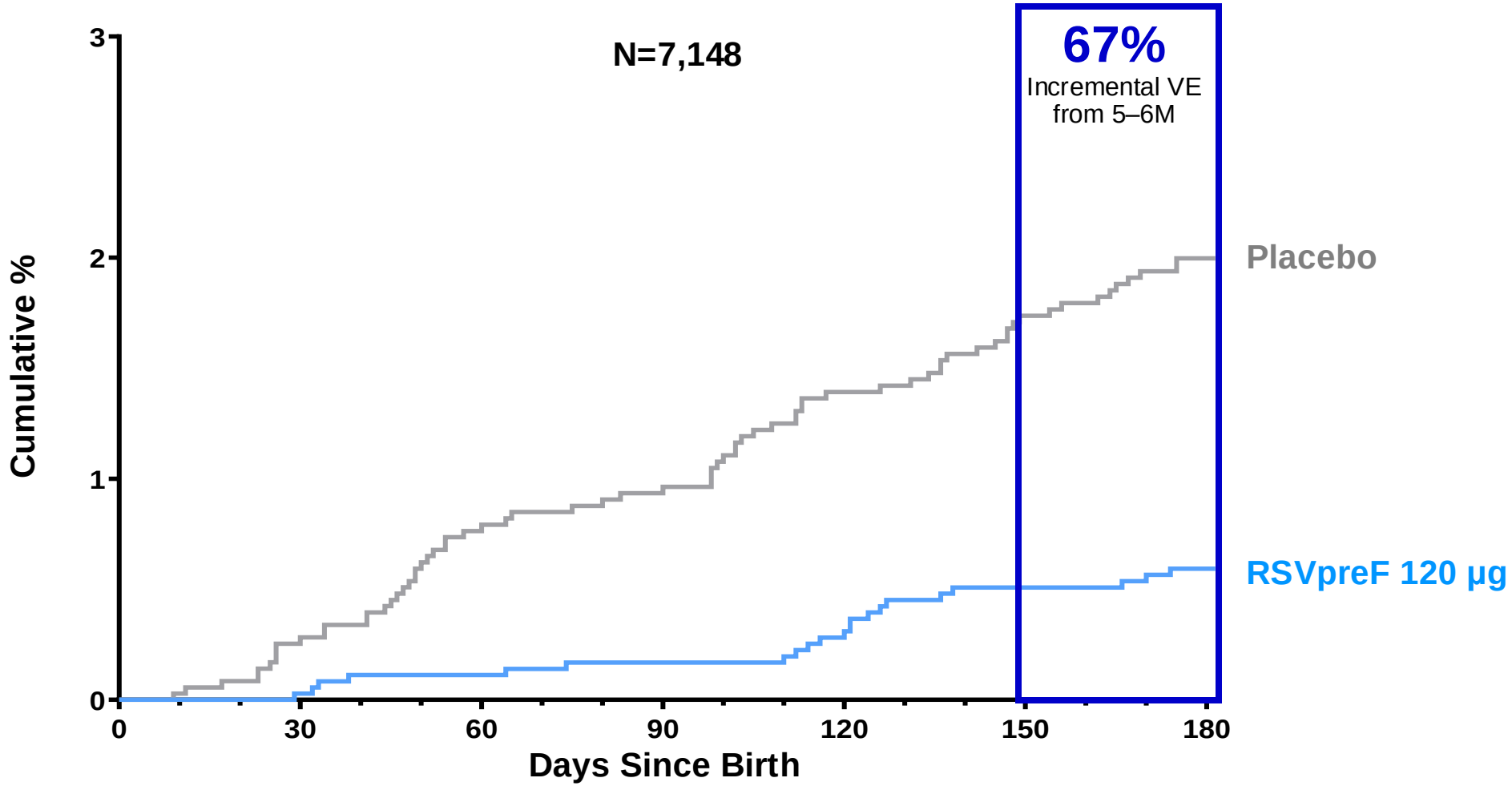
Matisse Phase III Final Overall Efficacy Results primary outcomes

Outcome	Time interval	RSVpreF N = 3585	Placebo N = 3563	Vaccine Efficacy % (95% CI)
RSV-Positive Severe Medically-attended LRTI	**0–90 days after birth**	6 (0.2)	34 (1.0)	**82.4 (57.5, 93.9)**
	0–180 days after birth	21 (0.6)	70 (2.0)	**70.0 (50.6, 82.5)**
RSV-Positive Medically-attended LRTI	**0–90 days after birth**	25 (0.7)	59 (1.7)	**57.6 (31.1, 74.6)**
	0–180 days after birth	67 (1.9)	132 (3.7)	**49.2 (31.4, 62.8)**

Incremental Efficacy for Each Month Against Severe MA-LRTIs Through 6 Months of Age



Incremental Cases each Month							
	RSVpreF	1	3	2	7	5	3
	Placebo	10	18	6	15	12	9

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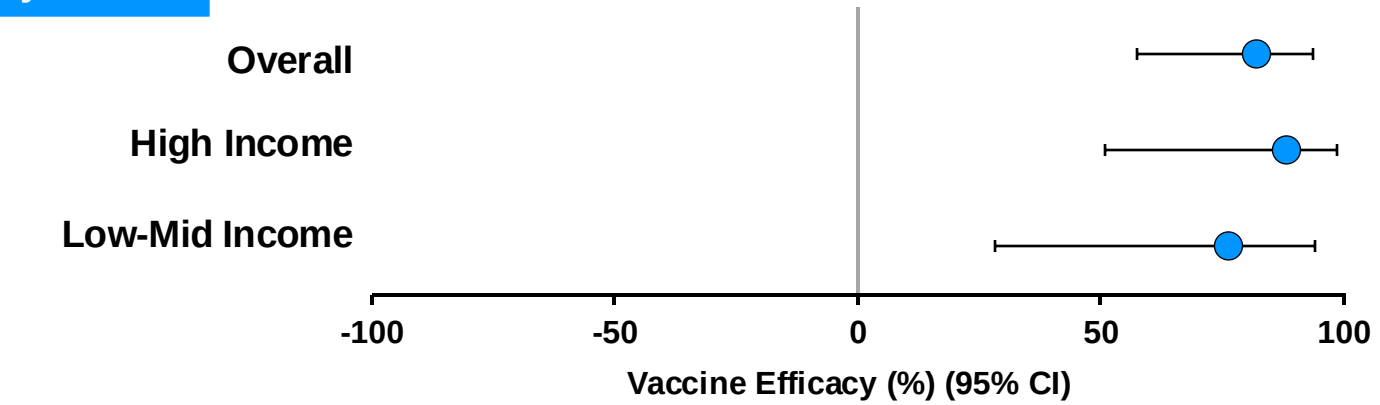
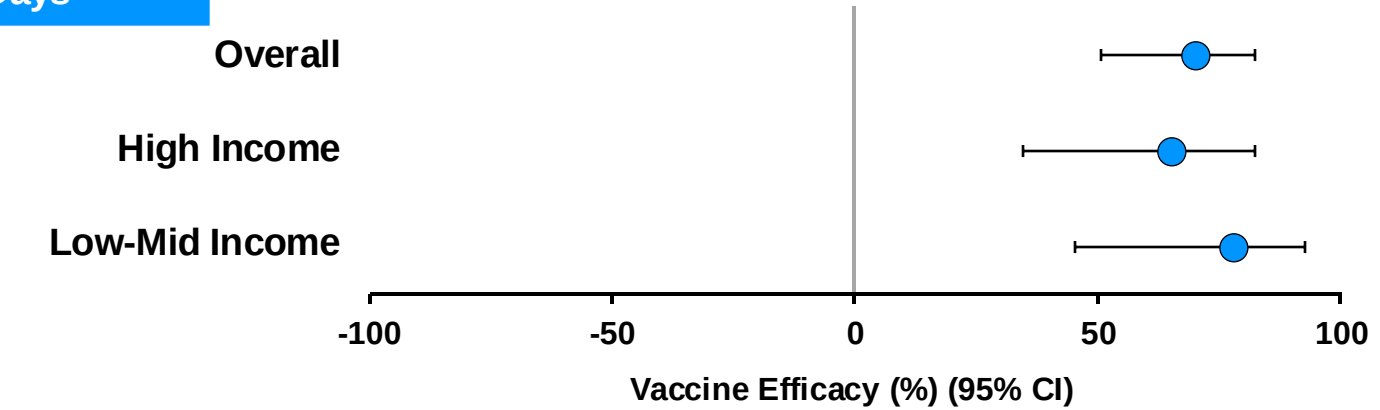
Efficacy Across Country Income Categories: RSV Severe MA-LRTI

RSV Severe MA-LRTI 90 Days



	RSVpreF/Placebo N=3585/3563	VE
Overall	6:34	82.4%
High Income	2:17	88.3%
Low-Mid Income	4:17	76.6%

RSV Severe MA-LRTI 180 Days

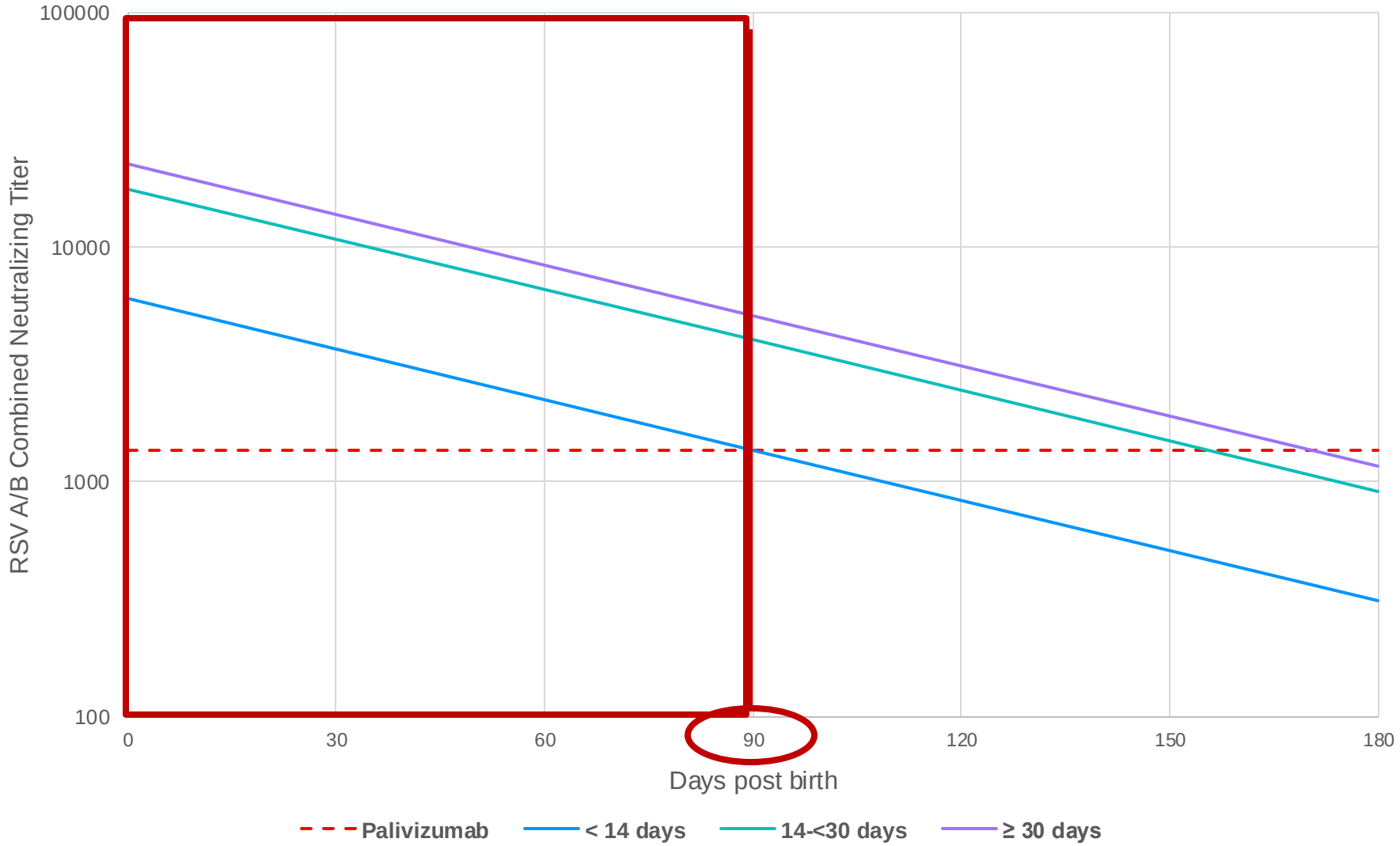


	RSVpreF/Placebo N=3585/3563	VE
Overall	21:70	70.0%
High Income	14:40	65.2%
Low-Mid Income	6:27	77.9%

USA = 46% of evaluable participants in study. Other countries include South Africa, Argentina, Japan, Taiwan, Spain, Netherlands, Chile, The Gambia, Finland, New Zealand, Brazil, Mexico, Philippines, Australia, Canada, Denmark, Korea. High-income = USA (66% evaluable participants in category), Japan (9%), Taiwan, Spain (5%), Netherlands (4%), Chile, Finland (3%), New Zealand (2%) Australia, Canada, Denmark, Korea, (1% or less) Low/Middle income = South Africa (44% evaluable participants in category), Argentina (39%), The Gambia (7%), Brazil, Mexico, Philippines (3%)

Slide content provided by Pfizer

Modelled duration of protection based on Neutralizing Antibody Titers at birth, based on timing of birth after vaccination



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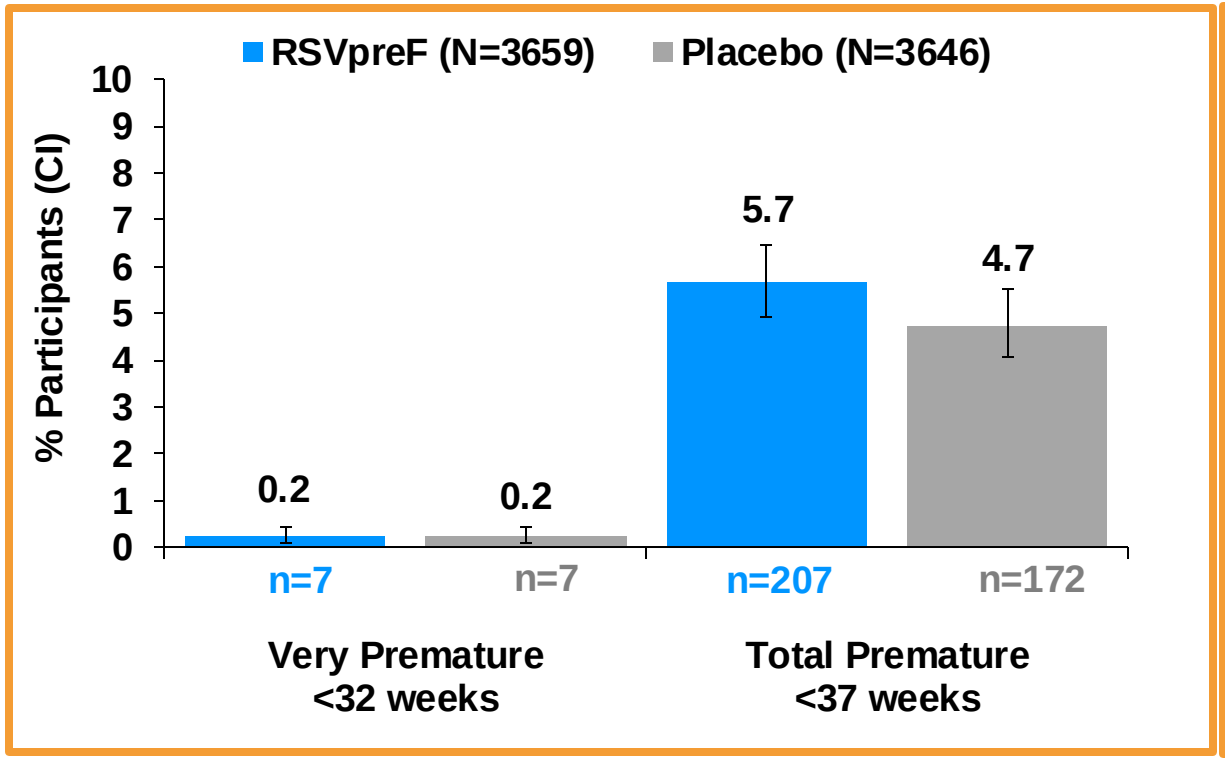
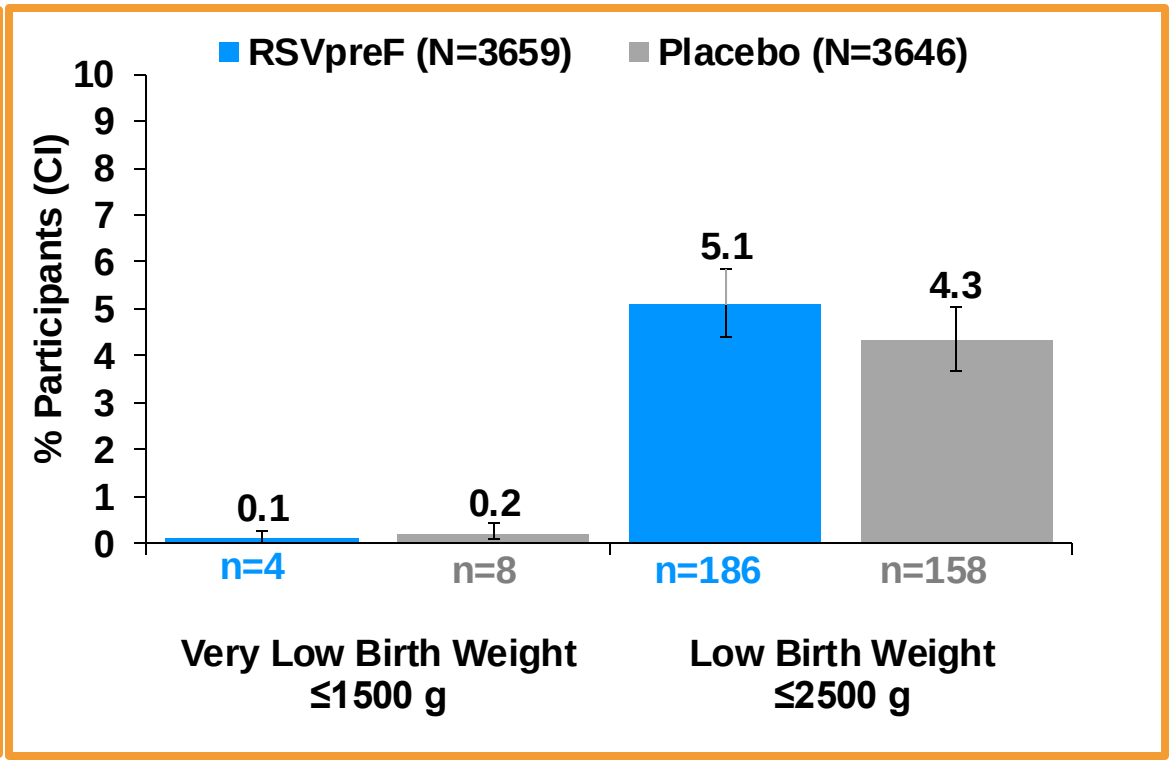
Birth Outcomes: Prematurity and Low Birth Weight





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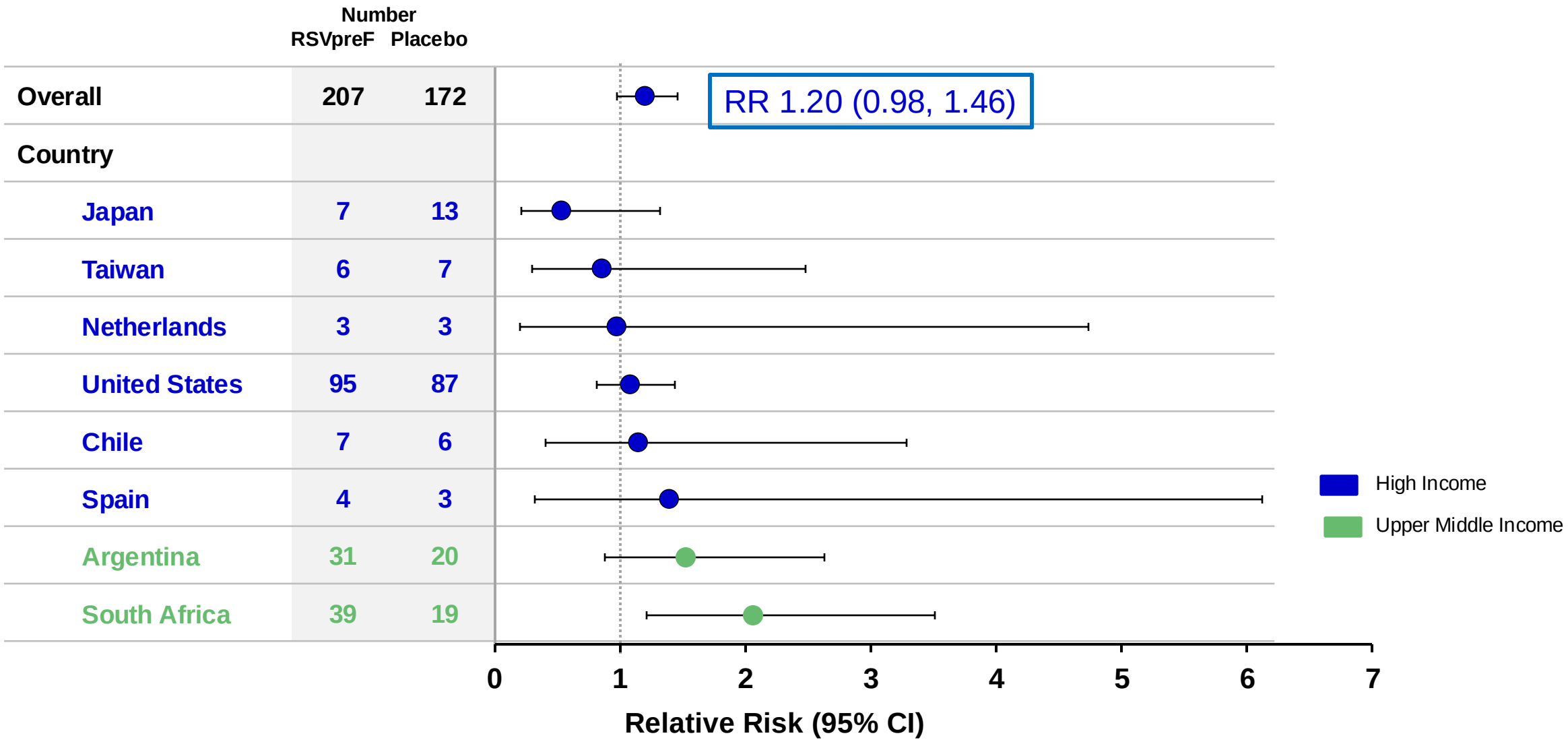
Preterm Births by Country

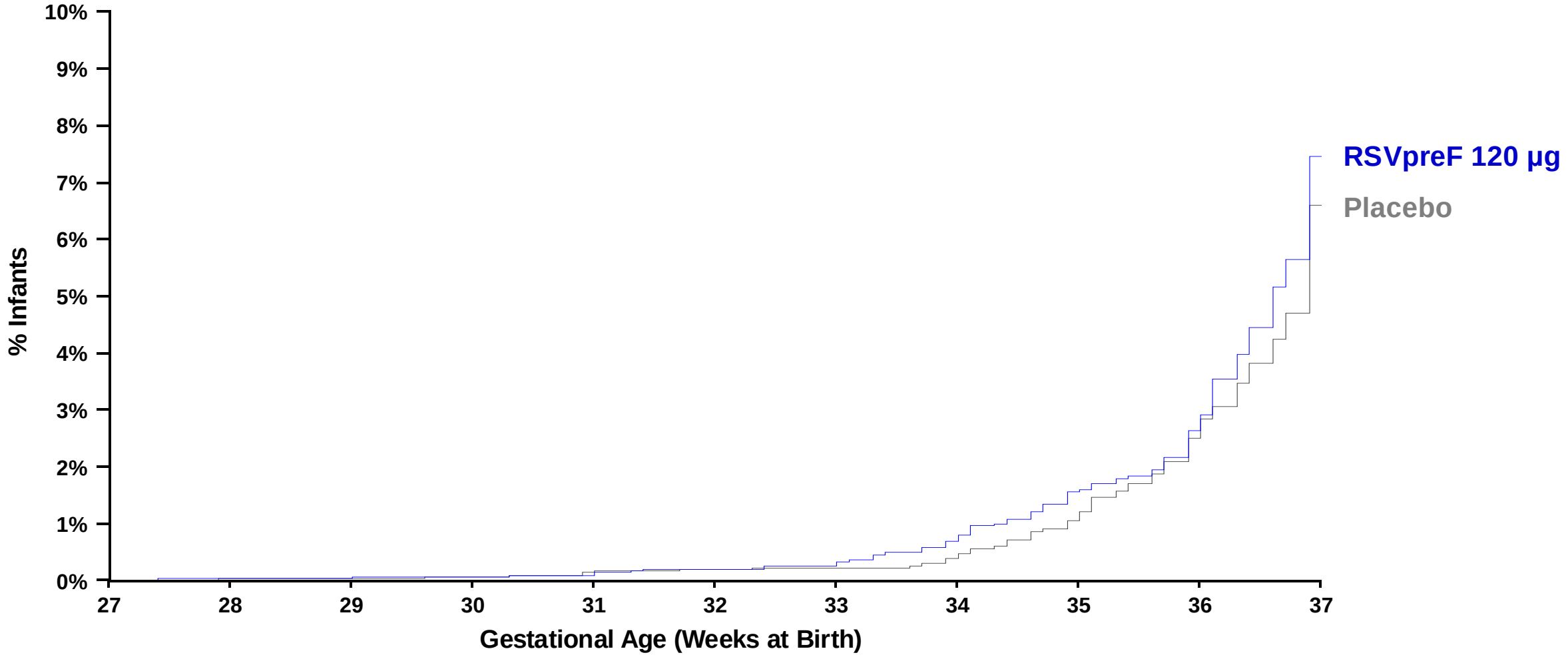
(countries with > 5 preterm births shown)



Final Analysis

Cumulative Distribution of Gestational Age at Birth among infants born < 37 weeks

Majority of Preterm Births Were Born Late Preterm and Groups are Similar < 33 Weeks



Slide content provided by Pfizer

Timing of delivery after vaccination

	Preterm		Term	
	RSVpreF 120 µg (N[a]=206)	Placebo (N[a]=172)	RSVpreF 120 µg (N[a]=3450)	Placebo (N[a]=3471)
Relative days of delivery from vaccination	n[b] (%)	n[b] (%)	n[b] (%)	n[b] (%)
≤7 days	8 (3.9)	9 (5.2)	0	2 (<0.1)
>7 days to ≤30 days	72 (35.0)	62 (36.0)	487 (14.1)	473 (13.6)
>30 days	126 (61.2)	101 (58.7)	2963 (85.9)	2996 (86.3)

Abbreviations: GA = gestational age; Note: Preterm is all maternal participants with infants <37 weeks GA at birth. Term is all maternal participants with infants ≥37 weeks GA at birth.

a. N = number of subjects in the specified vaccine group. This value is the denominator for the percentage calculations. b. n = Number of subjects in the specified category.

Slide content provided by Pfizer

Infant Deaths Overall and by Subcategory

Event Type	RSVpreF 120 µg N=3659 n	Placebo N=3646 n	RR (CI)
Total Infant death due to any cause (n=22)	**8**	**14**	**0.57 (0.24, 1.36)**
Infant death due to RSV	0	1	-
Preterm deaths (<37 weeks at birth)	1*	2	0.50 (0.05, 5.49)
Neonatal deaths (<30 days after birth)	3*	5	0.60 (0.14, 2.50)

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*A single preterm infant died in the neonatal (<30 days) period. The infant was in the RSVpreF group and from South Africa. The infant is represented in both subcategories: preterm and neonatal.

Hypertensive disorders among pregnant persons MATISSE

Table 3 Select Pregnancy-related Serious Adverse Events in Study 1 in Pregnant Individuals Occurring at any Time Following Vaccination[a]

Serious Adverse Reaction	ABRYSVO N=3,682 n (%)	95% CI	Placebo N=3,675 n (%)	95% CI
All Maternal SAEs	598 (16.2)	(15.1, 17.5)	558 (15.2)	(14.0, 16.4)
Pre-eclampsia	68 (1.8)	(1.4, 2.3)	53 (1.4)	(1.1, 1.9)
Gestational hypertension	41 (1.1)	(0.8, 1.5)	38 (1.0)	(0.7, 1.4)
Premature rupture of membranes	15 (0.4)	(0.2, 0.7)	16 (0.4)	(0.2, 0.7)
Preterm premature rupture of membranes	15 (0.4)	(0.2, 0.7)	10 (0.3)	(0.1, 0.5)
Hypertension	13 (0.4)	(0.2, 0.6)	6 (0.2)	(0.1, 0.4)
Maternal death[b]	1 (<0.1)	(0.0, 0.2)	0	(0.0, 0.1)
Fetal Death[c]	10 (0.3)	(0.1, 0.5)	8 (0.2)	(0.1, 0.4)

[a] Includes all SAEs from vaccination to 6 months post-delivery (up to approximately 10 months, depending on the gestational age at the time of vaccination). In Study 1, eclampsia occurred in 5 participants (3 in the ABRYSVO group and 2 in the placebo group) and HELLP syndrome occurred in 5 participants (2 in the ABRYSVO group and 3 in the placebo group).

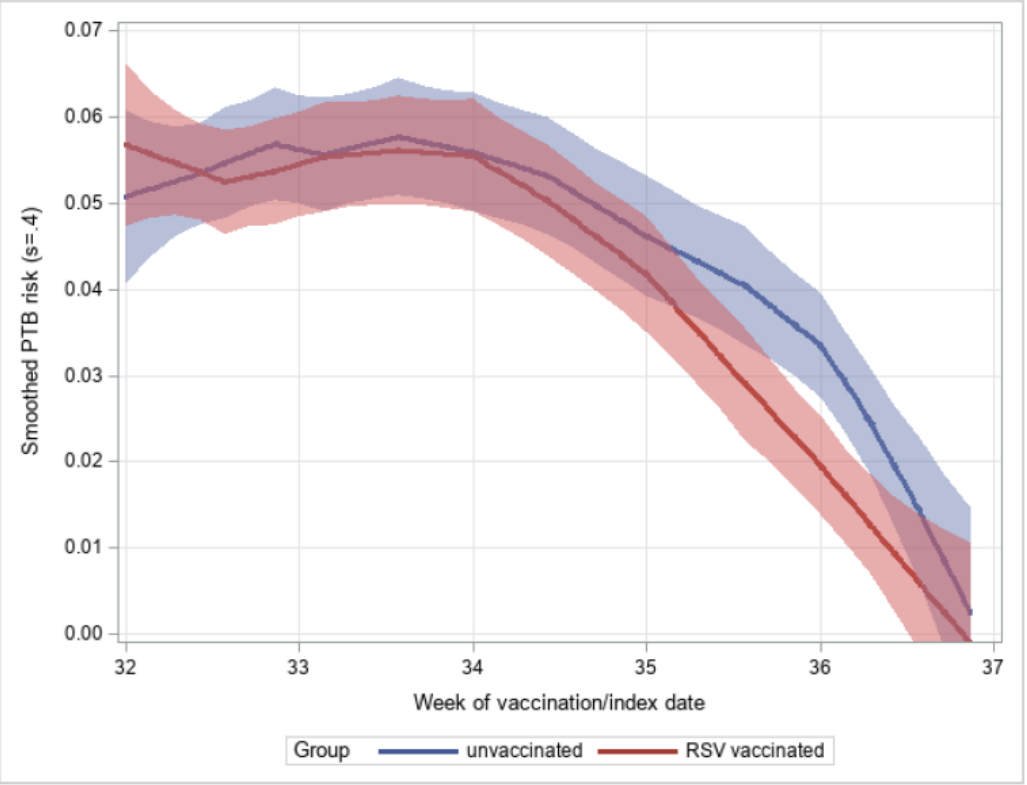
[b] There was one maternal death in the ABRYSVO group due to postpartum hemorrhage that was not likely to be associated with vaccination.

[c] A total of 18 intrauterine deaths were reported for the index pregnancy: 10 intrauterine deaths in the ABRYSVO group (0.3%) and 8 intrauterine deaths in the placebo group (0.2%). The intrauterine deaths represented various clinical conditions and presentations resulting in fetal demise without clear evidence of a common pathophysiology.

From: Food and Drug Administration. ABRYSVO package insert. https://www.fda.gov/media/168889/ download?attachment

Post-authorization evaluations of safety of RSVPreF

- U.S. CDC. Preliminary findings in the Vaccine Safety Datalink (VSD) shows rate of preterm births was 4.1% among vaccinated pregnant persons during 2023-2024 respiratory season
  - Within VSD's expected historical range of the incidence of preterm births at 32-36 weeks' gestation (3.1–6.1%)
  - Target trial emulation design (propensity score matched to be vaccinated): ptb rate 4.0% among vaccinated vs. 4.5% unvaccinated, RR 0.90 (0.80-1.00)



Global regulatory & policy approvals of RSVPreF maternal vaccine (September 2024)

Regulatory approval (GA window)	NITAG recommendations	Country roll-out
Australia (24 - 36 weeks)	Yes (28-36 weeks, with vaccination possible after 36 weeks, year-round)	Planned for 2025
Argentina (32 - 36 weeks)	Yes (32-36.6 weeks), seasonal	**Since March 2024,134,000 women vaccinated (57% coverage)**
Canada (32 - 36 weeks)	Yes, 32 through 36 weeks (based on individual decision making)	Private market (reimbursed in Ontario)
European Union & European Economic area (30 countries) (24 - 36 weeks)	Austria (24-36 weeks), seasonal; Belgium (28-36 weeks), seasonal; Italy (Sicily) (24-36 weeks, better between 32-36 weeks), seasonal; Italy (Lazio) (32-36 weeks), seasonal; Italy (Campania) (third trimester); Luxembourg (32-36 weeks), seasonal; France (32-36 weeks), seasonal; Slovenia (24-36 weeks)	Austria, private market; Belgium, private market; Italy, to start fall 2024; **Lux, national program started Aug. 2024;** **France, started Sept. 2024;** Slovenia, expected to start 16 Sept. 2024
United Kingdom (28 - 36 weeks)	Yes (28-36 weeks), the vaccine can be given up until delivery, year-round	**National Immunization Program started in August 2024 for Scotland and Sep 2024 for England, Wales, and Northern Ireland**
United States (32 - 36 weeks)	Yes (32-36 6/7 weeks), seasonal (Sept – Jan, most of US)	**October 2023 to January 2024 and second year of vaccine use started September 1, 2024**
Uruguay (32 - 36 weeks)	Yes (32-36.6 weeks)	**National Immunization Program started 19 August 2024, through end September.**
(24-36 wks) Bahrain; Brazil; Dominican Republic; Japan; Macau; Qatar; Saudi Arabia; Thailand; UAE	N/A*	N/A
(32-36 wks) Hong Kong; Singapore; Switzerland	N/A*	N/A

* = NITAG recommendations unknown or not yet available. Yellow highlight indicates upper middle-income country. Blue font means vaccination started.

SAGE Recommendations October 2024

- SAGE recommends that all countries introduce products for the prevention of severe RSV disease in young infants.
- There are two effective licensed approaches: a vaccine given to pregnant persons in the latter part of pregnancy to protect infants through transplacental transfer of maternal antibodies; and a long-acting monoclonal antibody administered directly to the infant.
- Decisions to use maternal vaccination and/or the long-acting monoclonal antibody should consider cost, financing, supply, anticipated coverage and feasibility of implementation within the existing health system.

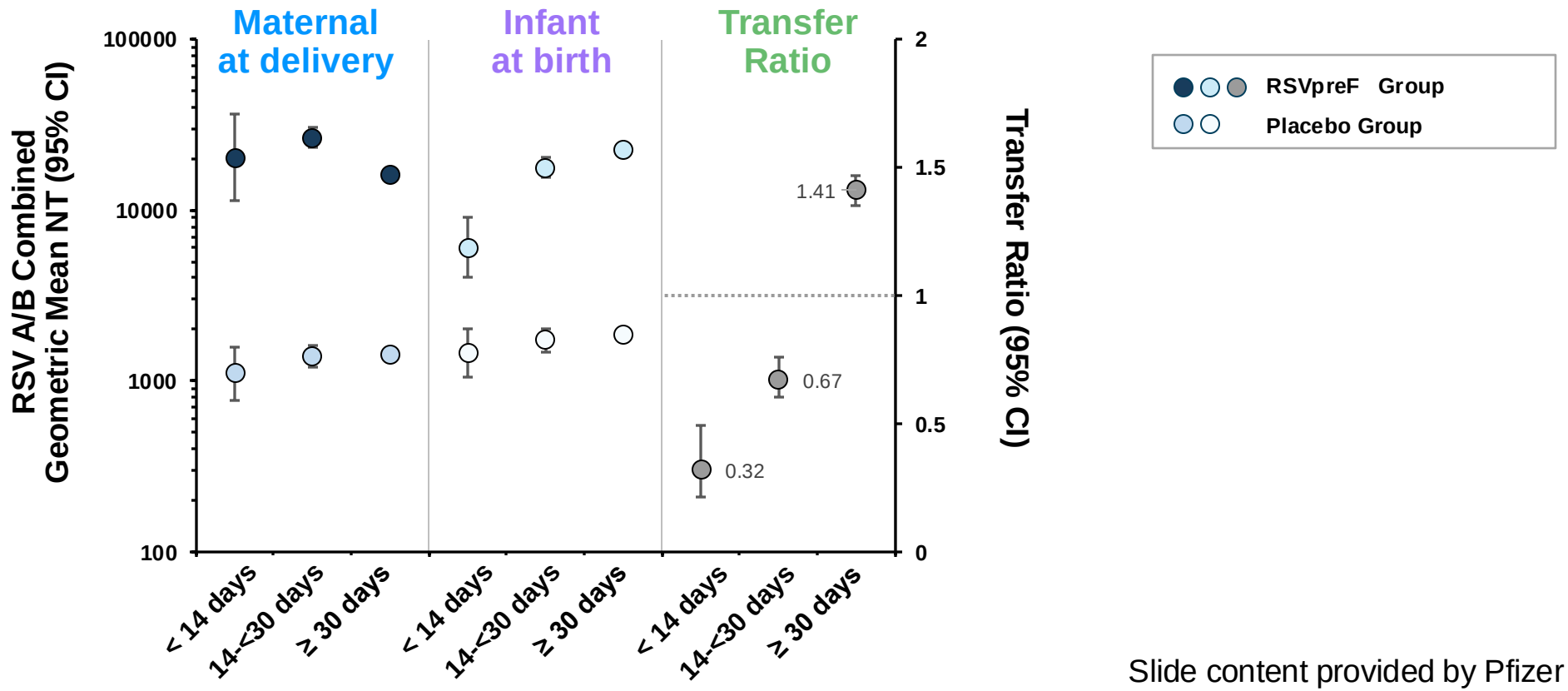
Thank you

World Health Organization

Extra slides

Maternal and Infant RSV Neutralizing Titers stratified by timing of delivery after vaccination

Evaluable Subset by Time from Vaccination to Delivery (#)
< 14 days (N=32)
14-30 days (N=147)
≥30 days* (N-931)

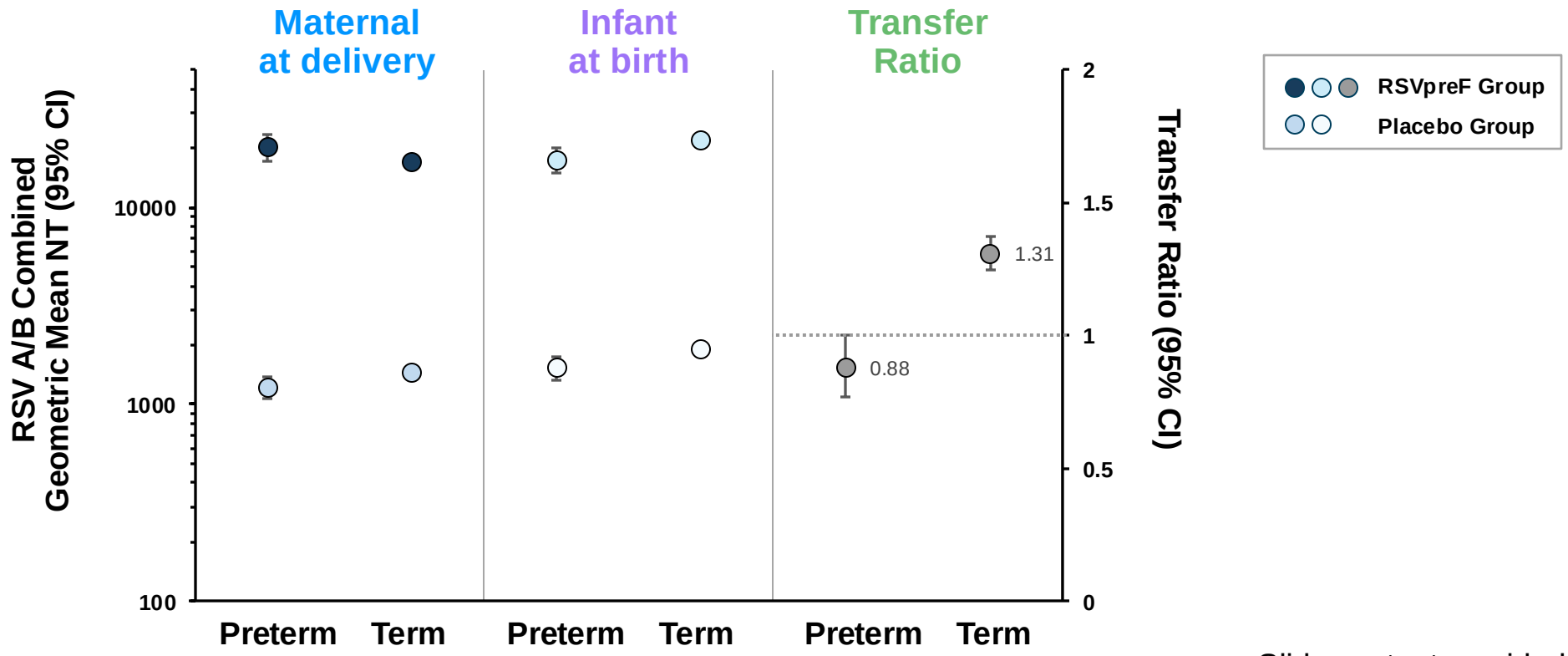


Slide content provided by Pfizer

+From convenience sample

Maternal and Infant RSV Neutralizing Titers stratified by Preterm vs. Term birth

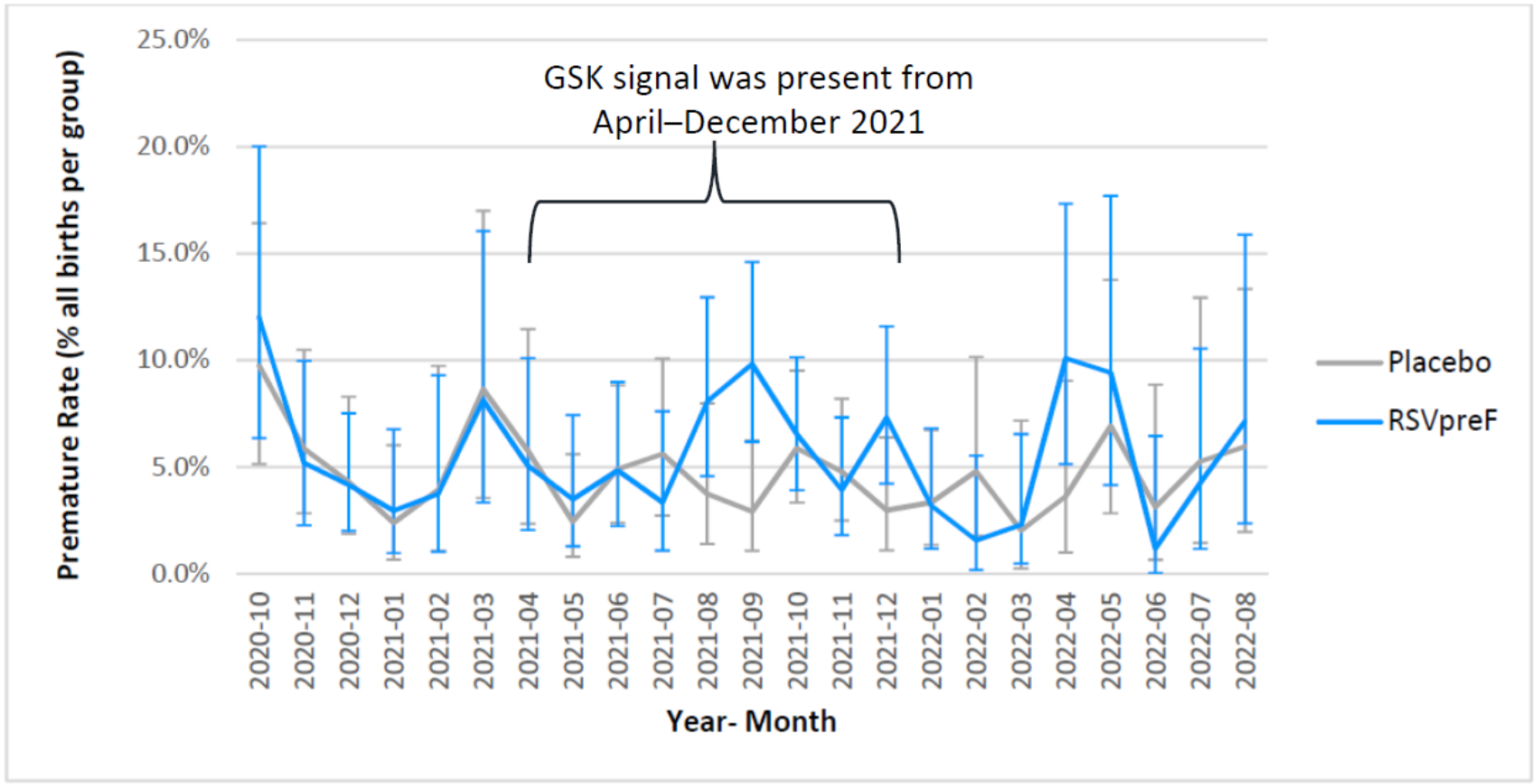
Trial Preterms Subgroup by GA at Delivery (N=379)*	
≥24 weeks to <28 weeks	N=2
≥28 weeks to <34 weeks	N=32
≥34 weeks to <37 weeks	N=345



* 331 Evaluable Available for Immunogenicity Analysis

Slide content provided by Pfizer

Preterm birth rate for vaccine and placebo recipients by calendar time—Pfizer Phase 3 trial, trial dosing interval (24–36 weeks gestation)



Data source: Pfizer response to ACIP, unpublished data, July 2023

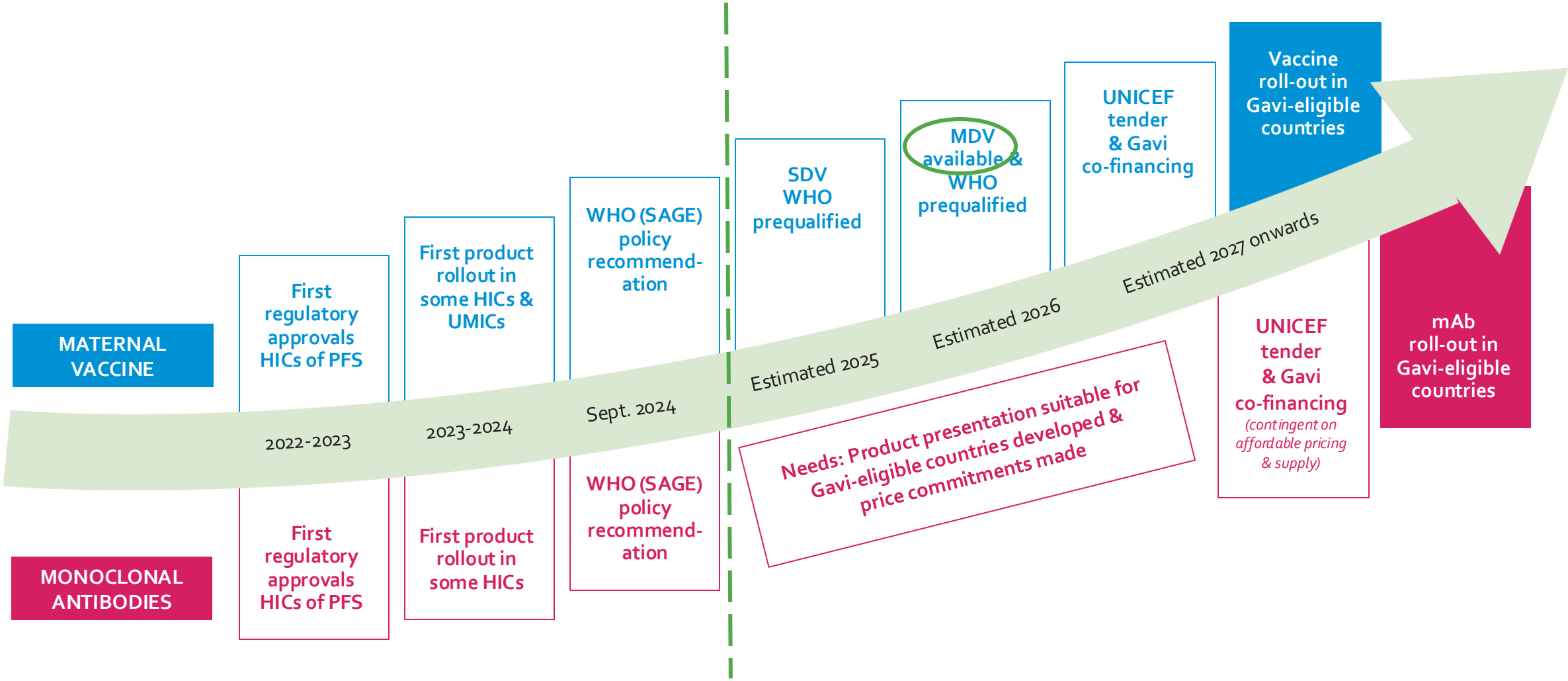
25

From ACIP presentation, September 22, 2023

RSVPreF access for LMICs

- Authorized vaccine formulation is a kit with single dose vial with lyophilized vaccine plus a separate prefilled syringe with diluent plus a vial adaptor
- EMA recently approved a variation for a 10+10 single dose vial:vial automated packaging presentation (can be used with AD syringe)
  - Formulation intended for use in LMICs
  - WHO Prequalification submission of single dose vial:vial formulation in May 2024; eligible for streamlined procedure (finalization pending WHO policy recommendation)
- Multidose Vial: Global Access commitment to MDV for lower income countries via public sector purchasers, including GAVI, as part of Pfizer's 'An Accord for a Healthier World'
  - Co-funded by Gates Foundation and Pfizer
  - Submission to EU beginning in 2025 and will also be submitted for WHO PQ
- Immunogenicity and safety trial in HIV+ pregnant women in South Africa
- Approval in principle of RSV immunization in GAVI Vaccine Investment Strategy in 2024, pending final GAVI Board approval

RSV immunization product availability for Gavi-eligible countries



Definitions: HIC = high-income country; PFS = pre-filled syringe; UMIC = upper- and middle-income country; WHO SAGE = World Health Organization Strategic Advisory Group of Experts; SDV = single-dose vial; MDV = multi-dose vial

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

RSV Maternal Vaccine impact study

- Phase IV efficacy trial
- 13,000 pregnant women in 4 African countries

Coprimary endpoints

  - Evaluate the efficacy of RSVpreF on RSV confirmed severe LRTI through 180 days of age.
  - Evaluate the safety of RSV-preF in relation to preterm births (born at <37 weeks GA) in women with gestational age staging GAIA Level of Certainty [LOC] 1 to 2A at time of enrolment.

- Anticipated start in early 2025

Demyelinating disorders/Guillain-Barré syndrome

- Within 42 days of vaccination, 2 related cases of Guillain-Barre syndrome (GBS) type neurological syndrome observed in RSVPreF recipients in RCT among elderly adults
  - Post-marketing surveillance ongoing
- No GBS or other demyelinating events were reported in the phase 2b or 3 trials among pregnant women
- Background rate of GBS in pregnant persons is much lower than among older adults
  - GBS in pregnancy in Vaccine Safety Datalink during 2004-15; 2.8 (95% CI 0.5-9.3) per million pyo (based on 2 cases)
- As of June 3, 2024, no *verified* cases of GBS-like syndromes have been reported among vaccinated pregnant persons in the US in post-authorization surveillance

1. Vaccines and Related Biological Products Advisory Committee May 18, 2023 Meeting Briefing Document- FDA
2. Myers TR, McCarthy NL, Panagiotakopoulos L, Omer SB. Estimation of the Incidence of Guillain-Barré Syndrome During Pregnancy in the United States. Open Forum Infect Dis. 2019 Mar 15;6(3):ofz071. doi: 10.1093/ofid/ofz071.
3. Sejvar JJ, Baughman AL, Wise M, Morgan O. Population Incidence of Guillain-Barré Syndrome: A Systematic Review and Meta-Analysis. Neuroepidemiology 2011;36:123–133

WHO SAGE prebrief, 24 September 2024

Benefit-risk analysis of maternal RSV vaccination in low- and middle-income countries

Ayaka Monoi[1], Akira Endo, Simon Procter, Sequoia Leuba, Stefan Flasche, Mark Jit[2],
Maternal RSV vaccine benefit-risk analysis advisory group
(Angela Guo, Bryan Nyawanda, Cheryl Cohen, Daniel Feikin, Erin Sparrow, Heather Zar, James Nokes, Jocelyn Moyes, Joyce Nyiro, Mihaly Koltai, Padmini Srikantiah, Patrick Munywoki, Philippe Beutels, Shabir Madhi)

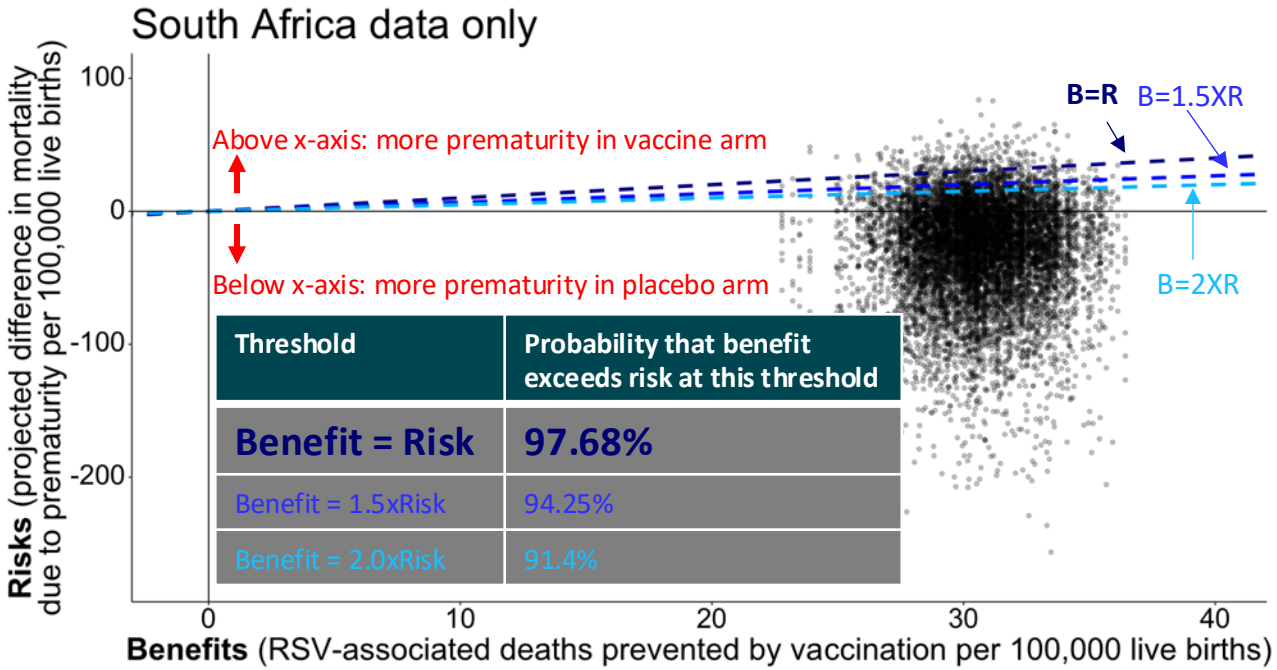
[1]ayaka.monoi@lshtm.ac.uk, [2]mark.jit@lshtm.ac.uk

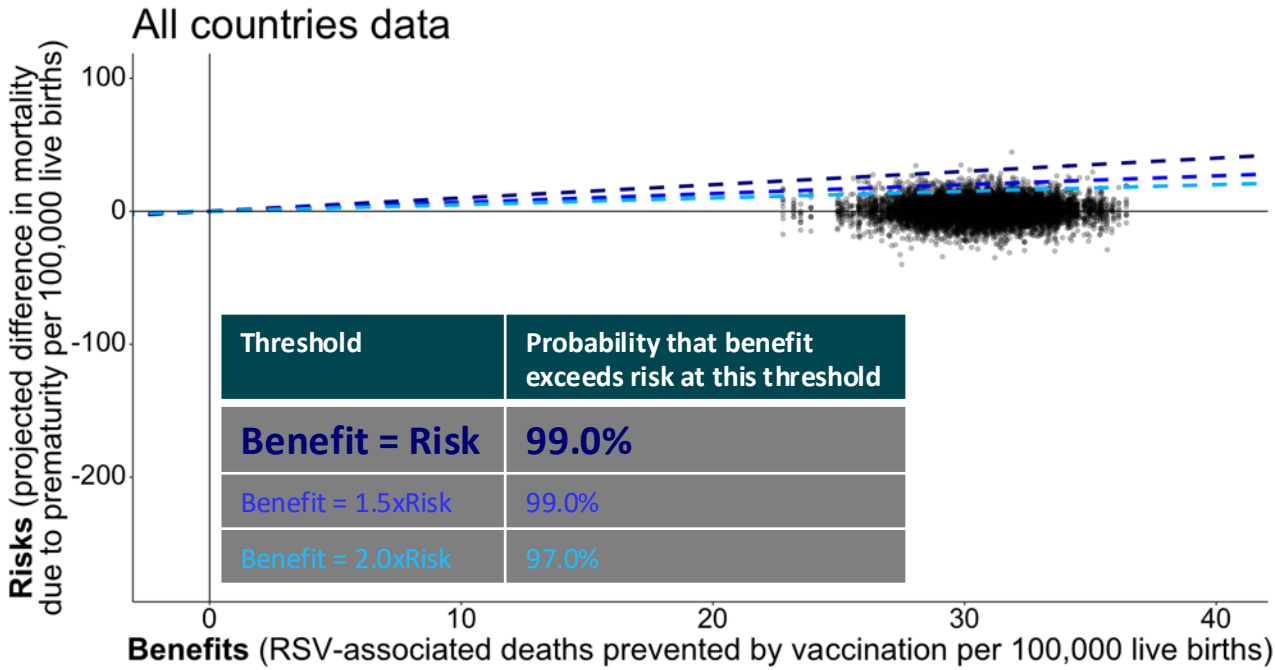
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

This presentation contains some unpublished data confidentially provided by Pfizer
Disclaimer: While the Analysis presented used data shared by Pfizer from the Phase 3 Matisse trial, Pfizer did not participate in the analysis of such data nor did Pfizer have any role in the conclusions drawn from the analysis presented by SAGE.

Updated benefit-risk analysis with vaccination at 27+weeks gestational age; Benefits outweigh risks.

Estimated risks and benefits of Abrysvo with trial birth outcomes born to mothers vaccinated at 27-36 weeks GA





Unpublished data provided by Pfizer

Disclaimer: While the Analysis presented used data shared by Pfizer from the Phase 3 Matisse trial, Pfizer did not participate in the analysis of such data nor did Pfizer have any role in the conclusions drawn from the analysis presented by SAGE.

Post-authorization evaluations of safety of RSVPreF

- NYC.* 2 hospitals, 2973 women; preterm 5.9% vaccinated vs. 6.7% unvaccinated
  - aOR PTB 0.87, 95% CI 0.62-1.20; cox PH HR 0.93, (0.64-1.34)
  - Hypertensive disorders of pregnancy, 20.1% vs. 18.1%; aOR 1.10, 95% 0.90-1.35; Cox PH HR 1.43, 1.16-1.77
- Argentina no increase in prematurity compared to baseline among >130,000 vaccinated
  - Formal analysis still pending
- Pfizer sponsored studies in the US (n=1) and EU (n=3)
- WHO initiative to develop global pregnancy minimal standard pharmacovigilance dataset, including data elements related to birth outcomes

*Son M, et al. 8 July 2024; JAMA Network Open

GACVS meeting, May 18, 2024

- Objective of RSV vaccine presentation was “for information”
- Presentation on results of MATISSE study with emphasis on safety aspects
- Discussion with GACVS members on results
  - “The numerical imbalance in preterm births between study groups is a safety signal, but, given the lack of statistical significance and absence of a plausible biological mechanism, it should not preclude use of this highly effective vaccine….”
  - “Post-marketing pharmacovigilance will be important to better understand this safety signal and should be conducted in countries in which the maternal vaccine is used.”
  - “Owing to low uptake of the vaccine to date, however, it will probably be several years before enough people have been vaccinated for definitive conclusions to be drawn from post-marketing evaluations.”
- GACVS will evaluate post-authorization pharmacovigilance data
- Report published in WER 9 AUGUST 2024, 99th YEAR. No 32, 2024, 99, 407–414

Maternal RSV vaccination

Recommendations from the PAHO and WHO Technical Advisory Groups

Webinar "Maternal vaccination for preventing respiratory syncytial virus-associated disease in infants"

17 December 2024

Outline

- People at highest risk of infectious and serious disease from RSV
- Recommendations from the PAHO TAG – November 2023
- Recommendations from the WHO SAGE – September 2024
- Conclusions

People at highest risk

Risk groups	Risk factors for severe disease
Infants and young children 0-5 years	• Age <6 months • Prematurity • Chronic lung or heart disease • Down syndrome • Immunocompromised (<18 years)
Older adults and adults with comorbidities	• Age ≥65 years • Adults with chronic lung or heart disease • Adults with weakened immune systems

Additional **risk factors for death** include, limited access to care and hospital capacity

Focus on maternal vaccination

When developing the agenda for its Technical Advisory Group (TAG) on immunization, PAHO chose to focus the topic on **maternal vaccination against RSV** because:

- Globally, RSV is the most common cause of pneumonia and bronchiolitis in infants.
- RSV is the leading cause of hospitalizations and deaths in first 6 months of life.
- In the Americas, most of RSV-associated hospitalizations are reported among children younger than 5 years, especially those younger than 6 months.
- Results from the multi-country clinical trial suggested that this vaccine had a high efficacy rate in preventing RSV disease in children younger than 6 months.

PAHO TAG November 2023

- PAHO welcomes the approval of Pfizer's (Abrysvo®) Bivalent Prefusion F (RSVpreF) vaccine in pregnant women to prevent RSV disease in infants by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), since it **addresses the considerable burden of disease in infants across the Americas** and **specifically targets pregnant women**, who are often excluded from vaccine clinical trials and therefore are delayed in reaping their benefits.

https://iris.paho.org/handle/10665.2/59314

PAHO TAG November 2023

- PAHO is encouraged by the results of the Phase 3 Maternal Immunization Study for Safety and Efficacy (MATISSE) study, which suggest **high vaccine efficacy** against severe RSV-associated disease in infants from birth through 6 months. In the trial, over 7000 pregnant women from 18 countries were included in the study. However, **data were collected only from upper-middle-income countries (UMIC) and high-income countries (HIC).** The impact study recommended by the SAGE in its October 2022 meeting in lower-middle-income countries is urgently needed to confirm the findings on vaccine safety and efficacy the MATISSE study outside of UMIC and HIC settings.

- PAHO notes the **high cost** of the RSVpreF vaccine in the United States and urges the PAHO Procurement and Supply Management Department and the PAHO Revolving Fund to negotiate a lower price for countries in the Americas to avoid inequitable implementation of this vaccine into the national immunization programs of the Region.

https://iris.paho.org/handle/10665.2/59314

PAHO TAG November 2023

- The PAHO assesses that maternal RSVpreF vaccine is best given in pregnant women at **32–36 weeks of gestation** to prevent RSV disease in infants while minimizing the risk of preterm birth. Any introduction of maternal RSVpreF vaccine should be accompanied by:
  - Identification of the optimal timing of vaccine administration according to country-specific RSV seasonality patterns.
  - Robust vaccine effectiveness and impact studies.
  - Well-designed safety, cost-effectiveness, economic burden, and affordability studies.
  - Studies of behavioral and social factors to facilitate vaccine uptake.
  - Integration with other prenatal immunization programs (e.g., influenza), services, and outreach operations.
  - Careful balance between the resources needed for the introduction of this vaccine and the requirements and goals of existing vaccination programs (e.g., maintaining measles elimination)
  - Documentation of the programmatic challenges of new vaccine introduction, especially in the context of a recovering national immunization program and limited financial resources.

https://iris.paho.org/handle/10665.2/59314

WHO SAGE September 2024

- SAGE recommended a single dose of vaccine in the third trimester of pregnancy, as defined in the local context (**≥28 weeks of gestation** in most settings).

- **No upper gestational limit** for vaccine administration was prescribed, except for women in active labour.

- The recommendation to **limit vaccination in the third trimester** is a precautionary approach to minimise potential adverse impacts of preterm births before the third trimester, which have the highest risk of mortality and serious sequelae while preserving the benefits and enhancing programmatic feasibility in low- and middle-income countries.

- Countries planning to introduce maternal RSV vaccine are encouraged to **establish post introduction safety monitoring** (including birth outcomes) among vaccinated pregnant individuals, starting before or at the time of vaccine introduction. However, this should not delay or preclude introduction.

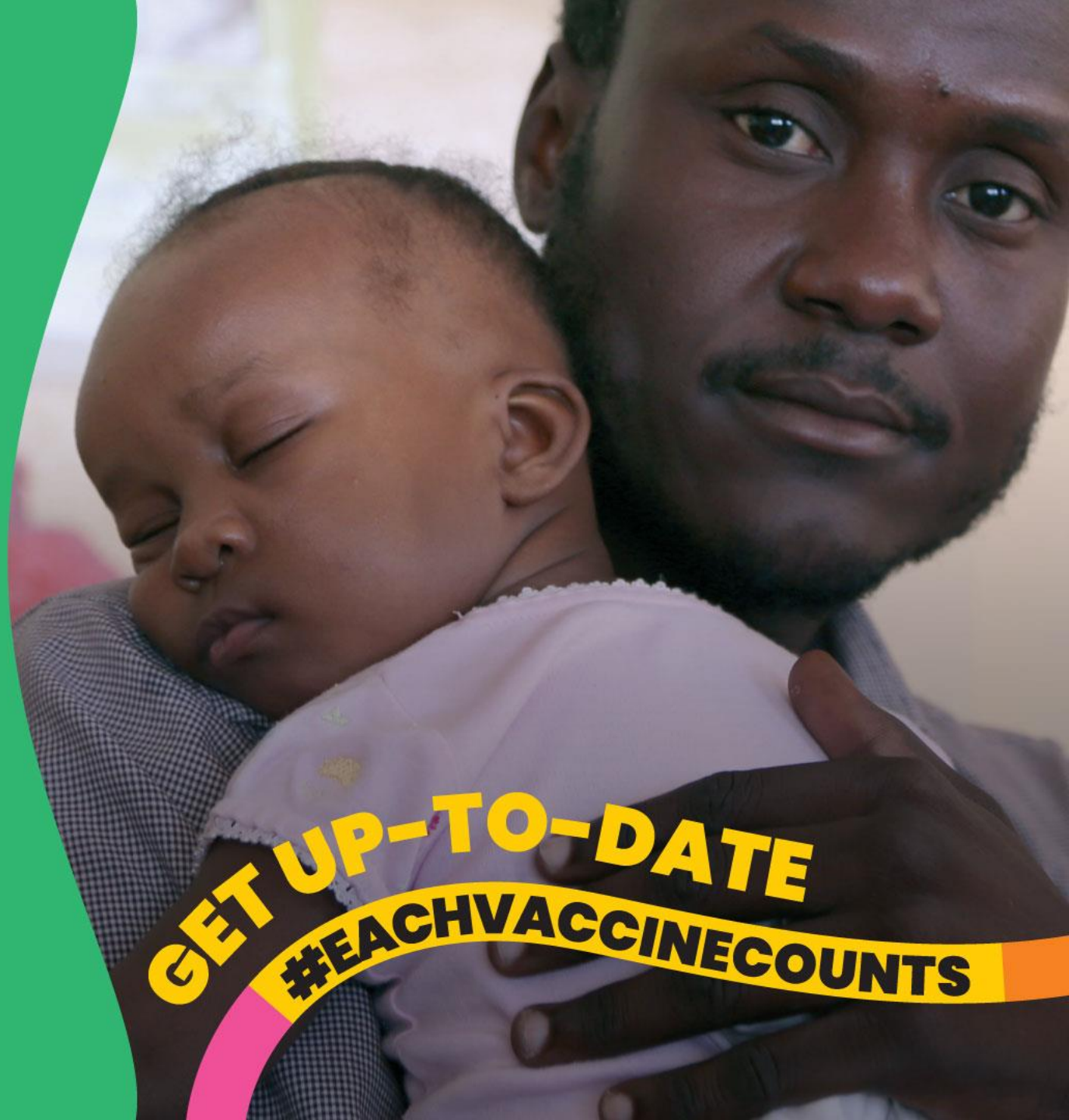
https://iris.who.int/bitstream/handle/10665/379717/WER9949-eng-fre.pdf

WHO SAGE September 2024

- **Programmatic considerations**
  - Maternal RSV vaccine could be administered at routine antenatal care contacts, at any healthcare contact, or during outreach activities.
  - A year-round approach to RSV immunization is preferable in most LMICs in tropical and sub-tropical regions where RSV circulates for much of the calendar year or seasonality patterns are not well-described.
  - Co-administration with other vaccines during pregnancy is acceptable.

https://iris.who.int/bitstream/handle/10665/379717/WER9949-eng-fre.pdf

THANK YOU



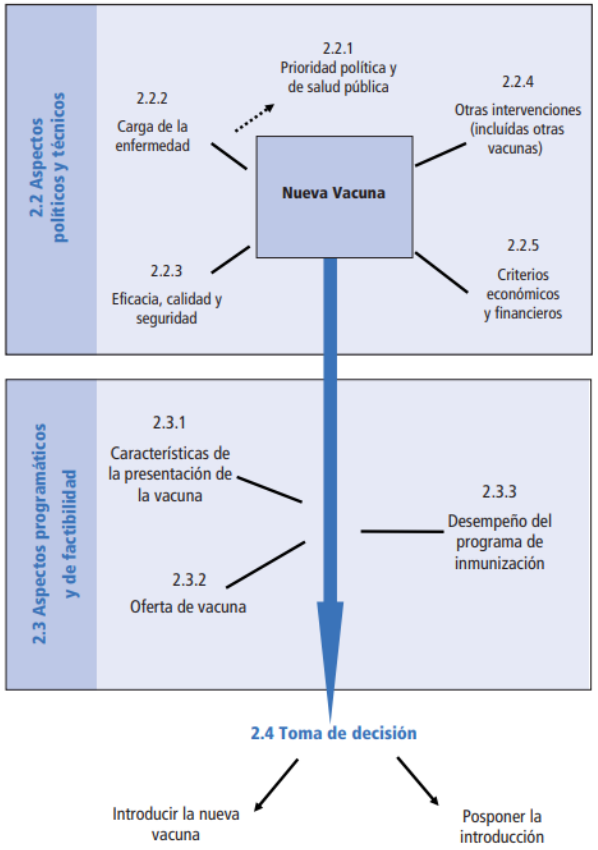
Estrategia de vacunación contra VSR: experiencia Argentina

Dra. María del Valle Juarez

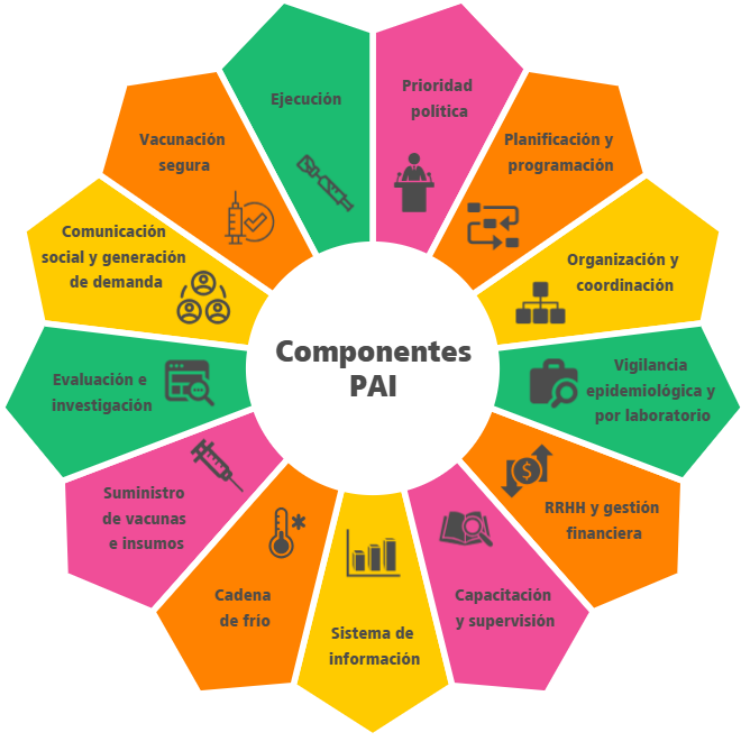
Diciembre de 2024

Contenido

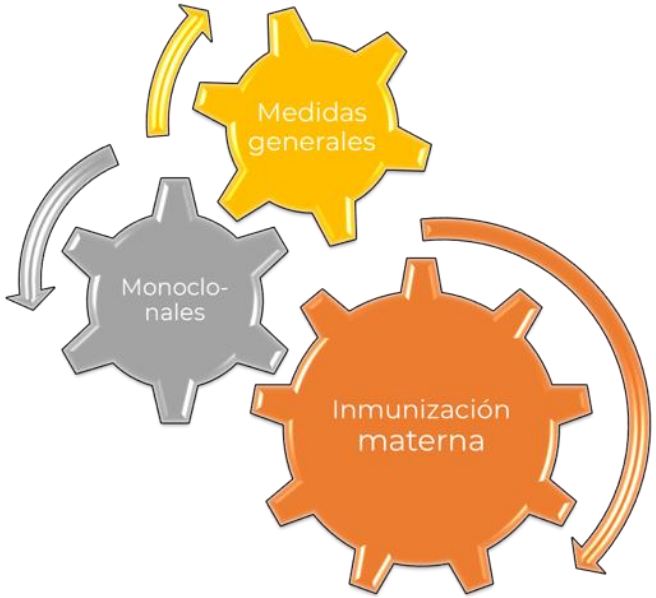
Como se tomo la decisión?



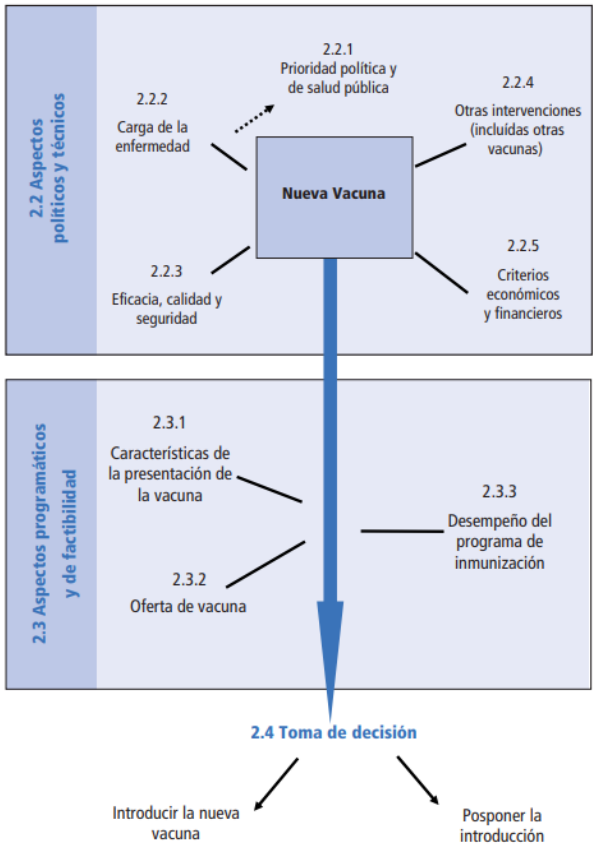
Como se implementó la estrategia?



Como seguimos?



Como se tomo la decisión?



1- Identificación del problema y estrategias novedosas de prevención desde el Ministerio de Salud.

2- Convocatoria para formación del grupo de trabajo de la Comisión Nacional de Inmunizaciones (CONAIN) para evaluar estrategias posibles.

3- Análisis de carga de enfermedad, estacionalidad, estrategias disponibles (seguridad y eficacia).

4- Recomendación de CONAIN y Consejo Federal de Salud.

Incorporación al Calendario Nacional de Vacunación.

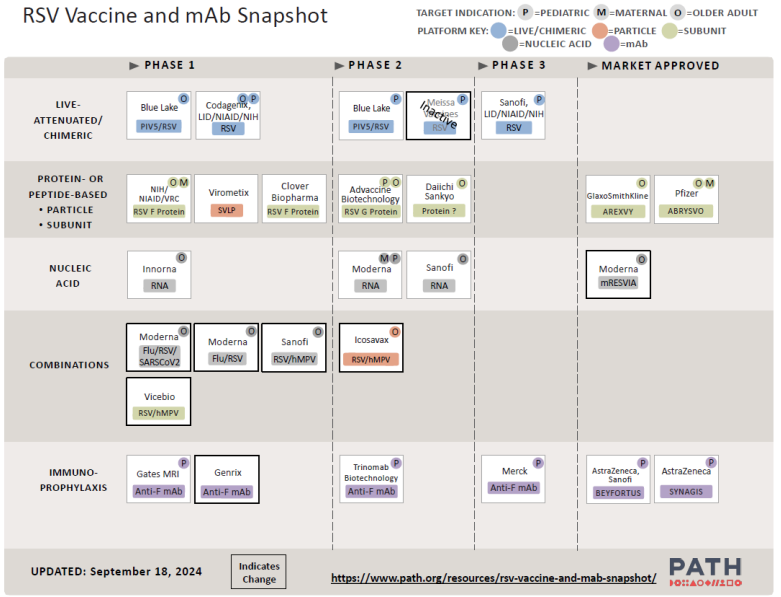
Carga de enfermedad por VSR

SALUD >

El brote de bronquiolitis supera en un 70% a los niveles prepandémicos en Argentina

El Ministerio de Salud nacional informó que ya se notificaron 50.594 en lo que va de 2023. Además, la Organización Panamericana de la Salud emitió un alerta epidemiológica para la región por el aumento de la actividad de los virus respiratorios

11 Jun, 2023 06:45 p.m. | Actualizado: 12 Jun, 2023 08:36 a.m. AR



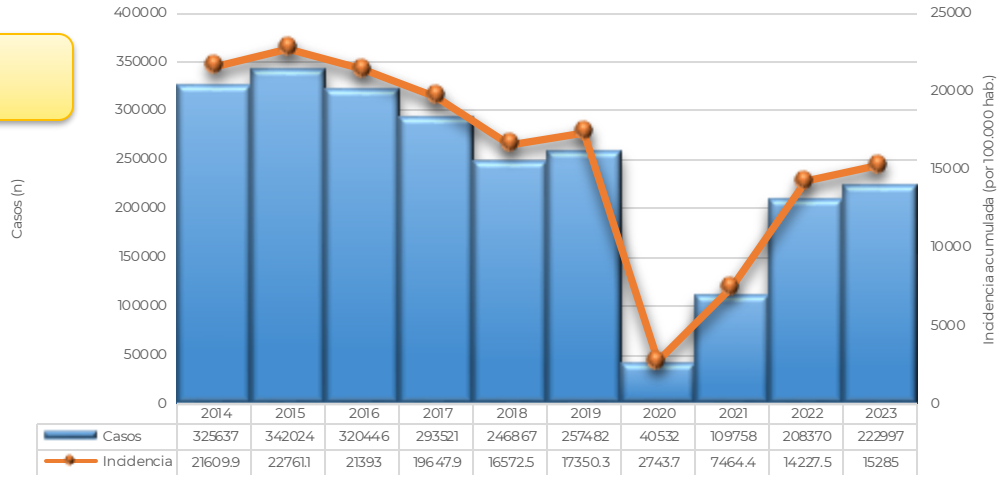
Nuevas tecnologías:

- Vacuna materna contra VSR
- Anticuerpos monoclonales de larga vida media

Carga de enfermedad por VSR

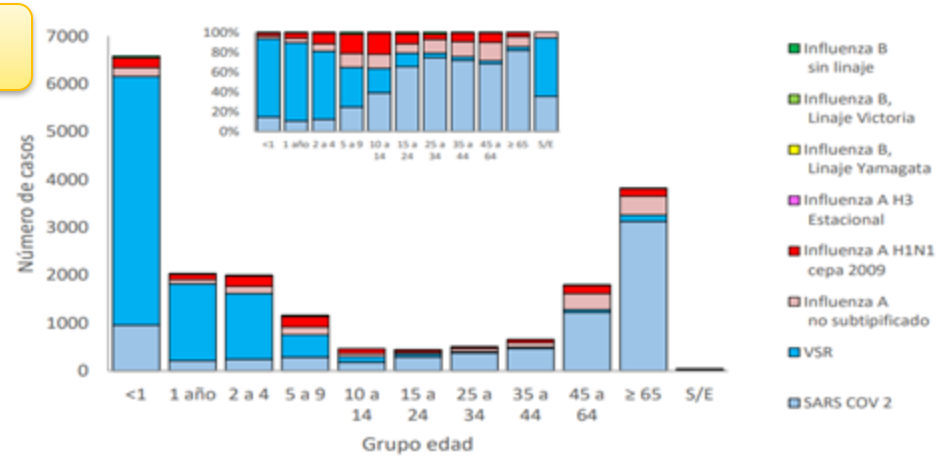
- **Menores de 1 año**: bronquiolitis (80% previamente sanos)
- **Menores de 2 años con ciertos factores de Riesgo** (cardiopatía congénita descompensada, displasia broncopulmonar, etc.)

Bronquiolitis



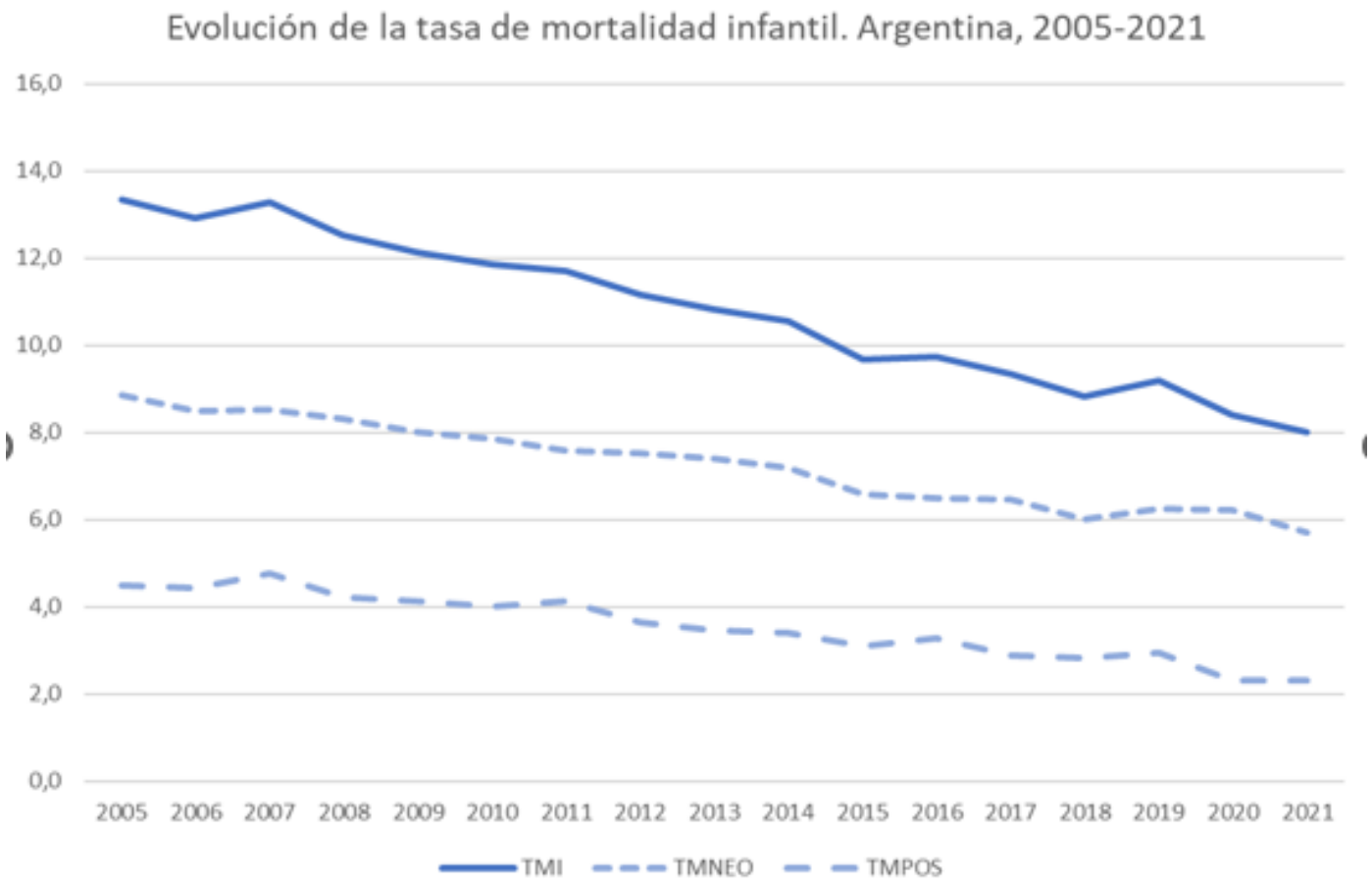
	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Casos	325637	342024	320446	293521	246867	257482	40532	109758	208370	222997
Incidencia	21609.9	22761.1	21393	19647.9	16572.5	17350.3	2743.7	7464.4	14227.5	15285

Hospitalizaciones



Fuente: Área de Vigilancia de la Salud de la Dirección de Epidemiología. SNVS 2.0. Ministerio de Salud

Morbimortalidad por VSR



Fuente: DEIS. Ministerio de Salud

- Menores de 1 año registran la mayor prevalencia de VSR.
- Durante 2021, en ausencia de circulación estacional de VSR se registró la menor tasa de mortalidad infantil de la historia.
- Reducción de 64% de la mortalidad por enfermedades respiratorias.

Factores de riesgo en la infancia

FACTORES ASOCIADOS A MORTALIDAD EN HOSPITAL[1]

- Desnutrición moderada a grave 3,69 (IC 95% 1,98–6,87)
- Enfermedad neurológica crónica 4,14 (IC 95% 2,12–8,08)
- Cardiopatía congénita 4,14 (IC 95% 2,39-7,32)
- **Edad menor de 6 meses** 1,99 (IC 95% 1,24-3,18)

FACTORES ASOCIADOS A MORTALIDAD EN EL HOGAR [2]

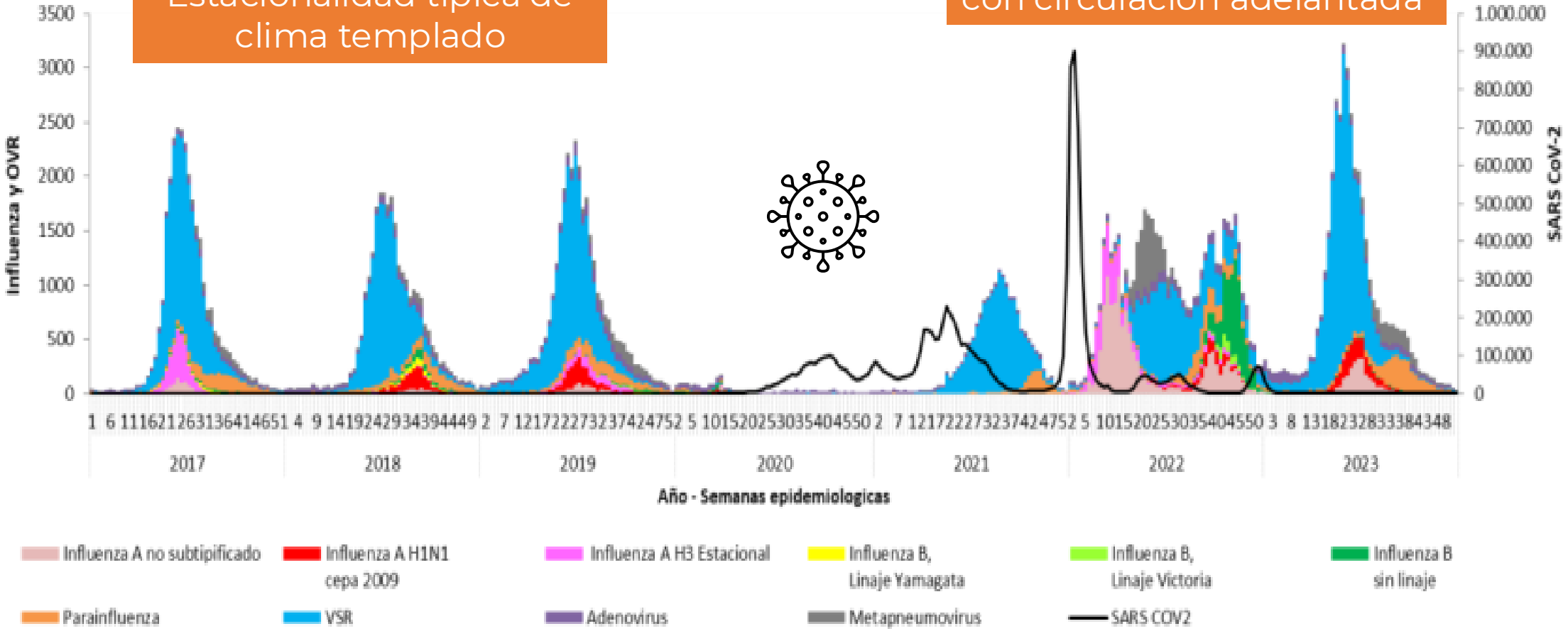
- **Ninguna visita al servicio de urgencias** 72,32 (IC 95% 4,82–1085,6)
- Requerimiento de cuidados intensivos neonatales 7,17 (IC 95% 2,21–23,27)
- Madre adolescente 4,89 (IC 95% 1,37–17,38)
- Falta de agua corriente 4,39 (IC 95% 1,11–17,38)
- **Hacinamiento** 3,73 (IC 95% 1,41–9,88)
- Vacunación incompleta para la edad 3,39 (IC 95% 1,20–9,62)

(1) *Gentile et al. Burden of Respiratory Syncytial Virus Disease and Mortality Risk Factors in Argentina: 18 Years of Active Surveillance in a Children's Hospital. The Pediatric Infectious Disease Journal 38(6):p 589-594, June 2019.*
(2) *Caballero M et al. Mortality Associated With Acute Respiratory Infections Among Children at Home. J Infect Dis. 2019 Jan 9;219(3):358-364.*

Estacionalidad

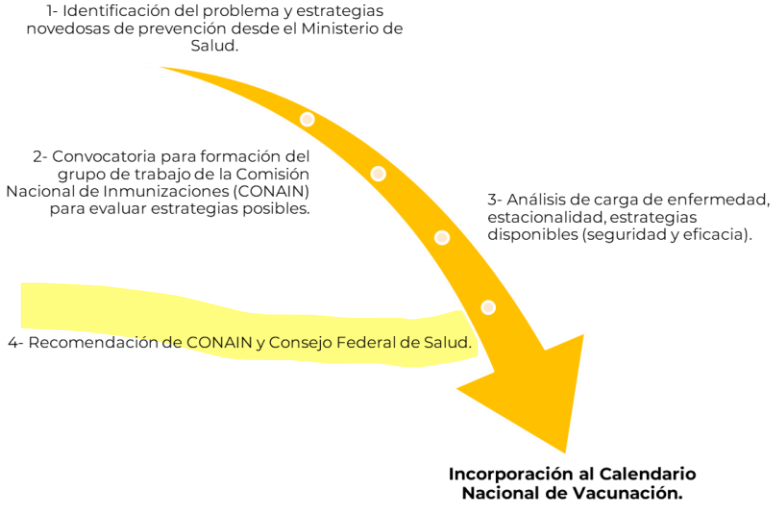
Estacionalidad típica de clima templado

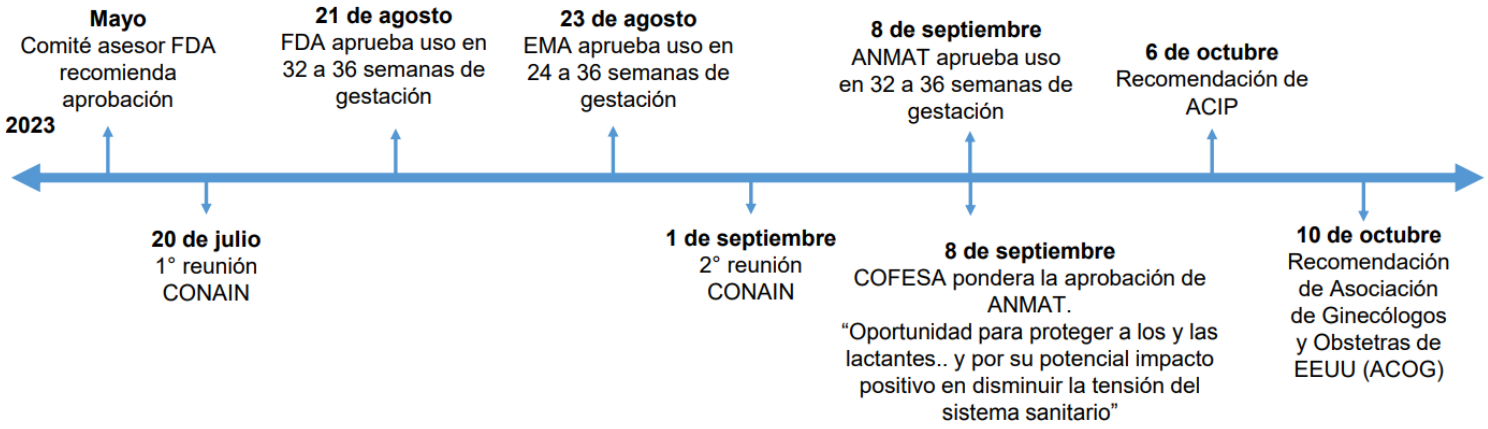
Recupera estacionalidad con circulación adelantada



Fuente: Área de Vigilancia de la Salud de la Dirección de Epidemiología. SNVS 2.0. Ministerio de Salud

Carga de enfermedad por VSR





Eficacia

Time period after birth	Trial dosing interval (24–36 weeks gestation) Vaccine efficacy[1] (99.5% or 97.58% CI)	Approved dosing interval (32–36 weeks gestation) Vaccine efficacy[2] (95% CI)
0–90 days after birth	81.8% (40.6, 96.3)	91.1% (38.8, 99.8)
0–180 days after birth	69.4% (44.3, 84.1)	76.5% (41.3, 92.1)

Seguridad

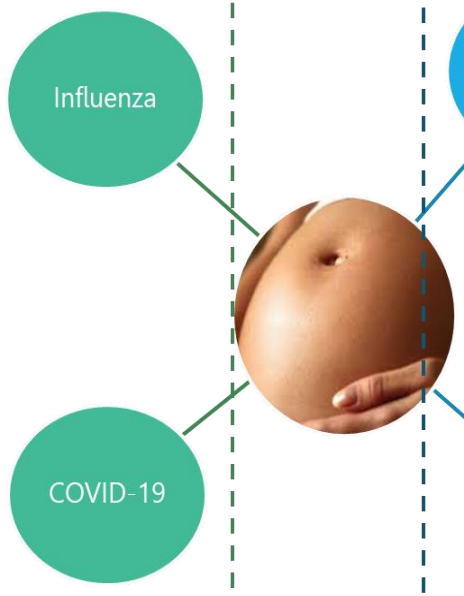
	Trial dosing interval (24–36 weeks gestation)[1]				Approved dosing interval (32–36 weeks gestation)[1,2]			
	RSVpreF vaccine group N=3,568		Placebo group N=3,558		RSVpreF vaccine group N=1,628		Placebo group N=1,604	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Preterm birth (<37 weeks gestation)	202	**5.7%** (4.9%, 6.5%)	169	**4.7%** (4.1%, 5.5%)	68	**4.2%** (3.3%, 5.3%)	59	**3.7%** (2.8%, 4.7%)
Low birth weight (≤2500 g)	181	**5.1%** (4.4%, 5.8%)	155	**4.4%** (3.7%, 5.1%)	67	**4.1%** (3.2%, 5.2%)	54	**3.4%** (2.5%, 4.4%)
Neonatal jaundice	257	**7.2%** (6.4%, 8.1%)	240	**6.7%** (5.9%, 7.6%)	102	**6.3%** (5.1%, 7.6%)	107	**6.7%** (5.5, 8.0%)

https://www.argentina.gob.ar/salud/inmunoprevenibles/conain/actas-informes

Implementación

Integrar la nueva estrategia dentro del componente de vacunación materna

- Se pueden indicar en **cualquier momento de la gestación**.
- Protegen principalmente a la gestante que tiene mayor riesgo de enfermedad grave por estas infecciones.
- Protegen indirectamente al recién nacido en los primeros meses de vida



Triple bacteriana acelular

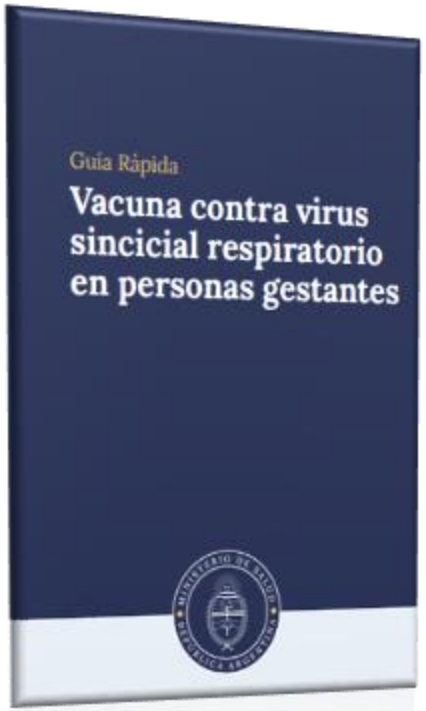
- **Triple bacteriana acelular a partir de las 20 semanas** de gestación.
- Protegen al recién nacido durante los primeros 6 meses de vida de padecer infecciones graves por Bordetella pertussis y tétanos neonatal.

VSR

- **VSR entre las semanas 32 y 36,6 de la gestación.**
- Protegen al recién nacido durante los primeros 6 meses de vida de padecer infecciones respiratorias agudas graves por VSR.

Materiales de capacitación

https://bancos.salud.gob.ar/sites/default/files/2024-02/lineamientos-vsr.pdf

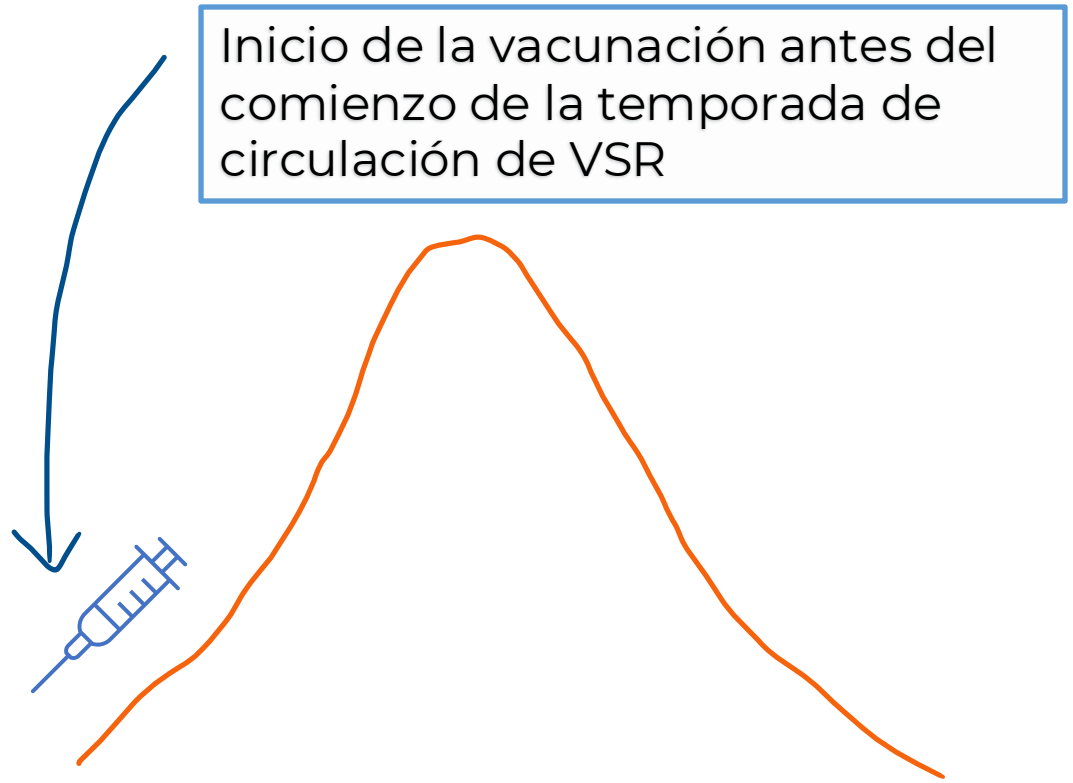


https://bancos.salud.gob.ar/sites/default/files/2024-02/guia-rapida-vsr.pdf

https://youtu.be/JdGdMkmYM3E

Ejecución de la estrategia

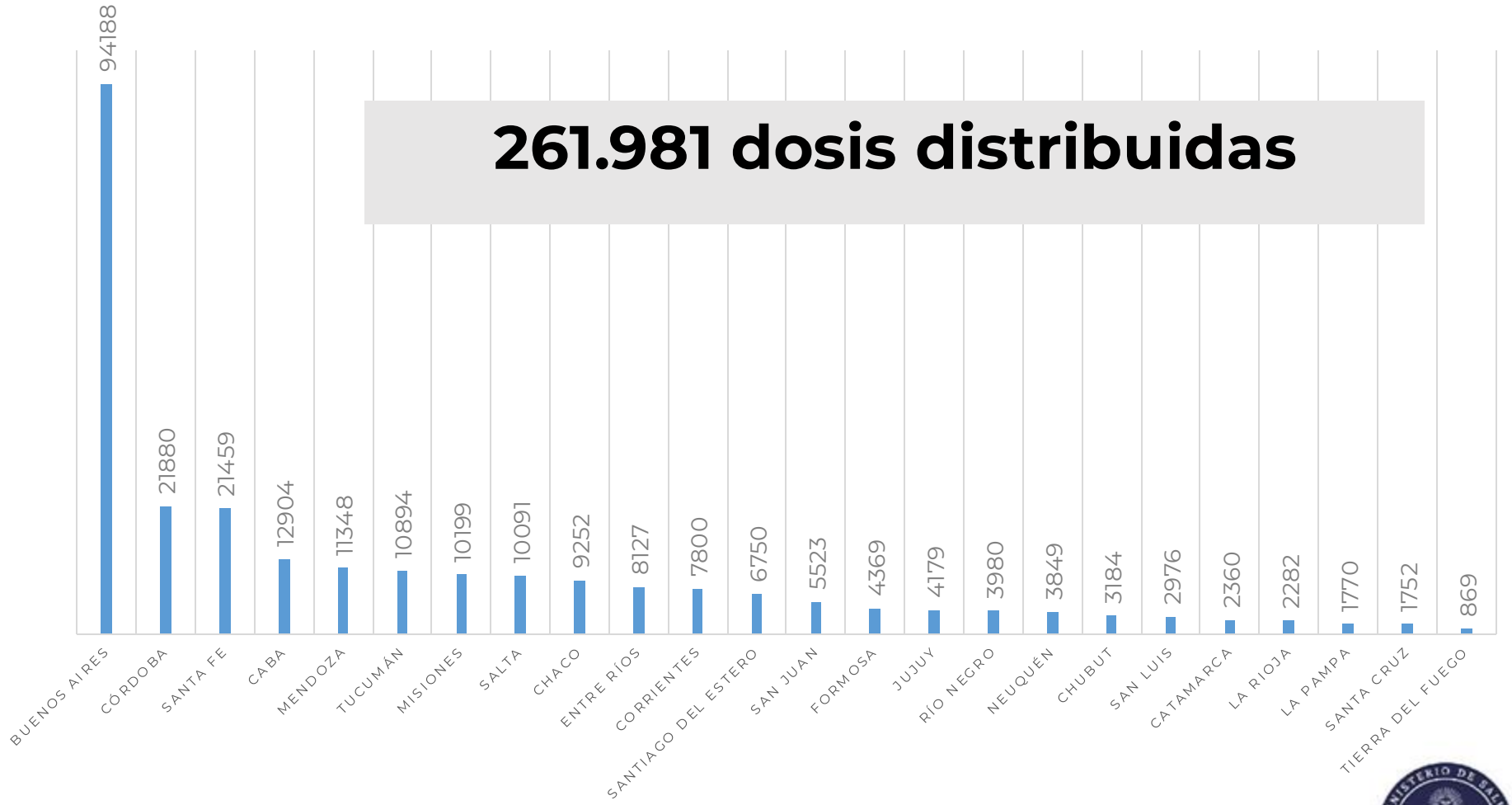
- Administración en forma gratuita en todos los vacunatorios públicos del país.
- Sin requerimiento de orden médica, solo certificando en que semana de gestación se encontraban.
- Coadministración con cualquier vacuna del embarazo.
- Revacunación en cada embarazo.



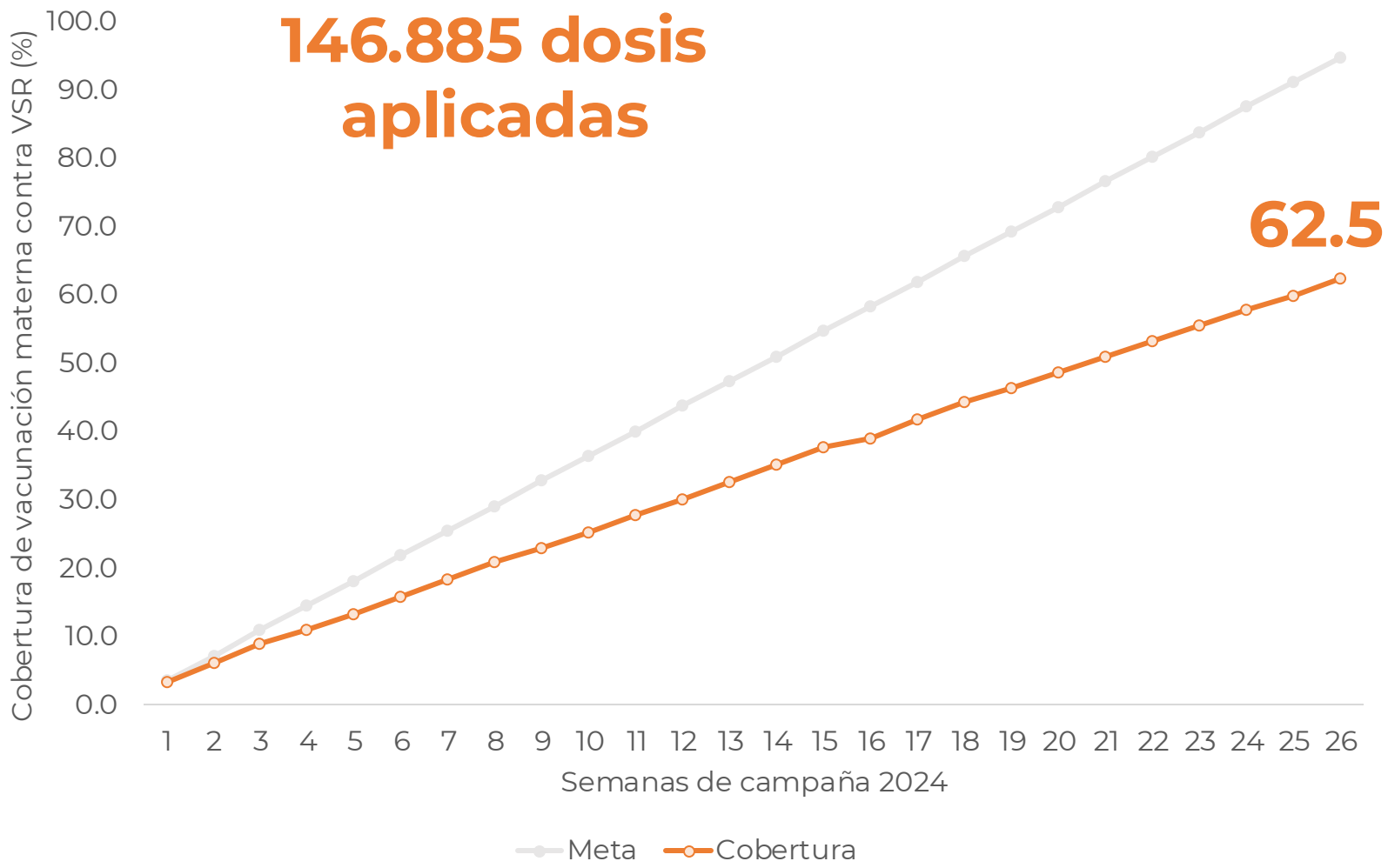
Vacunación entre marzo y agosto (6 meses)

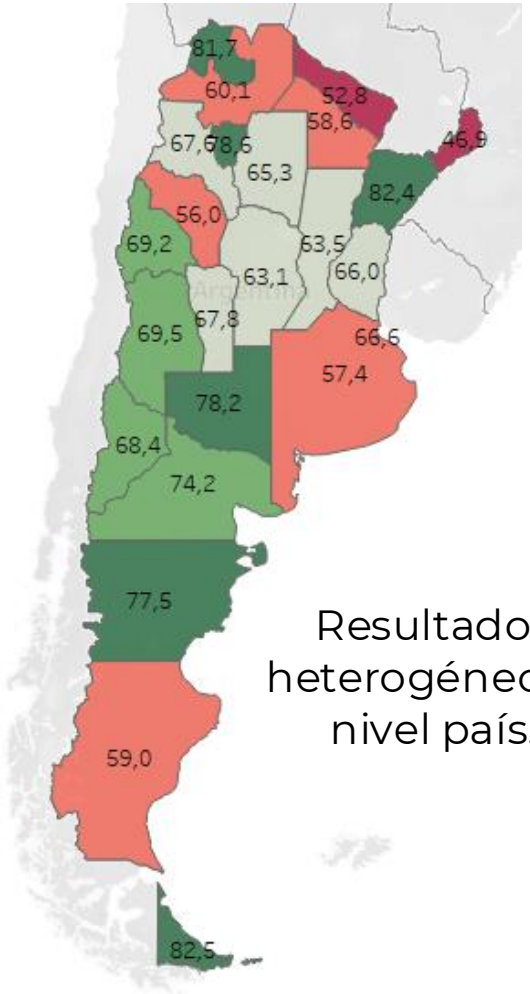
Logística y distribución

- En el primer envío, entre el 16-23 de febrero, se distribuyó el 50% de las dosis.
- El segundo envío se realizó un mes después.



Coberturas de vacunación materna contra VSR





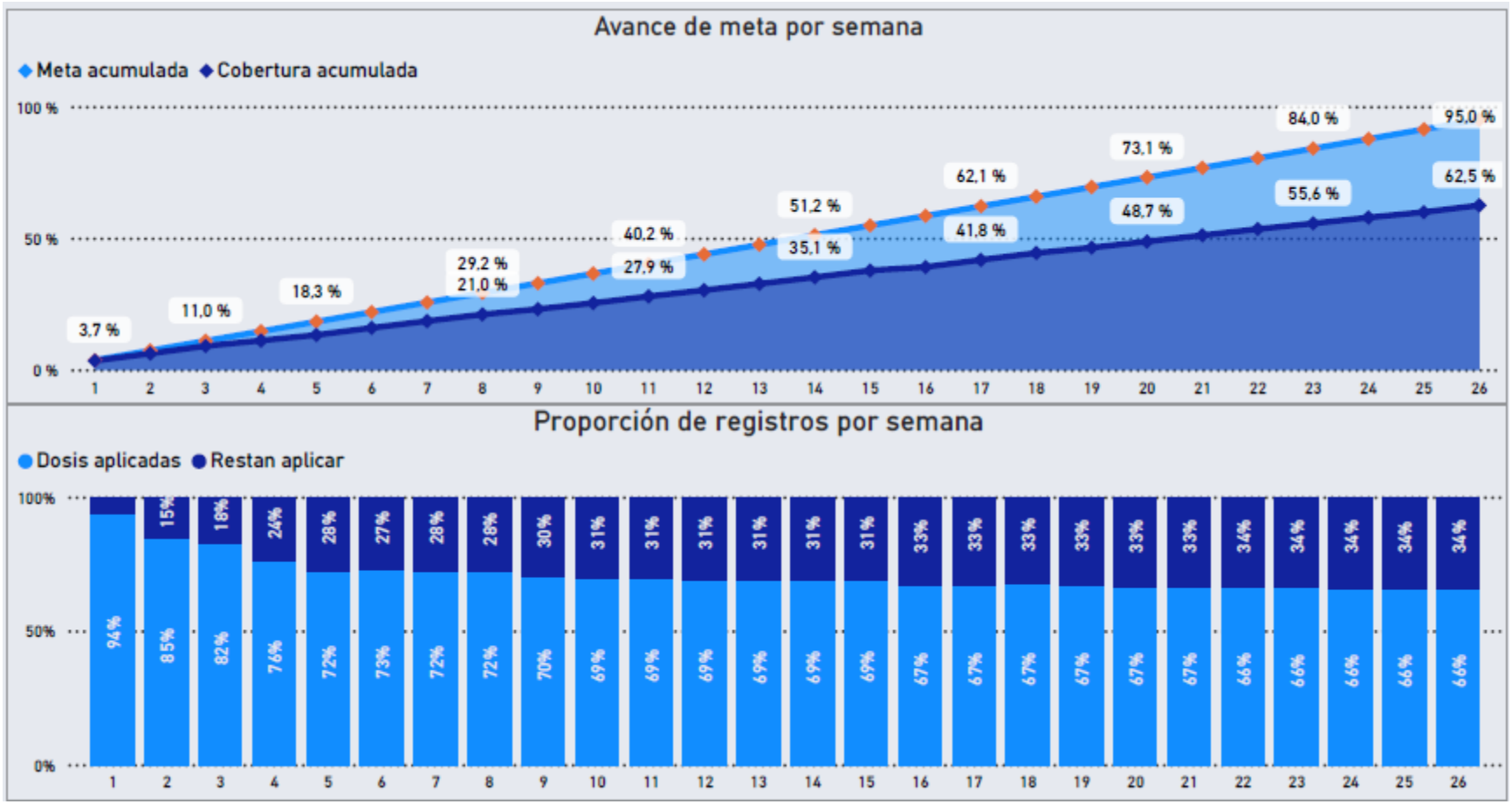
Resultados heterogéneos a nivel país.

Fuente: Área de datos. DiCEI. Ministerio de Salud. Informe 13-11-2024

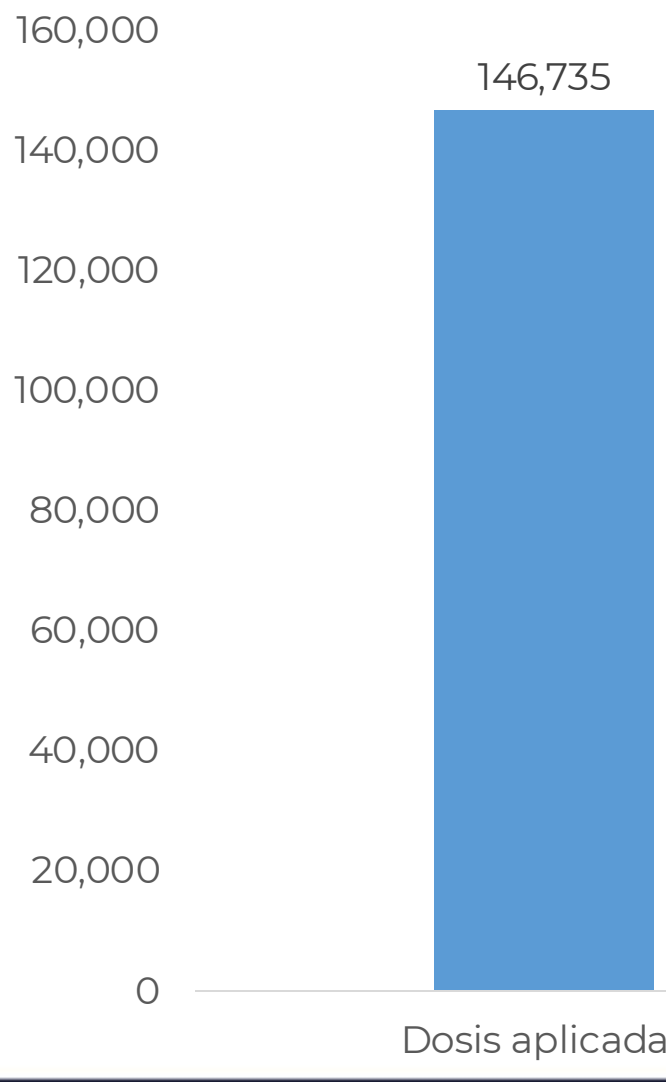
Avances semanales de coberturas de vacunación

62,5%

Los primeros dos meses de campaña las coberturas se mantuvieron por encima del 70%.



Vigilancia de seguridad de la vacunación materna contra VSR



Área de vigilancia de ESAVI. DiCEI. Ministerio de Salud. Octubre 2024.

- ✓ Sistema de vigilancia pasivo.
- ✓ A través de plataforma SISA
- ✓ Cobertura nacional

232
ESAVI

Tasa de ESAVI
158/100.000
dosis aplicadas

154
ESAVI graves

Tasa de ESAVI grave
104/100.000
dosis aplicadas

Vigilancia de seguridad de la vacunación materna contra VSR

TIPO DE ERROR PROGRAMÁTICO*	N	TASA
Fuera del rango de edad gestacional aprobado (<32 o ≥37 semanas)	25	17,0
Revacunación	17	11,6
Persona no gestante	3	2,0
Error en la preparación	1	0,7
Vía de administración equivocada	1	0,7

* En cuatro eventos se desconoce el motivo del error

Tasa de error programático: 34,7 cada 100.000 dosis aplicadas

Errores más frecuentes relacionados con la ventana estrecha de vacunación

Fuente: Área de vigilancia de ESAVI. DiCEI. Ministerio de Salud.

Vigilancia de seguridad de la vacunación materna contra VSR

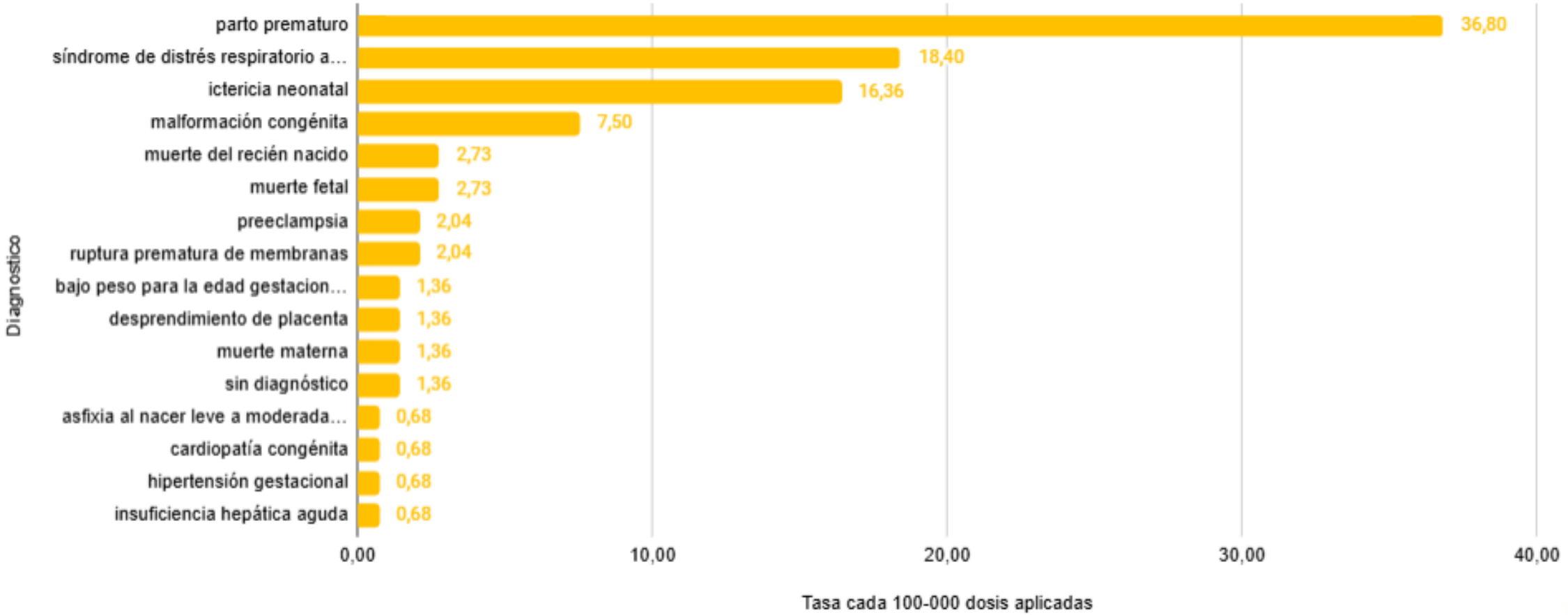
EVENTO	N	TASA
Reacción alérgica	3	2,04
Inflamación localizada aguda	5	3,41
Fiebre	2	1,36
Dolor en el sitio de inyección	1	0,68
Síntomas tipo gripales	1	0,68

Tasa de eventos relacionados al producto:
8,2 cada 100.000 dosis aplicadas

Fuente: Área de vigilancia de ESAVI. DiCEI. Ministerio de Salud.

Vigilancia de seguridad de la vacunación materna contra VSR

ESAVI GRAVES: 154



Fuente: Área de vigilancia de ESAVI. DiCEI. Ministerio de Salud.

Vigilancia de seguridad de la vacunación materna contra VSR

Parto prematuro

Total: 54 eventos / 146.735 d.a.

Tasa: 36,8 / 100.000 d.a. (0,03 %)

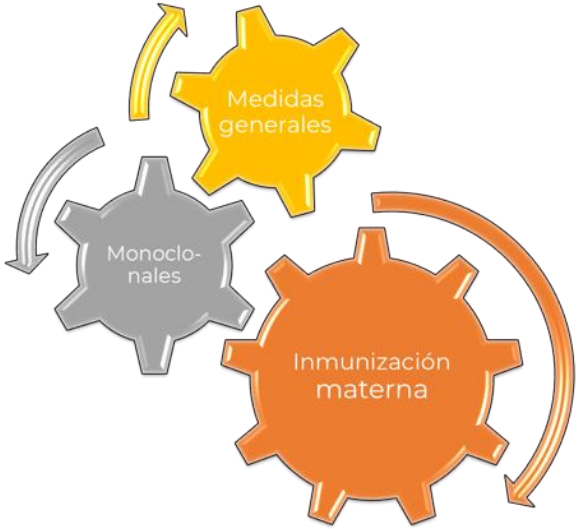
Promedio de días desde la vacunación: 10,9 días

El 85% fueron prematuros tardíos (34-36 semanas)

Todos los prematuros tuvieron evolución favorable

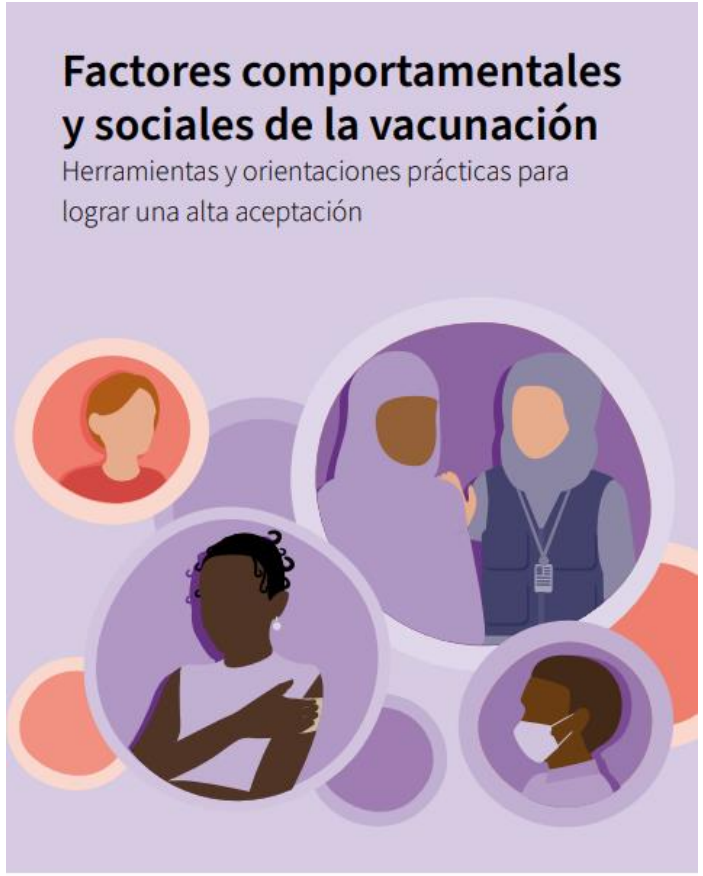
Fuente: Área de vigilancia de ESAVI. DiCEI. Ministerio de Salud.

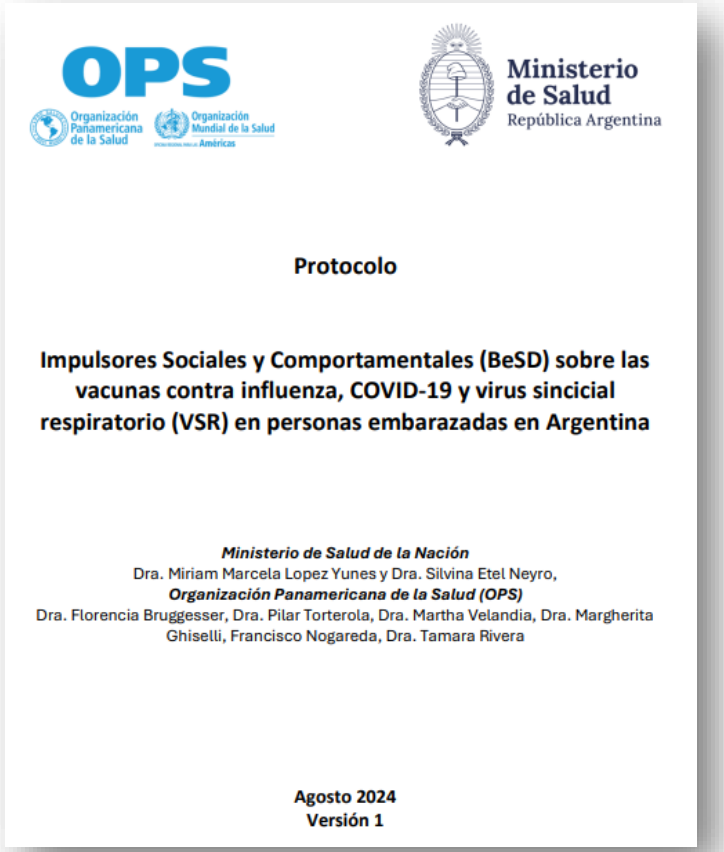
Como seguimos?



- Implementación de unidades centinela de vigilancia de seguridad para complementar la vigilancia pasiva.
- Medición de la efectividad en el primer año de implementación utilizando información producida por las unidades centinela de IRAB.
- Estudio sobre la aceptabilidad
- Definición de momento de inicio de la estrategia estacional en 2025.
- Decisión de revacunación en cada embarazo.
- Consolidar una estrategia integrada de prevención de la enfermedad grave por VSR en menores de 6 meses en Argentina.

Estudio sobre la aceptabilidad





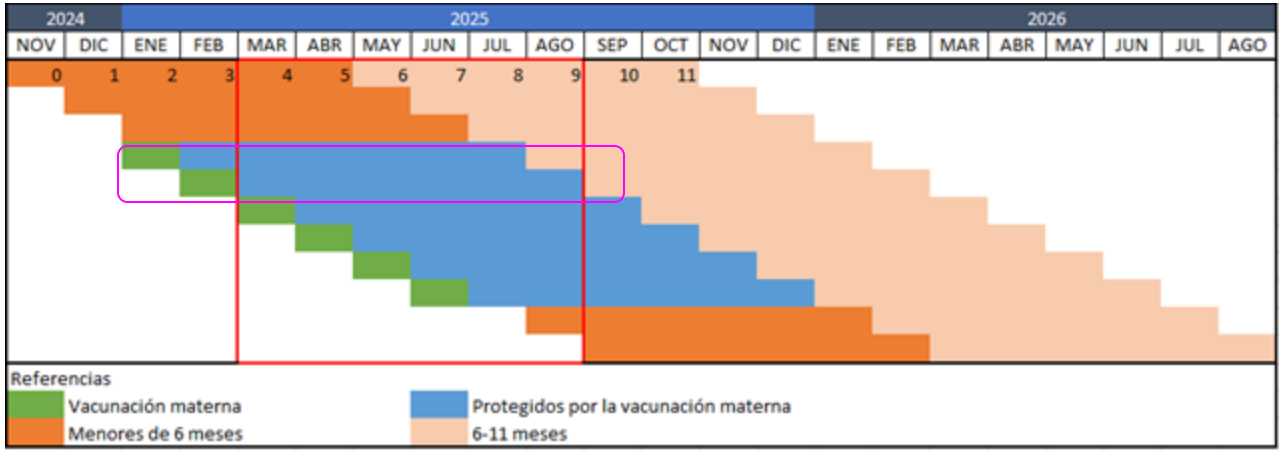
OBJETIVO

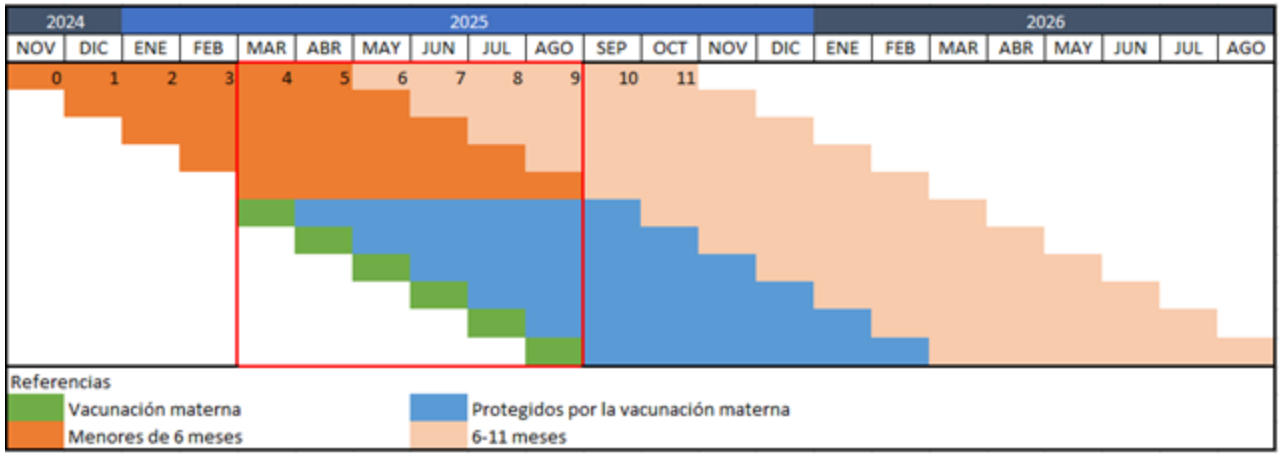
Implementar la herramienta validada para **identificar y analizar las causas de aceptación o de reticencia frente a las vacunas contra influenza, COVID-19 y VSR entre una muestra de personas embarazadas en Argentina**.

Provincias de Buenos Aires(región sexta), San Juan, Santa Fe, Salta, Chaco, Neuquén y en la Ciudad Autónoma de Buenos Aires (CABA)

https://iris.who.int/bitstream/handle/10665/361748/9789240055438-spa.pdf?sequence=1

Programación temporada 2025





Población objetivo a proteger	Meses protegidos durante temporada	
	Inicio Enero 2025	Inicio Marzo 2025
43664	**5**	5
43664	**6**	4
43664	**5**	3
43664	**4**	2
43664	**3**	1
43664	**2**	0

LA ESTRATEGIA INICIARÁ EN ENERO DE 2025

Fuente: Grupo de trabajo de VSR. Comisión Nacional de Inmunizaciones.

Poblaciones no alcanzadas por la estrategia de vacunación materna

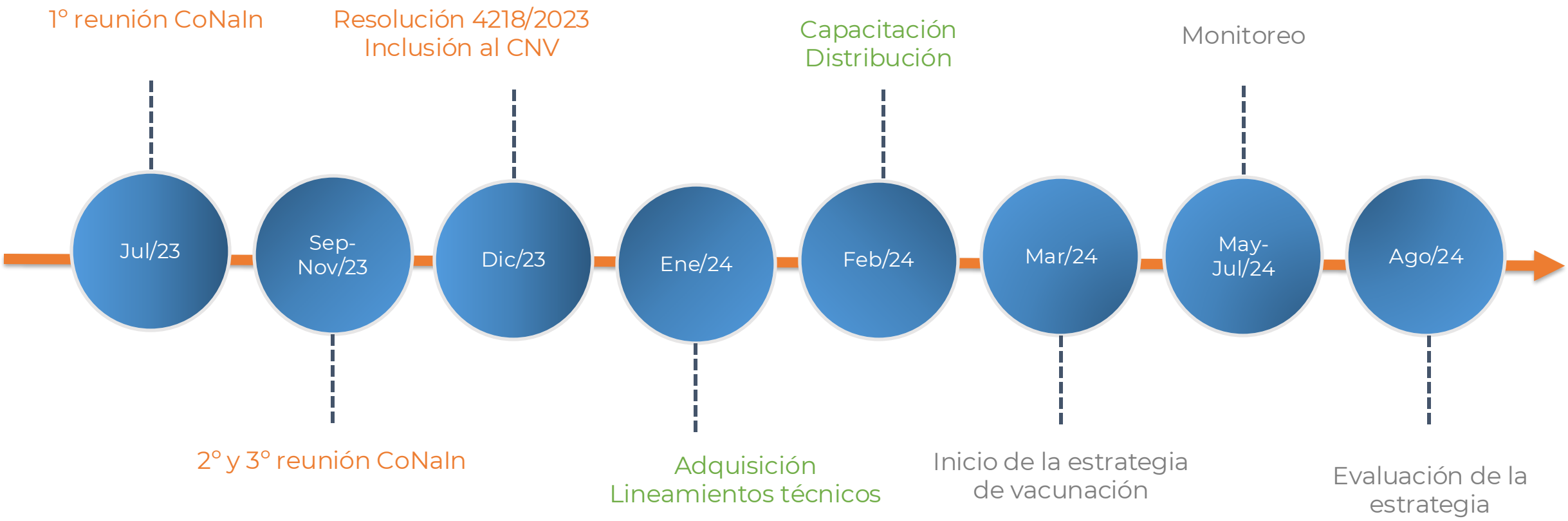
- Nacidos antes de las 32 semanas de vida
- Población de riesgo en su segunda temporada (DBP, cardiópatas, prematuros, etc.)
- Nacidos con menos de 2 semanas de intervalo entre la vacunación y el nacimiento o gestantes no vacunadas
- Nacidos fuera de la temporada de indicación de vacunación

INMUNIZACION MATERNA

ANTICUERPOS MONOCLONALES

Estrategia integrada

Proceso de toma de decisión



Fuente: Dirección de Control de Enfermedades Inmunoprevenibles. Ministerio de Salud

Muchas gracias

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