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SIMRI
società italiana per le malattie respiratorie infantili

XXVIII CONGRESSO NAZIONALE SIMRI

Il respiro: scienza e terapia per la salute del bambino

Torino, 10-12 ottobre 2024

Università degli Studi di Messina
Dipartimento di Patologia umana dell'adulto e dell'età evolutiva Gaetano Barresi
UOC Pediatria
Dir. Prof.ssa M. Wasniewska

La gravidanza: un'opportunità per le vaccinazioni del neonato

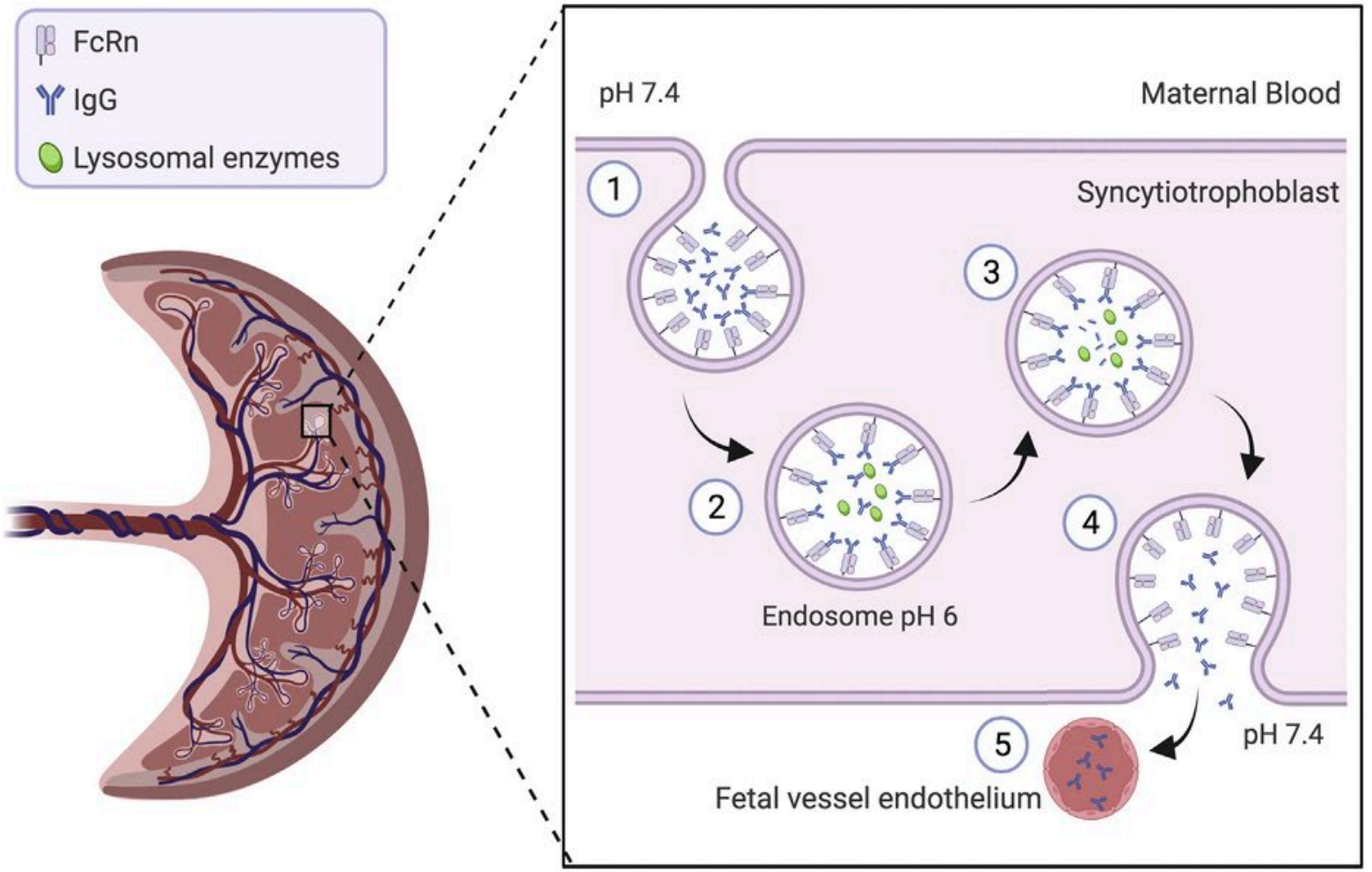
Sara Manti

smanti@unime.it

- La gravidanza: un’opportunità **REALE** per le vaccinazioni del neonato

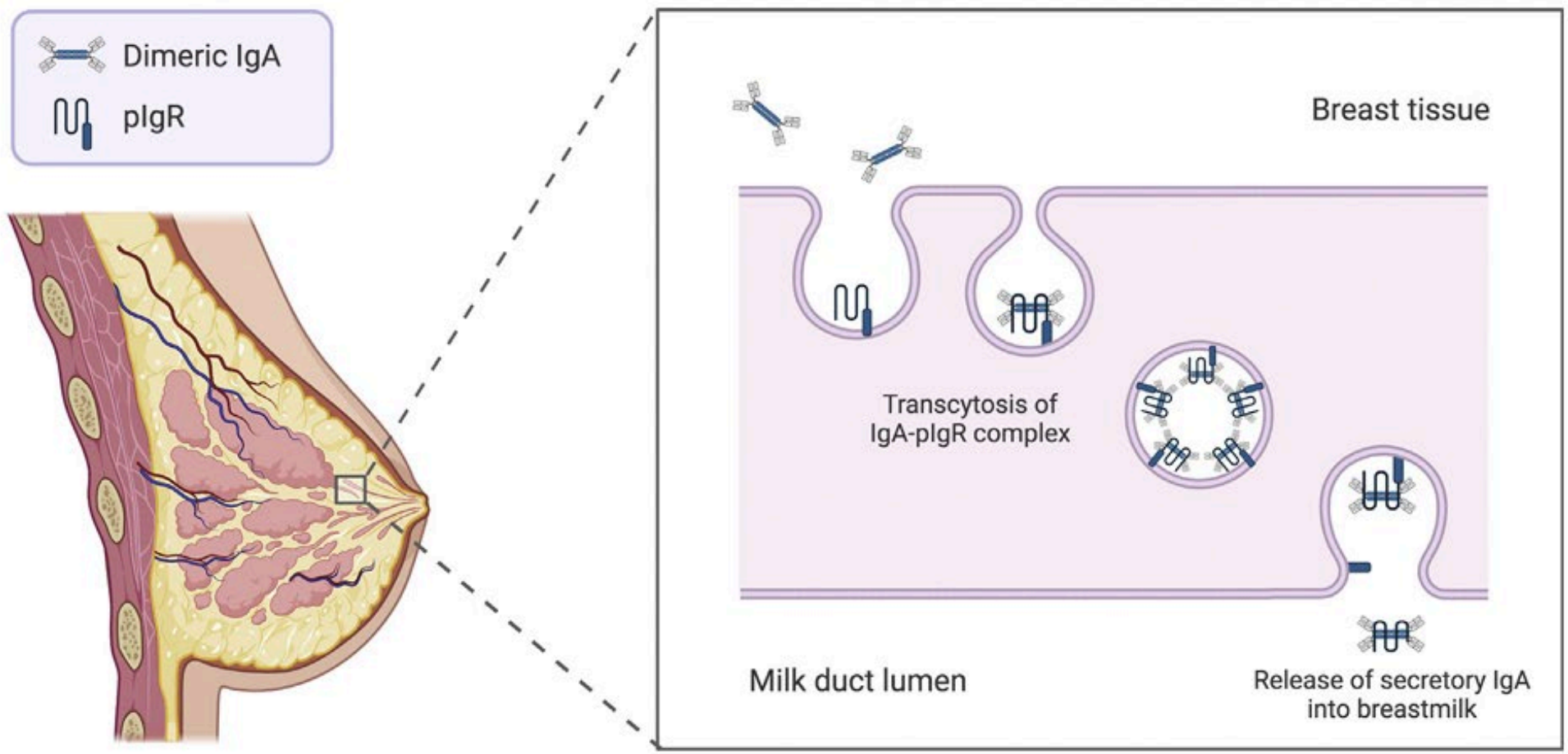
- La gravidanza: un’opportunità **FUTURA** per le vaccinazioni del neonato

Placental transfer of IgG antibodies from maternal to fetal circulation



Etti M et al. Expert Review 2022

Transfer of secretory IgA antibodies from maternal breast tissue to breast milk



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THE LANCET

Macklin R. 2010

The art of medicine

Enrolling pregnant women in biomedical research

Maternal immunization:

US FDA regulatory considerations

1960

1961

NEONATAL TETANUS IN NEW GUINEA

EFFECT OF ACTIVE IMMUNIZATION IN PREGNANCY

BY

F. D. SCHOFIELD, M.D., M.R.C.P., D.T.M.&H.

V. M. TUCKER, S.R.N.

Department of Public Health, Territory of Papua and New Guinea

AND

G. R. WESTBROOK, S.R.N.

A.O.G. Mission, Wingei, Sepik District, New Guinea

1961 **BRITISH MEDICAL JOURNAL**

1993

Research in this population **should be performed only if it is relevant to the particular health needs of a pregnant woman or her foetus**… or if **it is supported by reliable evidence from animal experiments**, particularly as to risks of teratogenicity and mutagenicity

2002

Guidelines on the Exposure to Medicinal Products During Pregnancy (EMA)

2005

Advisory Committee on Immunization Practices (**ACIP**) **established** general **principles on the immunization of pregnant and breastfeeding women** and cited the following rationale for maternal immunizations: (a) to protect the mother, (b) to protect the fetus, (c) to protect the neonate, or (d) to protect the young infant

2008

Guidelines on the Exposure to Medicinal Products During Pregnancy (EMA/FDA)

2009

Maternal vaccination: a review of current evidence and recommendations

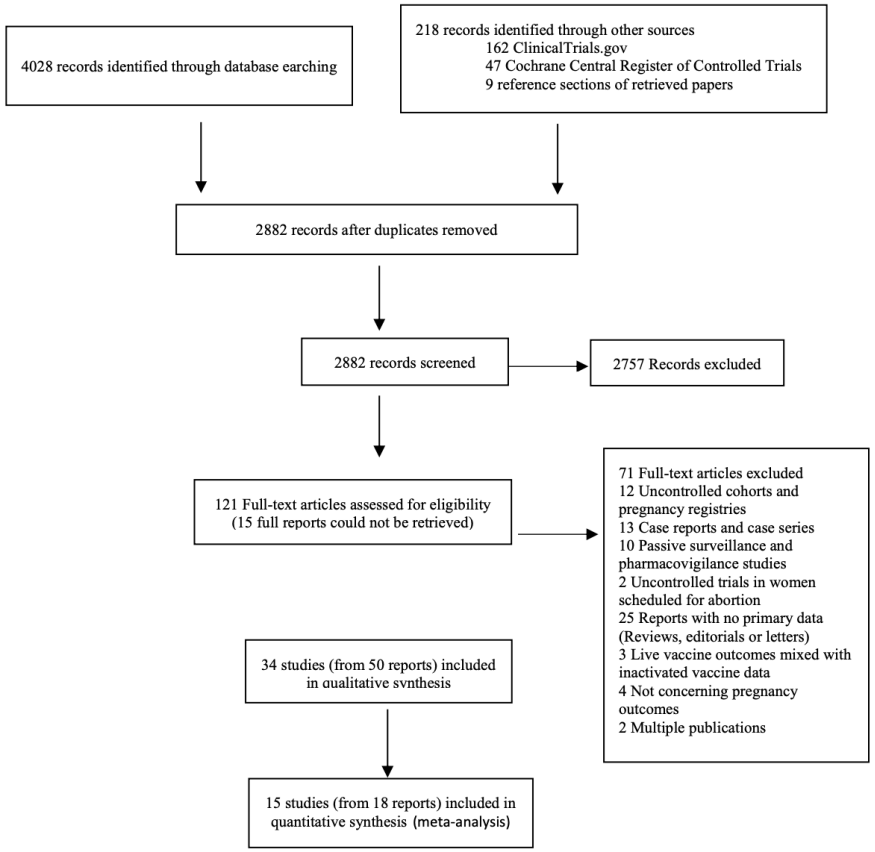
Worldwide: coverage rates vary from 1.7%-95%
In Europe: 10%
UK and Galles: 50%

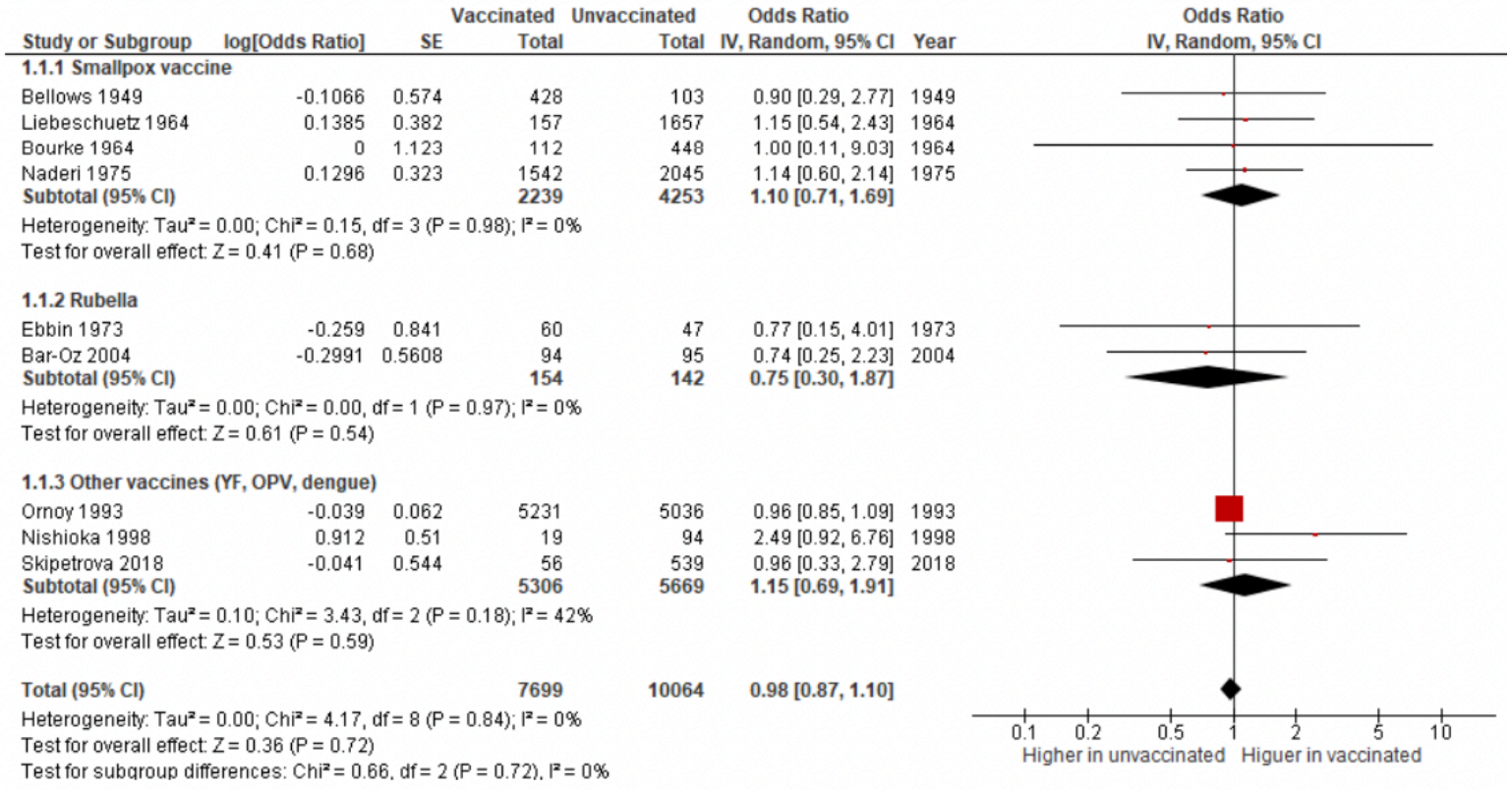
Vaccine Brand name (manufacturer)	Number of doses recommended	Recommended dosing schedule (gestation)	Contraindications
Influenza AFLURIA (Seqirus Pty. Ltd), Agriflu (Seqirus Inc), FLUAD (Seqirus Inc), Fluarix (GSK), Flublok (Protein Sciences Corporation), Flucelvax (Seqirus Inc), FluLaval (ID Biomedical Corporation of Quebec), FluMist, Fluvirin (Sequris Vaccines Ltd), Fluzone (Sanofi Pasteur)	One dose	Vaccine can be administered during any trimester. Administration before the start of flu season is recommended **Administration during the 1st trimester is suggested. Since the risk of fetal death and adverse birth outcomes is greatest for women who are infected during their first trimester of pregnancy** **Trivalent influenza vaccine or quadrivalent influenza vaccine strains**	Contraindicated in individuals with a history of severe allergic reaction (eg, anaphylaxis) or life-threatening reaction to a previous dose of an influenza vaccine **The live attenuated influenza vaccine, which is administered intranasally, is contraindicated during pregnancy because of the theoretical risk of placental transmission of the virus to the fetus.**

Etti M et al. Expert Review 2022

Safety of Administering Live Vaccines during Pregnancy: A Systematic Review and Meta-Analysis of Pregnancy Outcomes

vaccines





No association was found between vaccination and **miscarriage** (OR 0.98, 95% CI 0.87–1.10), **stillbirth** (OR 1.04, 95% CI 0.74–1.48), **malformations** (OR 1.09, 95% CI 0.98–1.21), **prematurity** (OR 0.99, 95% CI 0.90–1.08) or **neonatal death** (OR 1.06, 95% CI 0.68–1.65) overall. However, increased odds of malformations (OR 1.24; 95% CI 1.03–1.49) and miscarriage after first trimester immunization (OR 4.82; 95% CI 2.38–9.77) was found for *smallpox vaccine*.

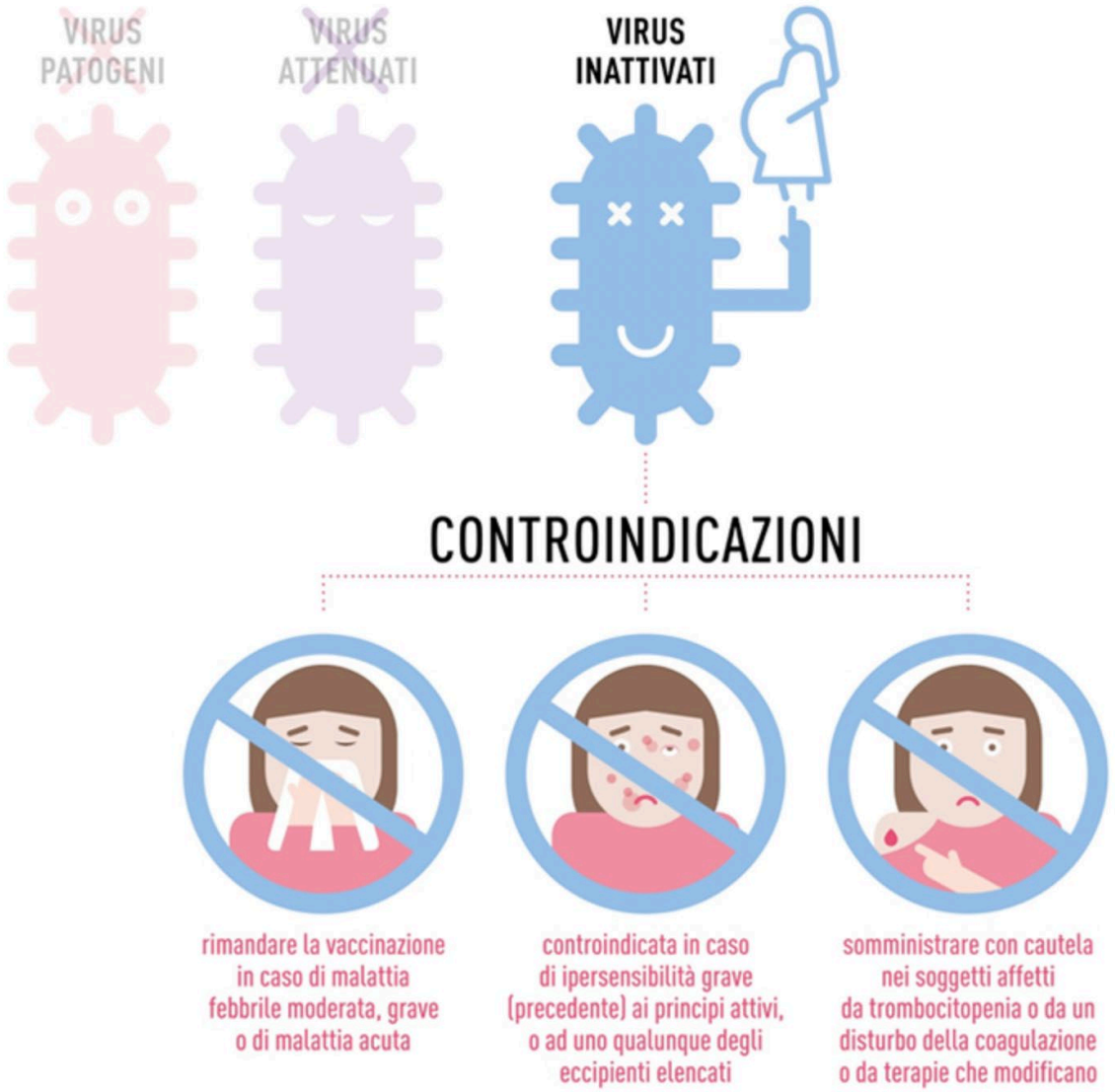
Laris-González A et al. Vaccine 2020

Il Vaccino Antinfluenzale In Gravidanza

Quando offrire il vaccino antinfluenzale in gravidanza

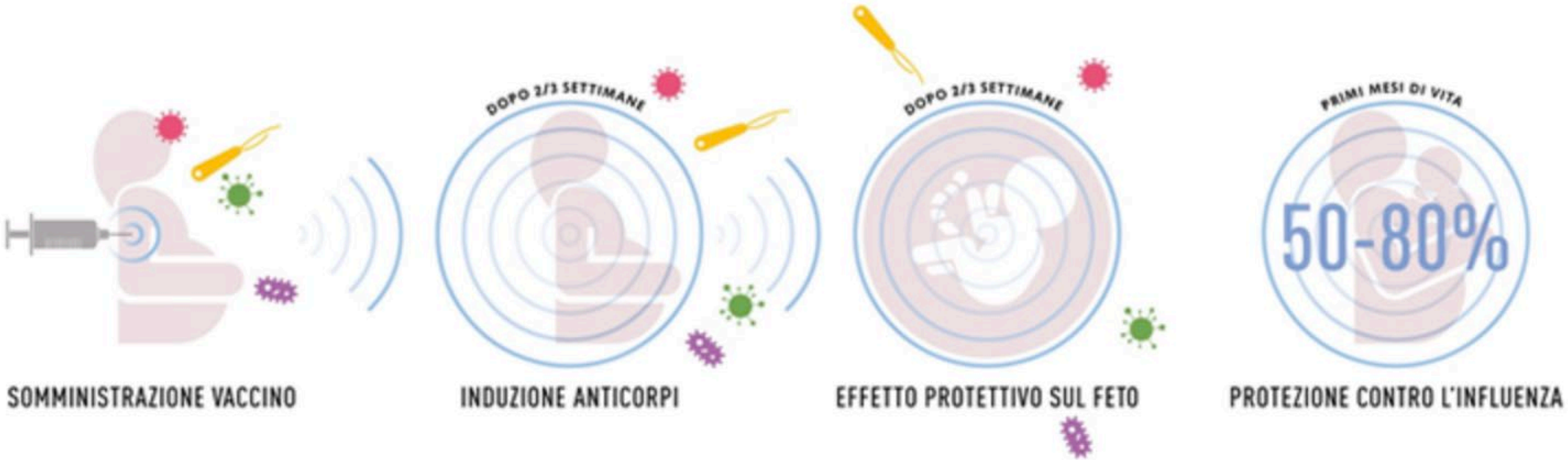
La gravidanza **NON** rappresenta una controindicazione alla vaccinazione con virus inattivati, come quella antinfluenzale. Per le donne sono valide le stesse raccomandazioni osservate per la popolazione generale[5]:

- La vaccinazione **DEVE** essere rimandata in caso di malattia febbrile moderata, grave o di malattia acuta;
- Rappresentano controindicazioni alla vaccinazione solo l'**ipersensibilità grave** (precedente reazione anafilattica) ai principi attivi, o ad uno qualunque degli eccipienti elencati o a qualunque componente che può essere presente in tracce come uova (ovalbumina, proteine del pollo)
- Cautela nei soggetti affetti da **trombocitopenia o da un disturbo della coagulazione o da terapie che modificano significativamente la coagulazione**, poiché in questi soggetti può manifestarsi sanguinamento a seguito della somministrazione intramuscolare.

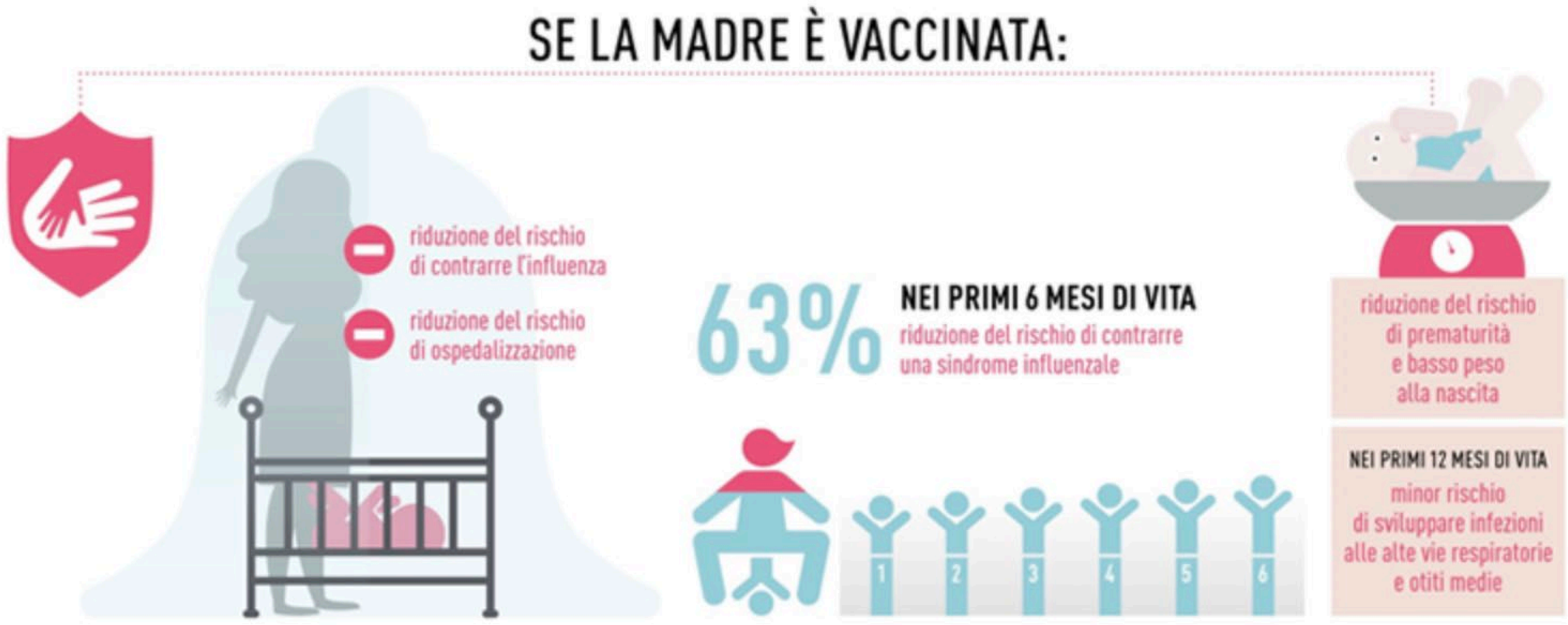


Il Vaccino Antinfluenzale In Gravidanza

Meccanismo d'azione del vaccino antinfluenzale



Meccanismo d'azione del vaccino antinfluenzale



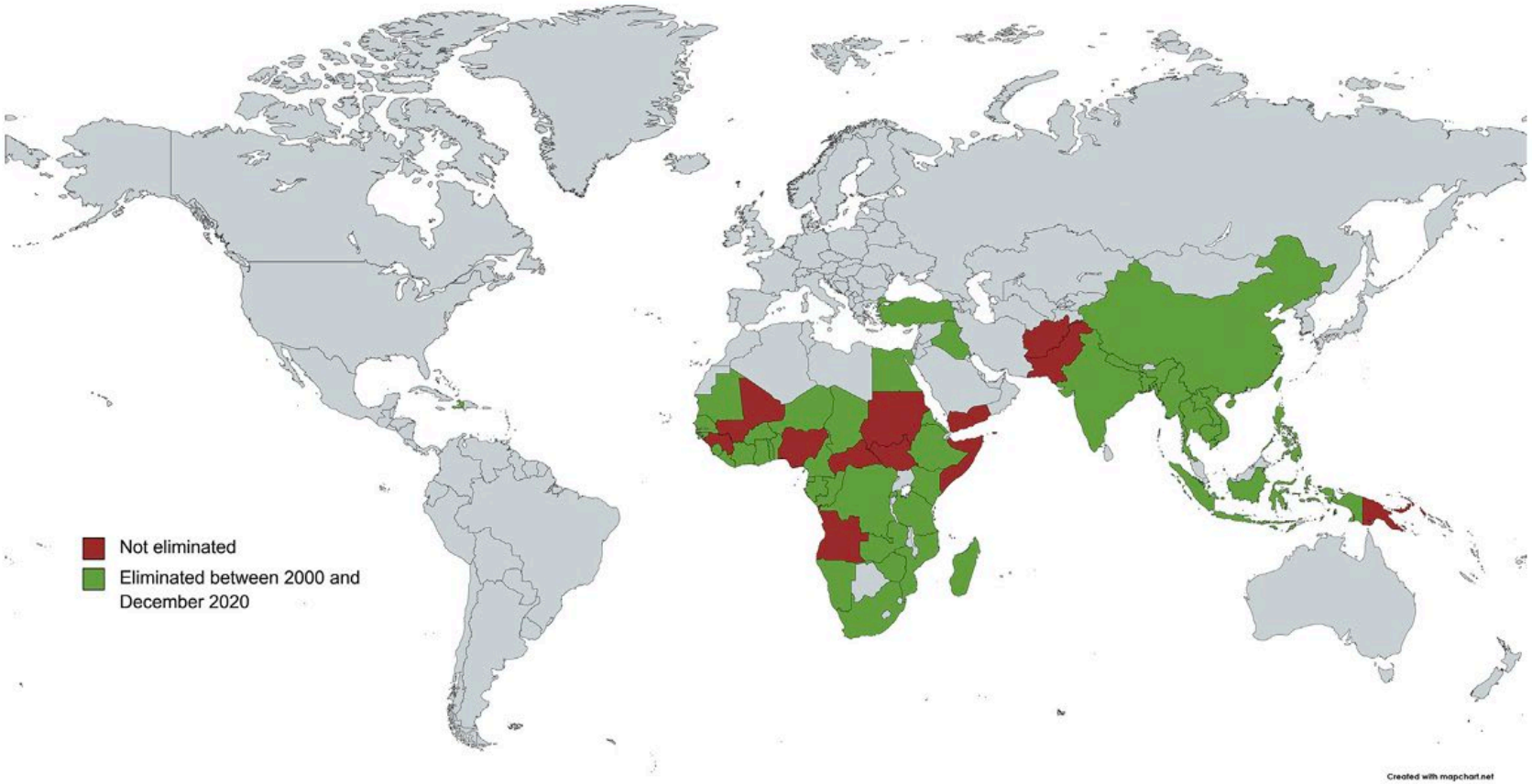
Maternal vaccination: a review of current evidence and recommendations

Vaccine Brand name (manufacturer)	Number of doses recommended	Recommended dosing schedule (gestation)	Contraindications
Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis (Tdap) Adcel (Sanofi Pasteur), Boostrix (GSK)	One dose	Between 27 and 36 weeks' gestation (can be given earlier if indicated, eg, for wound management or pertussis outbreak) If no history of previous vaccination and dose not administered during pregnancy, give dose immediately postpartum	Contraindicated in individuals who have had a severe allergic reaction (eg, anaphylaxis) after a previous dose of a Tdap vaccine or who have a severe allergy to any vaccine component

Etti M et al. Expert Review 2022

Maternal vaccination: a review of current evidence and recommendations

FIGURE 3
Global elimination status of maternal and neonatal tetanus



As of December 2020, 12 out of 59 "at-risk" countries identified by the WHO in 2000 had not yet eliminated the disease.[40] Figure reproduced with permission from the World Health Organization.
Countries shaded in green represents maternal and neonatal tetanus eliminated between 2000 and December 2020

Countries shaded in red represents maternal and neonatal tetanus not eliminated.

WHO, World Health Organization.

Etti M et al. Expert Review 2022

Vaccination in Pregnancy against Pertussis: A Consensus Statement on Behalf of the Global Pertussis Initiative

Safety and Vaccine Effectiveness
Vaccination against pertussis in pregnancy is safe for pregnant women and newborns and highly effective in preventing pertussis in young term and preterm infants.
Timing of vaccination
Vaccination against pertussis in the third trimester of pregnancy is highly effective in the prevention of pertussis in both term and preterm infants.
A growing body of evidence supports that vaccination early in the third trimester is associated with higher newborn anti-*B. pertussis* antibody concentrations compared with vaccination in the late third trimester. More data are required to confirm this observation and whether vaccination early in the third trimester is associated with higher vaccine effectiveness compared to later in the third trimester.
More studies are needed to determine whether vaccination in the second trimester is associated with higher newborn anti-*B. pertussis* antibody concentrations and vaccine effectiveness compared with vaccination in third trimester of pregnancy.
There is currently no evidence to suggest that timing of vaccination in pregnancy affects post-primary and post-booster vaccination antibody concentrations in infants, although more formal studies designed to answer this question are needed.
Anti-*B. pertussis* antibodies in breast milk
Vaccination in pregnancy induces anti-*B. pertussis* antibodies in breast milk until 12 weeks post-partum. The added benefit of breastfeeding in infants of vaccinated women to clinical protection is unclear.

Abu-Raya B, et al. Vaccine 2022

Comunicato stampa

La pertosse è una minaccia seria, allarme della Società Italiana di Pediatria

"Abbiamo assistito a un aumento dei ricoveri per pertosse dell'800% rispetto al 2022 e al 2023, che hanno riguardato nella maggior parte dei casi neonati e lattanti non vaccinati sotto i 4 mesi di età. Il 95% delle madri di questi bambini non era vaccinata e l'80% non aveva ricevuto alcuna informazione sulla disponibilità di una vaccinazione prenatale'

In Italia da gennaio a maggio 2024 sono stati registrati 110 casi di pertosse, con oltre 15 ricoveri in terapia intensiva di piccoli lattanti e tre neonati deceduti.

Maternal vaccination: a review of current evidence and recommendations

Summary of COVID-19 vaccines and evidence of safety and recommendations for use in pregnancy

Vaccine platform	Commercial developer (candidate name)	Mechanism of action	Assessment of safety in pregnancy	Recommendations for use during pregnancy
mRNA	Pfizer/BioNTech (BNT162b2)	Nucleoside-modified mRNA expressed in lipid nanoparticles that encodes the spike protein for the SARS-COV-2 virus	Pfizer/BioNTech commenced a global Phase 3 study recruiting pregnant women in early 2021	Initial safety data supports the safe use of mRNA vaccines in pregnant women
	Moderna (mRNA-1237)	Nucleoside-modified mRNA encoding the pre-fusion stabilized spike (S) protein and the S1—S2 cleavage site encapsulated within a lipid nanoparticle	Real-world data from >90,000 women have not identified any safety signals[22]	
Nonreplicating viral vector	Oxford-AstraZeneca (AZD1222)	Modified chimpanzee adenovirus (replication deficient) containing the gene encoding the spike (S) protein	Pregnancies that occurred in clinical trials were recorded and followed up until 3 months after birth. Compared with women who received the control vaccine, there was no increased risk of miscarriage and no instances of stillbirth.[23]	No previous studies among pregnant women. However, adenovirus-vectored Zika vaccine studies in pregnant mice did not identify any safety signals
	Janssen (Ad26.COV2.S)	Recombinant, replication-incompetent human adenovirus type 26 that encodes the full length of the stabilized conformation of the spike (S) protein		
	Sputnik V (Gam-COVID-Vac)	Combined recombinant adenovirus-based vaccine (rAd5 and rAd26), both containing the gene encoding the full-length spike (S) protein		

Etti M et al. Expert Review 2022

Maternal vaccination: a review of current evidence and recommendations

Summary of COVID-19 vaccines and evidence of safety and recommendations for use in pregnancy

Vaccine platform	Commercial developer (candidate name)	Mechanism of action	Assessment of safety in pregnancy	Recommendations for use during pregnancy
Protein subunit	Novavax (NVX-Cov2373)	Full length recombinant spike (S) protein nanoparticle administered with a saponin-based adjuvant (Matrix-M)	No direct safety data available	Recombinant vaccines are generally considered safe for use during pregnancy Safety of saponin-based adjuvant in pregnancy unknown
Inactivated whole virus	Sinovac (CoronaVac)	Inactivated whole virus particle containing aluminum hydroxide adjuvant	No direct safety data available	Inactivated vaccines generally considered safe for use during pregnancy.
	Sinopharm (BBIBP-CorV)	Inactivated whole virus particle containing aluminum hydroxide adjuvant		Aluminum hydroxide (used in human papillomavirus vaccine) and CpG 1018 (used in hepatitis B virus vaccine adjuvants) both considered safe for use during pregnancy
	Valneva (VLA2001)	Inactivated whole virus particle containing aluminum hydroxide and CpG 1018 adjuvants		Safety of the Alhydroxiquim-II adjuvant unknown in pregnancy
	Bharat Biotech (BBV152)	Inactivated whole virus particle containing Alhydroxyquim-II adjuvant		

Etti M et al. Expert Review 2022

0037743-04/12/2023-DGPRE-DGPRE-P

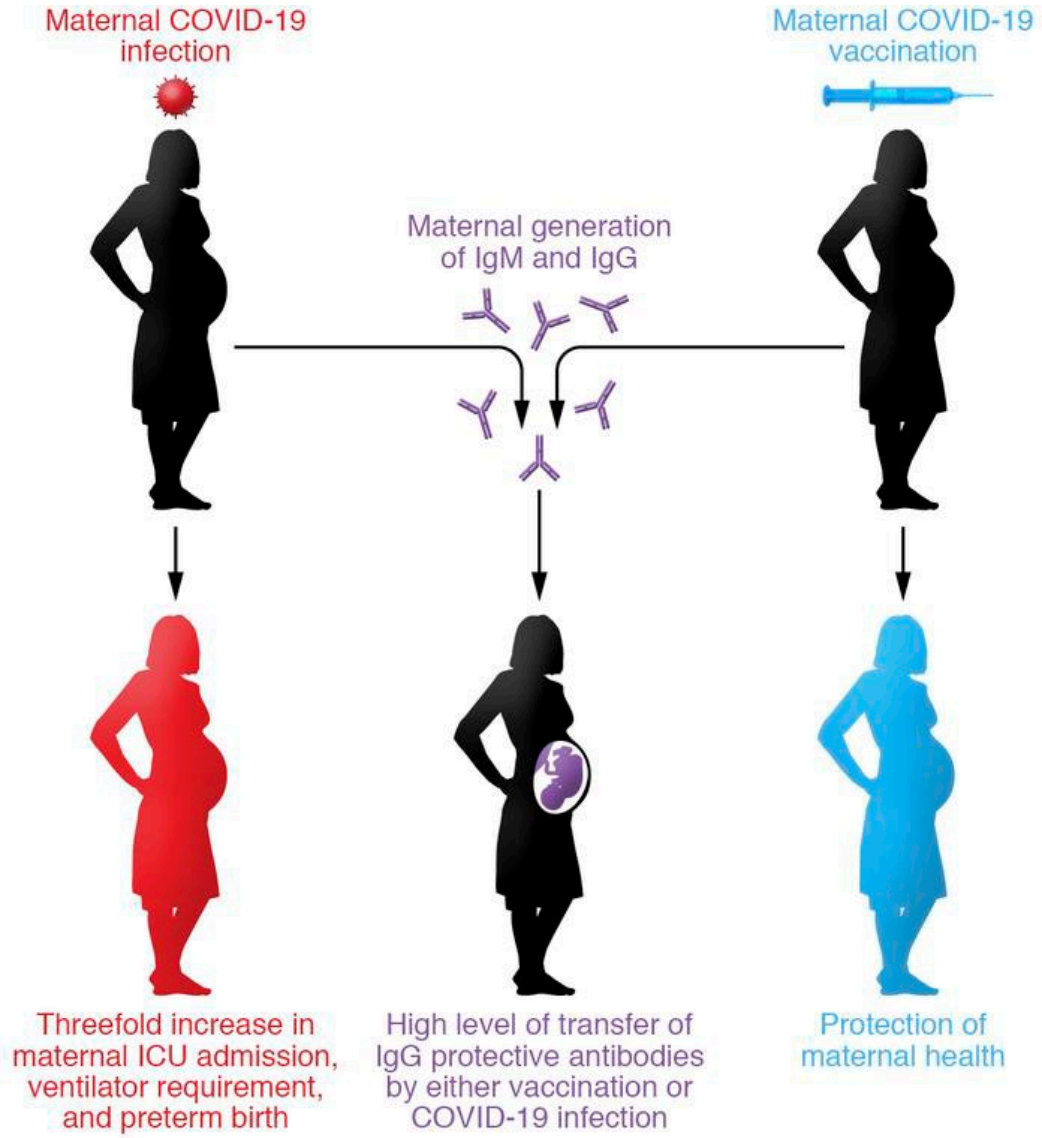
Ministero della Salute

DIREZIONE GENERALE DELLA PREVENZIONE SANITARIA
Ufficio 5 - Prevenzione malattie trasmissibili e profilassi internazionale
Ufficio 11- Gestione Sanitaria delle emergenze

OGGETTO: integrazione delle indicazioni e raccomandazioni per la campagna di vaccinazione autunnale/invernale 2023/2024 anti COVID-19.

Comirnaty Omicorn XBB 1.5 --- Nuvaxovid XBB 1.5.

- La vaccinazione primaria anti COVID-19 e le dosi di richiamo (terza e quarta dose) con vaccini a mRNA sono raccomandate a tutte le donne in gravidanza in qualsiasi momento della gestazione, specialmente in caso di maggior rischio di sviluppare una malattia grave da COVID-19 (donne con fattori di rischio come età ≥30 anni, BMI >30 kg/m2, comorbidità, cittadinanza di Paesi ad alta pressione migratoria).
- La dose di richiamo con formulazione bivalente dei vaccini a mRNA Comirnaty Original/Omicron e Spikevax Original/Omicron (quarta dose) è raccomandata in gravidanza nei dosaggi autorizzati allo scopo.
- Tra la somministrazione della dose di richiamo e l'ultima dose precedente di un vaccino anti-COVID-19 o la precedente infezione da SARS-CoV-2 deve trascorrere un intervallo di almeno 120 giorni.
- La vaccinazione primaria e le dosi di richiamo (terza e quarta dose) possono essere somministrate contestualmente alle vaccinazioni raccomandate in gravidanza contro l'influenza e la pertosse.



Burd I et al. J Clin Invest. 2021

Il 42% delle donne intervistate ha dichiarato di aver aderito alla vaccinazione per tetano, difterite, pertosse.

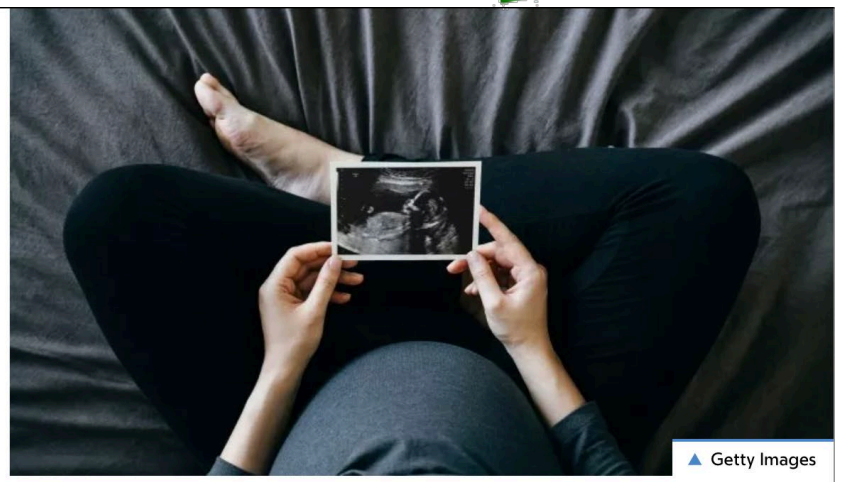
Il 33% a quella per l'influenza

Il 22% a quella per il **COVID-19**

la Repubblica

Solo due italiane su 10 si vaccinano contro Covid durante la gravidanza

di Simone Valesini



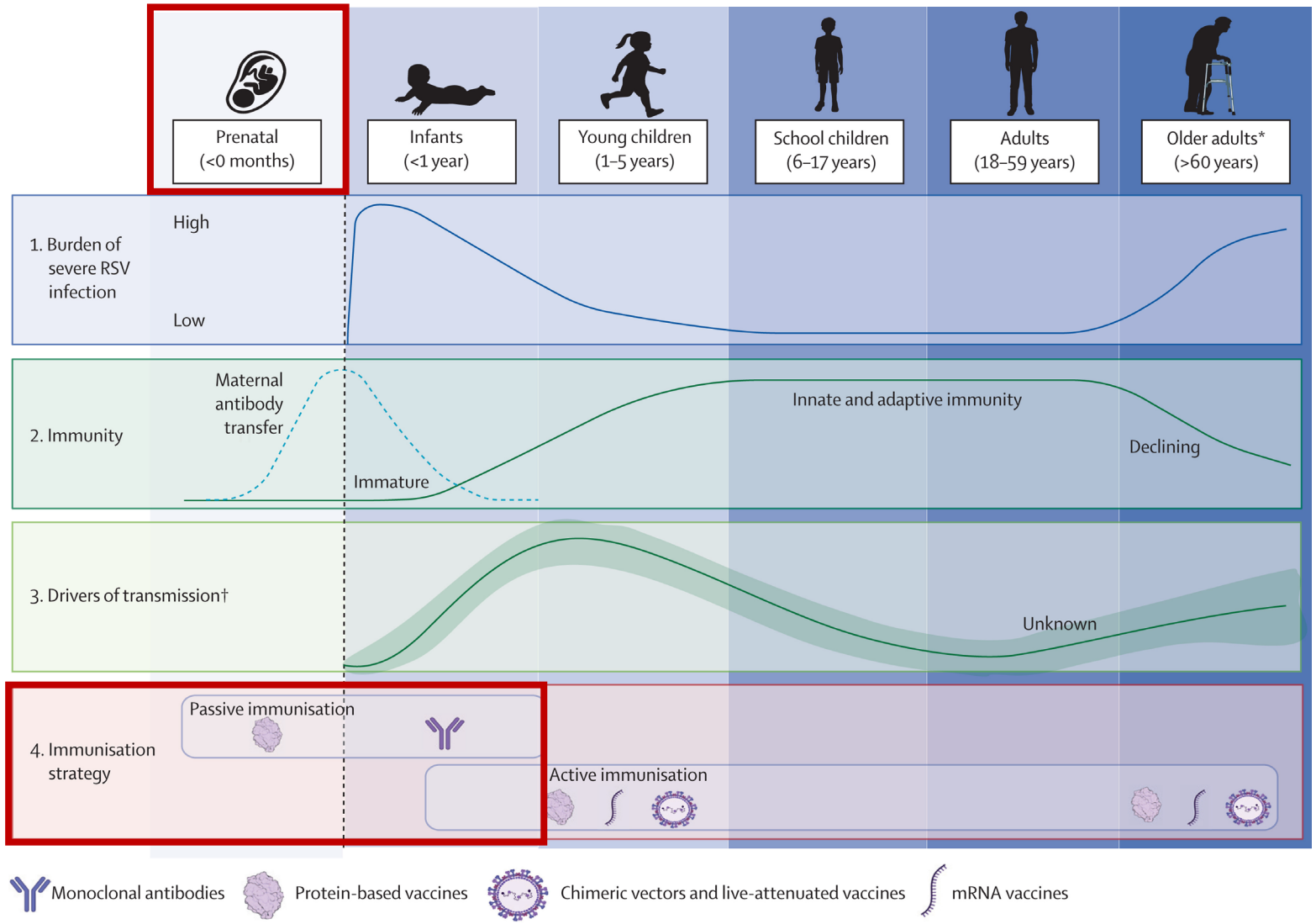
Un convegno al senato ha affrontato il tema della prevenzione primaria nelle donne incinte, con un focus sulle vaccinazioni. Un campo in cui, stando ai dati presentati, c'è ancora molto lavoro da fare

11 APRILE 2024 ALLE 12:49

3 MINUTI DI LETTURA

THE LANCET

The respiratory syncytial virus vaccine and monoclonal antibody landscape: the road to global access



Terstappen J et al. The Lancet. 2024

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

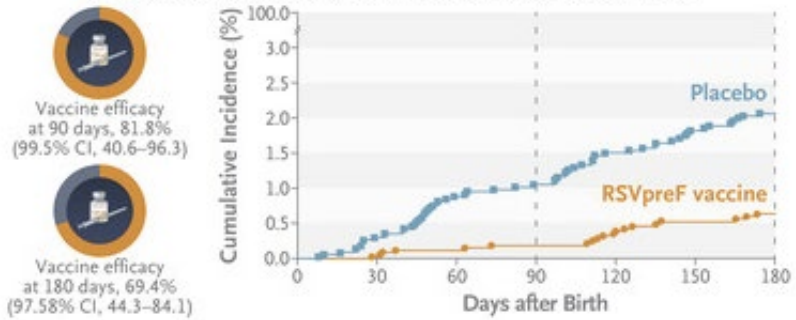
B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, 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*

RESEARCH SUMMARY

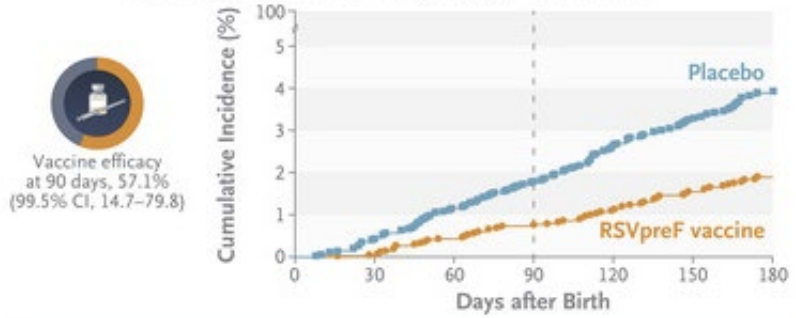
Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

Kampmann B et al. DOI: 10.1056/NEJMoa2216480

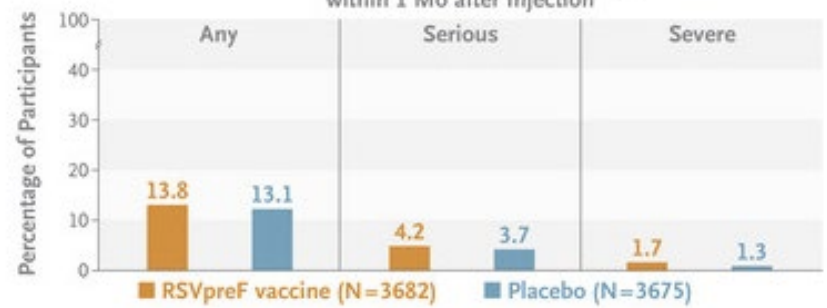
Severe RSV-Associated Lower Respiratory Tract Illness



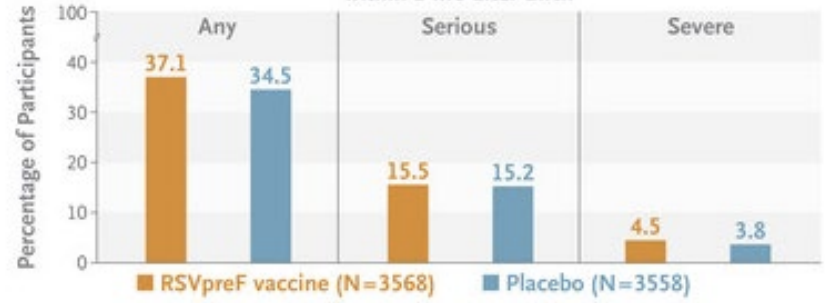
RSV-Associated Lower Respiratory Tract Illness



≥1 Adverse Event in Maternal Participants
within 1 Mo after Injection



≥1 Adverse Event in Infant Participants
within 1 Mo after Birth



CLINICAL TRIAL

Design: An international, phase 3, randomized, placebo-controlled trial examined the efficacy and safety of vaccinating women with an uncomplicated singleton pregnancy at 24 through 36 weeks' gestation to prevent RSV-associated illness in infants.

Intervention: 7392 women were randomly assigned to receive one 120-μg dose of RSVpreF vaccine or placebo. The two primary efficacy end points were medically attended severe RSV-associated lower respiratory tract illness and medically attended RSV-associated lower respiratory tract illness in infants within 90, 120, 150, and 180 days after birth.

RESULTS

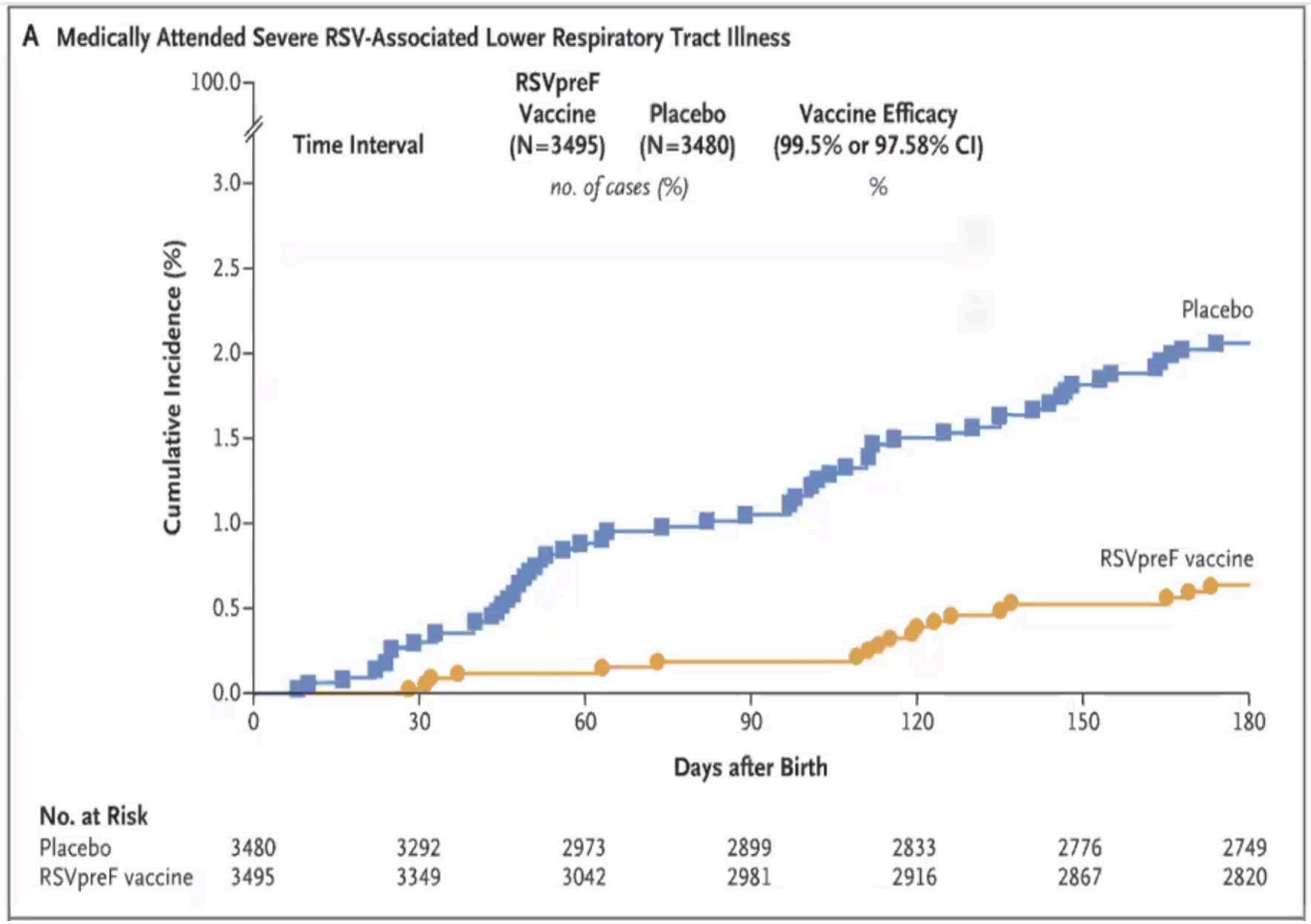
Efficacy: At this prespecified interim analysis, the RSVpreF vaccine was effective against medically attended severe RSV-associated lower respiratory tract illness within 90 days after birth, and protection was maintained through 180 days. The statistical success criterion for vaccine efficacy was not met for medically attended RSV-associated lower respiratory tract illness (the second primary end point).

Safety: No safety signals were detected in maternal participants or in infants and toddlers up to 24 months of age. The incidences of adverse events reported within 1 month after injection or within 1 month after birth were similar in the two groups.

LIMITATIONS AND REMAINING QUESTIONS

- Women with high-risk pregnancies were excluded from the trial, which limits generalizability of the results, since the offspring in such cases could be at higher risk for severe illness.
- Given the small sample size, safety data were limited.
- Limited data were available from low-income countries, where the vaccine could have the greatest effect.

Che efficacia ha il vaccino anti-RSV somministrato in gravidanza nella prevenzione dell'infezione grave da RSV nel neonato?

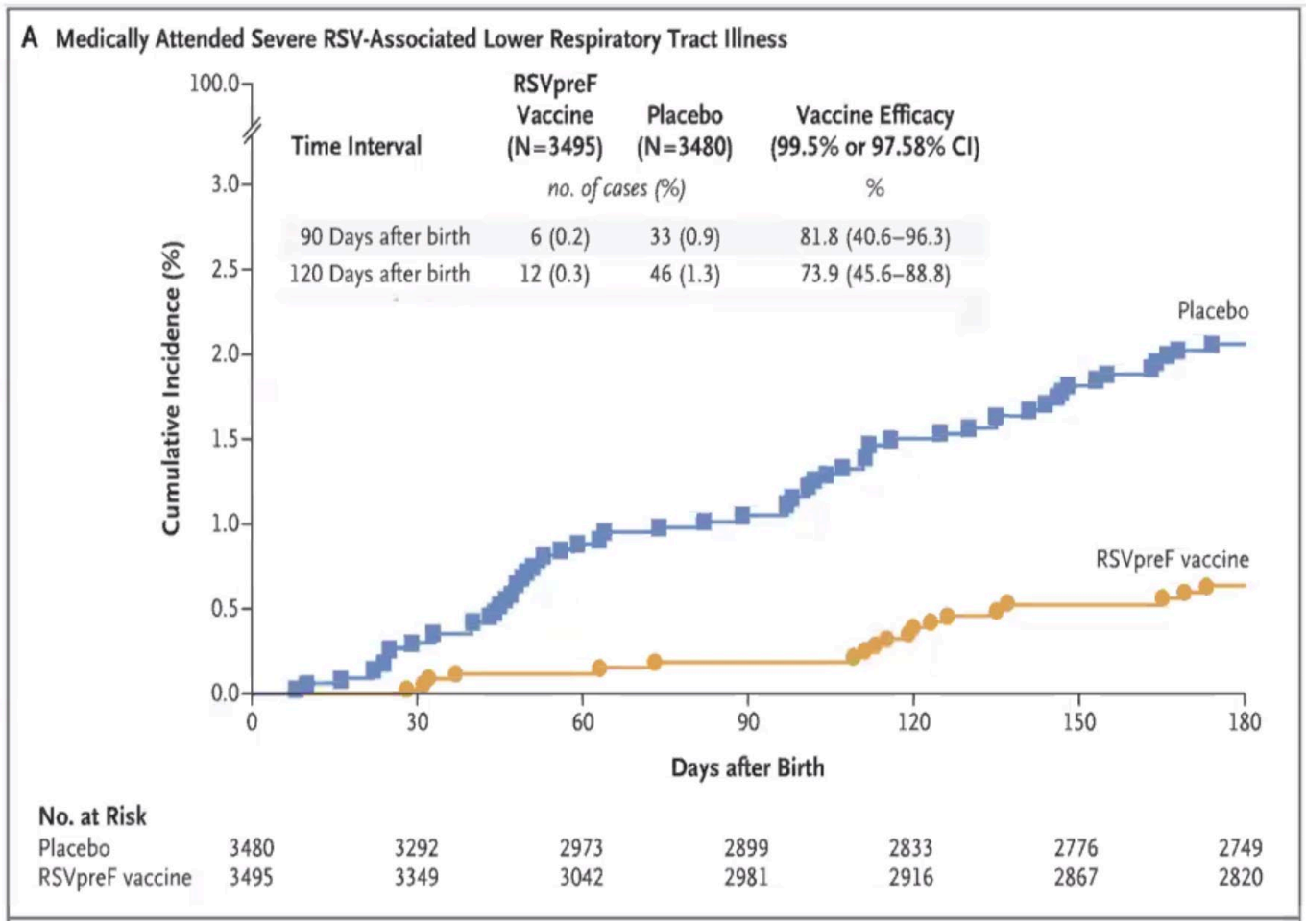


Nei **primi 3 mesi** dopo la nascita la protezione del bambino (effectiveness) è

81.8%

Kampmann B., et al.,
N Engl J Med 2023; 388:1451-1464

Che efficacia ha il vaccino anti-RSV somministrato in gravidanza nella prevenzione dell'infezione grave da RSV nel neonato?



Nei **primi 3 mesi** dopo la nascita la protezione del bambino (effectiveness) è

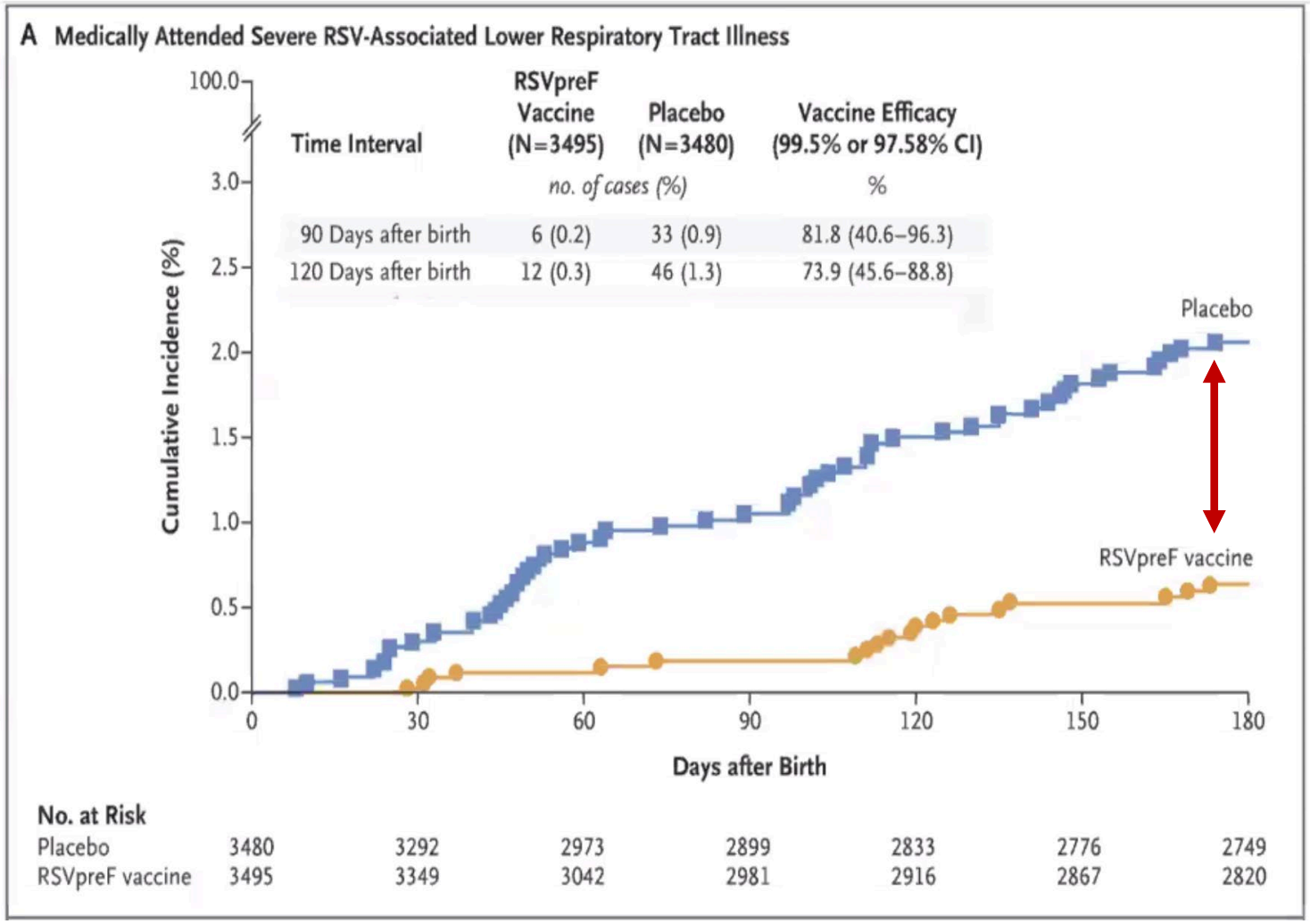
81.8%

Se si valutano **i primi 4 mesi** dopo la nascita l'efficacia è

73.9%

Kampmann B., et al.,
N Engl J Med 2023; 388:1451-1464

Che efficacia ha il vaccino anti-RSV somministrato in gravidanza nella prevenzione dell'infezione grave da RSV nel neonato?



Nei **primi 3 mesi** dopo la nascita la protezione del bambino (effectiveness) è

81.8%

Se si valutano **i primi 4 mesi** dopo la nascita l'efficacia è

73.9%

Se si valutano **i primi 6 mesi** dopo la nascita l'efficacia è

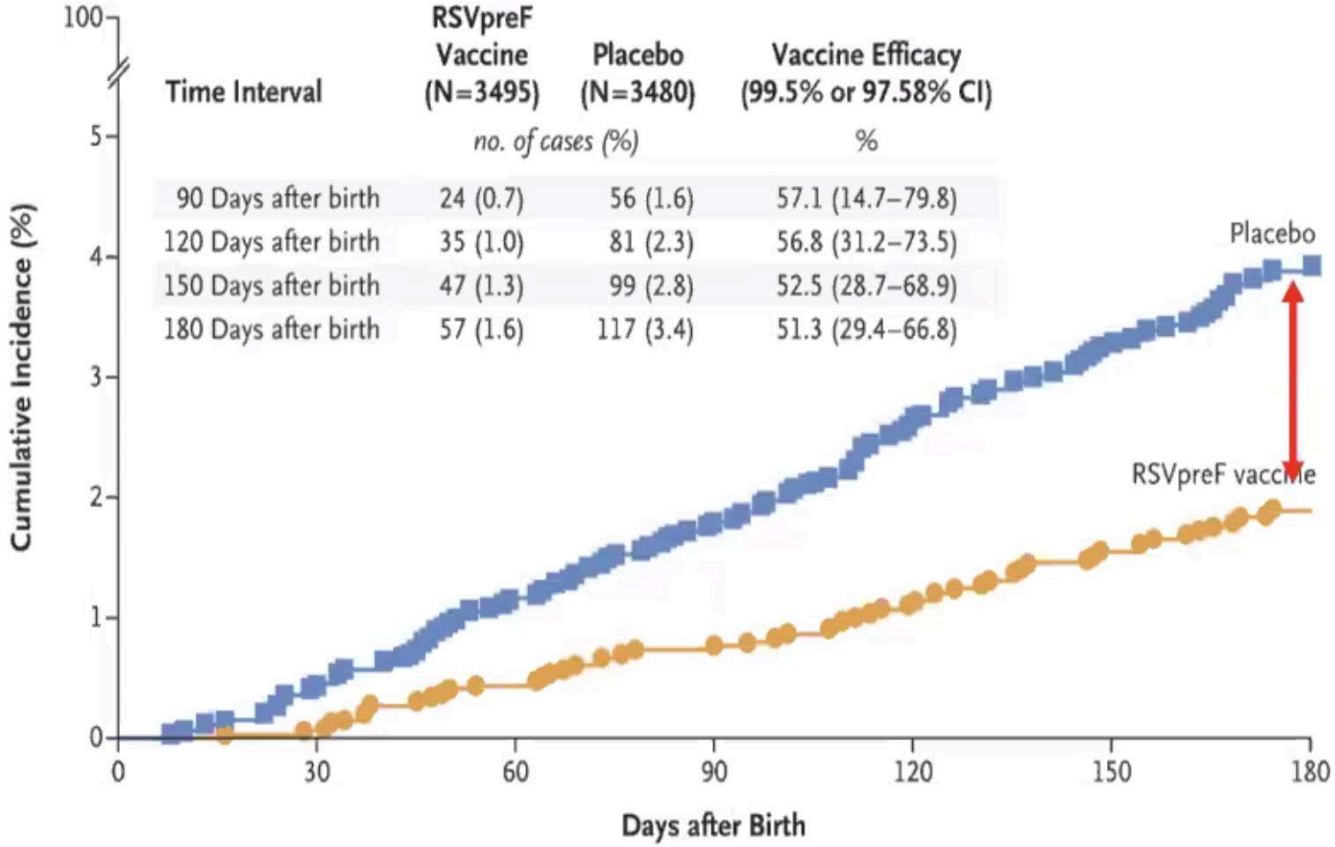
69.4%

Kampmann B., et al.,
N Engl J Med 2023; 388:1451-1464

Che efficacia ha il vaccino anti-RSV somministrato in gravidanza nella prevenzione delle infezioni delle basse vie respiratorie da RSV nel neonato?

Medically Attended RSV-Associated Lower Respiratory Tract Illness

Time Interval	RSVpreF Vaccine (N=3495)	Placebo (N=3480)	Vaccine Efficacy (99.5% or 97.58% CI)
	no. of cases (%)		%
90 Days after birth	24 (0.7)	56 (1.6)	57.1 (14.7–79.8)
120 Days after birth	35 (1.0)	81 (2.3)	56.8 (31.2–73.5)
150 Days after birth	47 (1.3)	99 (2.8)	52.5 (28.7–68.9)
180 Days after birth	57 (1.6)	117 (3.4)	51.3 (29.4–66.8)



No. at Risk							
Placebo	3480	3288	2964	2879	2804	2738	2700
RSVpreF vaccine	3495	3348	3035	2968	2898	2845	2792

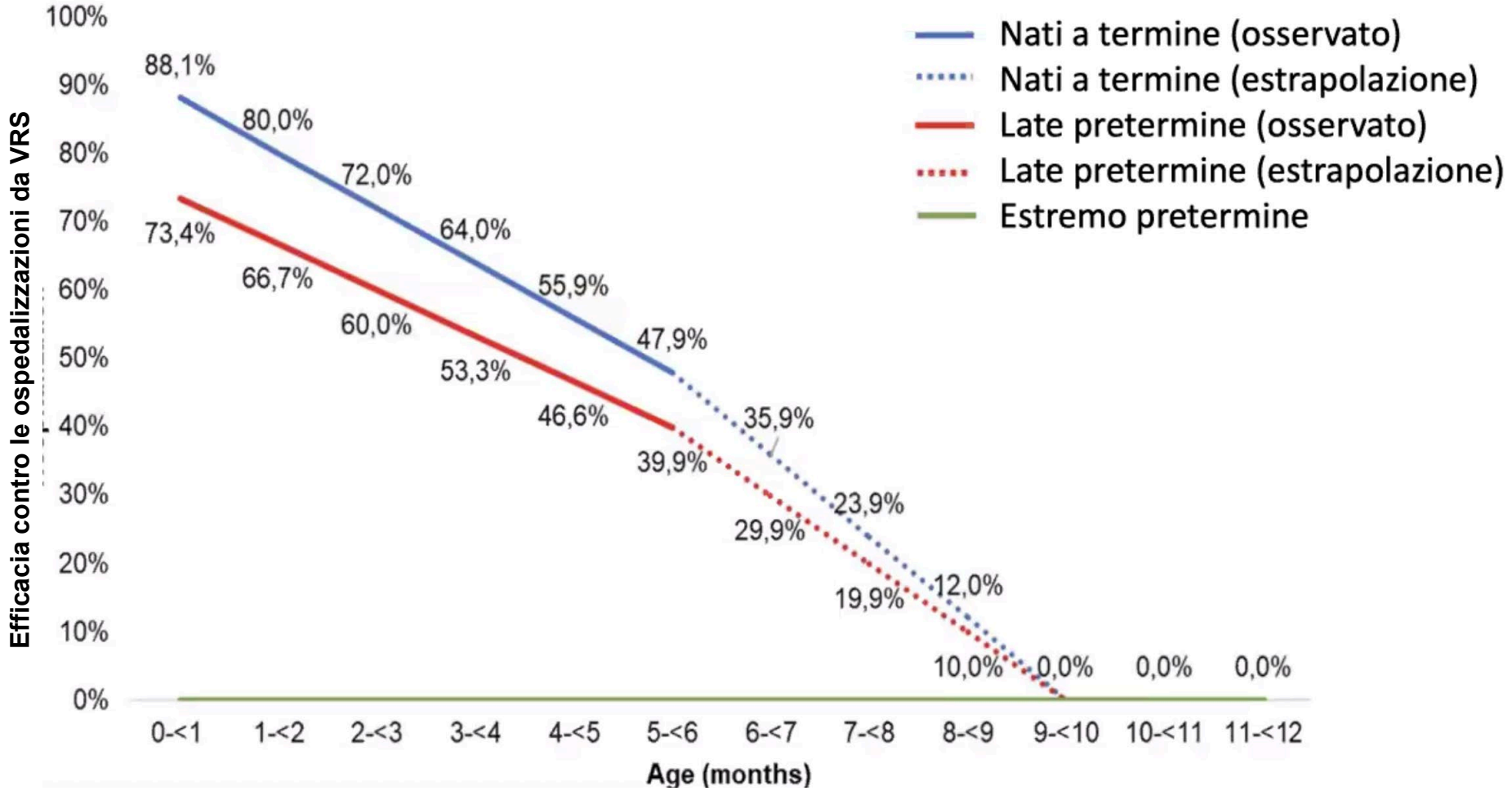
Nei **primi 3 mesi** dopo la nascita la protezione del bambino (effectiveness) è **57.1%**

Se si valutano **i primi 4 mesi** dopo la nascita l'efficacia è **56.8%**

Se si valutano **i primi 6 mesi** dopo la nascita l'efficacia è **51.3%**

Kampmann B., et al.,
N Engl J Med 2023; 388:1451-1464

Quanto dura la protezione indotta dalla vaccinazione materna?
Efficacia nella prevenzione delle ospedalizzazioni



Alvarez AJ et al. Inf Dis Ther. 2024

Cochrane Database of Systematic Reviews | Review - Intervention

Respiratory syncytial virus vaccination during pregnancy for improving infant outcomes

Emily WEM Phijffer, Odette de Bruin, Fariba Ahmadizar, Louis J Bont, Nicoline AT Van der Maas, Miriam CJM Sturkenboom, Joanne G Wildenbeest, Kitty WM Bloemenkamp Authors' declarations of interest

Version published: 02 May 2024 Version history

25 RCTs - 17,991 pregnant women

Selection criteria: We included randomised controlled trials (RCTs) comparing maternal RSV vaccination with placebo or no intervention in pregnant women of any age. The primary outcomes were hospitalisation with clinically confirmed or laboratory-confirmed RSV disease in infants. The secondary outcomes covered adverse pregnancy outcomes (intrauterine growth restriction, stillbirth, and maternal death) and adverse infant outcomes (preterm birth, congenital abnormalities, and infant death).

(mainly due to selection bias). All studies were funded by pharmaceutical companies. Maternal RSV vaccination compared with placebo reduces infant hospitalisation with laboratory-confirmed RSV disease (risk ratio (RR) 0.50, 95% confidence interval (CI) 0.31 to 0.82; 4 RCTs, 12,216 infants; high-certainty evidence). Based on an absolute risk with placebo of 22 hospitalisations per 1000 infants, our results represent 11 fewer hospitalisations per 1000 infants from vaccinated pregnant women (15 fewer to 4 fewer). No studies reported infant hospitalisation with clinically confirmed

Virus respiratorio sinciziale, l'Fda approva il primo vaccino per le donne in gravidanza per prevenire l'RSV nei neonati

Martedi 22 Agosto 2023 *Redazione*

La Food and Drug Administration (Fda) degli Stati Uniti ha approvato Abrysvo (Respiratory Syncytial Virus Vaccine), il vaccino bivalente RSV prefuso F (RSVpreF) d, per la prevenzione della malattie delle basse vie aeree (LRTD) e della LRTD grave causata da virus respiratorio sinciziale (RSV) nei neonati dalla nascita fino a sei mesi di età, attraverso l'immunizzazione attiva di donne in gravidanza a 32-36 settimane di età gestazionale.

30 August, 2024

RSV Vaccine Guidance for Pregnant People

Recommendations

Timing

CDC recommends one dose of Pfizer's Abrysvo for people who are 32 0/7 weeks' through 36 6/7 weeks' gestation. Pregnant people who are more than 36 weeks 6 days pregnant should not be vaccinated, as it is unlikely there will be enough time for the antibodies to develop, cross the placenta, and protect the infant. Instead, their infant should receive RSV immunization (i.e., nirsevimab) just before or at the start of the RSV season.

If an infant requires protection against severe RSV outside of the recommended seasonal administration for maternal RSV vaccination, healthcare providers should administer nirsevimab.

30 August, 2024

RSV Vaccine Guidance for Pregnant People

Recommendations

Revaccination for subsequent pregnancies

At this time, if a pregnant person has already received a maternal RSV vaccine during any previous pregnancy, CDC does not recommend another dose of RSV vaccine during subsequent pregnancies. If their mother was **not** vaccinated during the **current** pregnancy, the infant should receive nirsevimab during October–March (ideally, in October if born during April–September or at birth if born during October–March).

CDC continues to evaluate data to determine whether there is sufficient benefit of revaccination in subsequent pregnancies.

Recommendations

Administration with other vaccines

There are multiple vaccines recommended for pregnant people. Maternal RSV vaccine can be administered during the same visit that a patient receives a Tdap, COVID-19, and/or influenza vaccine.

Contraindications

Pfizer's Abrysvo should not be administered to a person with a history of severe allergic reaction, such as anaphylaxis, to any component of this vaccine. Information about Abrysvo can be found in the manufacturer's package insert.

Precautions

Patients with a minor acute illness, such as a cold, can receive maternal RSV vaccination. If a patient has moderate or severe acute illness, with or without fever, vaccination should generally be deferred until the patient's health improves.

ABRYSVO®
Respiratory Syncytial Virus Vaccine

Maternal Safety

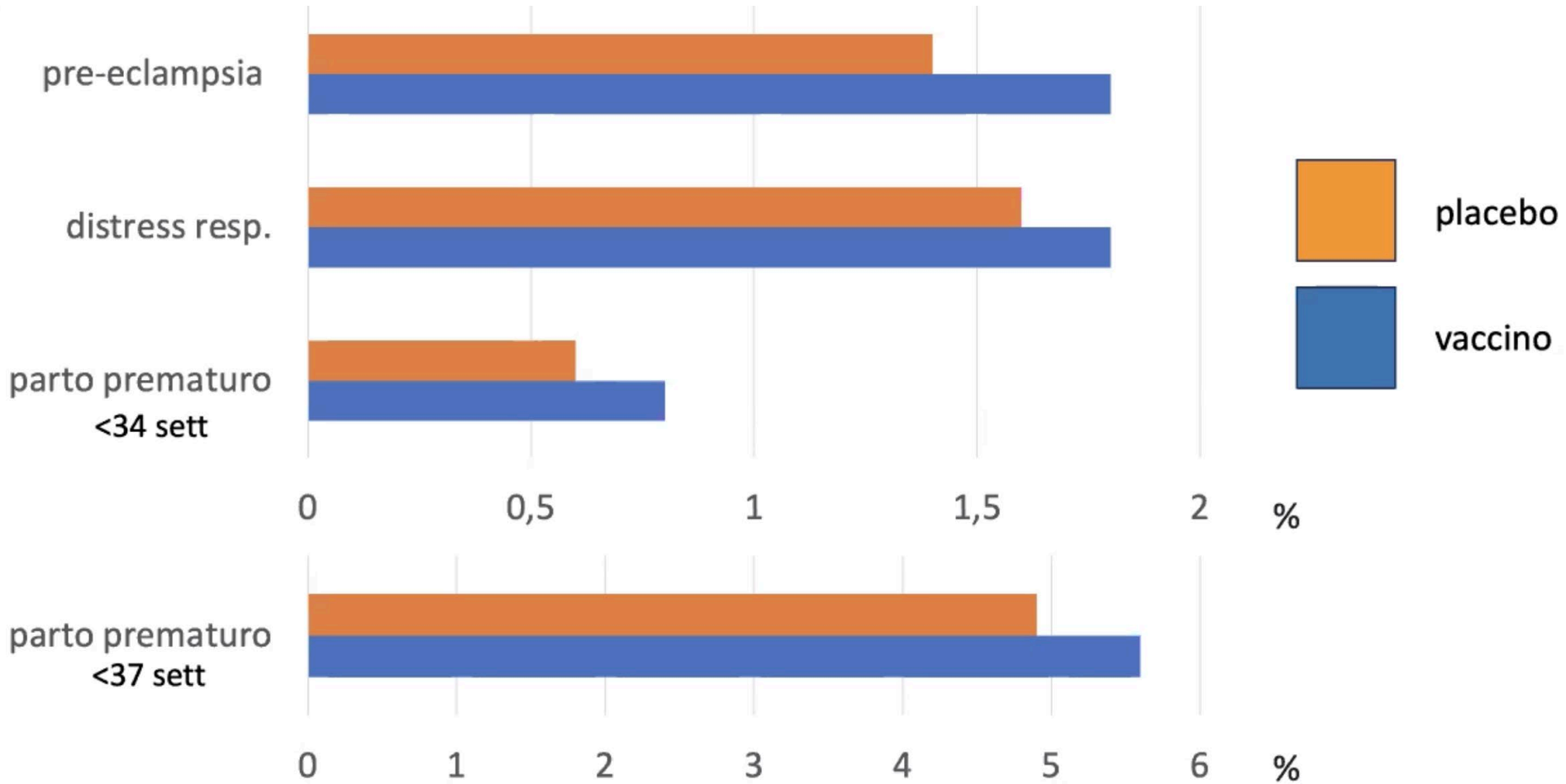
Solicited adverse reactions within 7 days of vaccination[1]

Systemic adverse reactions (ANY)*	ABRYSVO N=3,663 (%)	Placebo N=3,638-3,639 (%)
Fever (≥38.0°C)	2.6%	2.9%
Fatigue	46.1%	43.8%
Headache	31.0%	27.6%
Muscle pain	26.5%	17.1%
Nausea	20.0%	19.2%
Joint pain	11.6%	10.5%
Diarrhea	11.2%	11.5%
Vomiting	7.8%	7.0%

Local adverse reactions (ANY)*	ABRYSVO N=3,663 (%)	Placebo N=3,639 (%)
Pain at the injection site	40.6%	10.1%
Redness	7.2%	0.2%
Swelling	6.2%	0.2%

https://abrysvomaternal.pfizerpro.com/about-abrysvo/safety#tabpanel-tab1

Eventi avversi gravi entro 6 mesi dalla vaccinazione



Kampmann B et al NEJM 2023

Respiratory Syncytial Virus Infection (RSV)

EXPLORE TOPICS

30 August, 2024

What is V-safe?

V-safe is an innovative vaccine safety monitoring system that allows you or your dependent to quickly and easily share how you feel after getting a vaccine. It takes just a few minutes to enroll, and then you will receive V-safe notifications through text messages or emails to complete **short, confidential health check-ins.** Your participation in V-safe makes a difference—it helps others know what to expect in the days following vaccination, and it helps CDC monitor the safety of vaccines for everyone.

V-safe features:

- **Receive health check-ins via text or email** after vaccination.
- **Enroll your dependents** and complete check-ins on their behalf.
- **Share** how you feel **after getting a vaccine dose.**

V-safe

Sign up with your smartphone, tablet, or computer at vsafe.cdc.gov

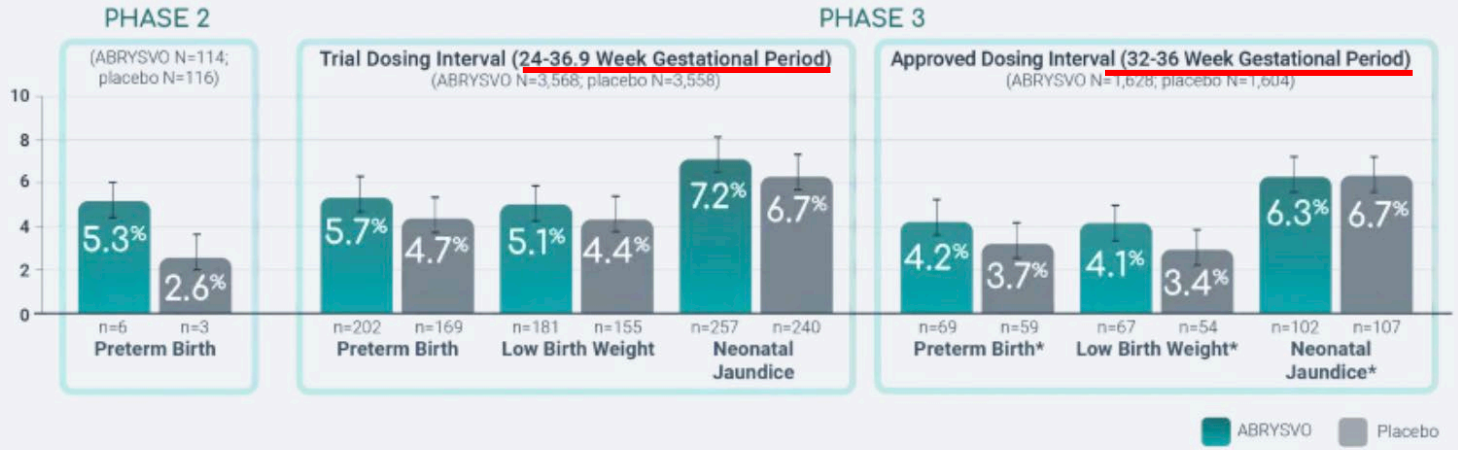
OR

Aim your smartphone's camera at this code

Infant Safety

ABRYSVO®
Respiratory Syncytial Virus Vaccine

Preterm births and additional safety outcomes[1,2]



*Additional preterm birth, low birth weight, and neonatal jaundice data (when vaccine was administered 32-36 weeks gestation) are shown above. These data are derived from the October 13, 2023 *MMWR*.[2]

- Within the trial dosing interval of the phase 3 ABRYSVO trial, there was an ~1% higher rate of preterm birth observed vs placebo[1]

To avoid the potential risk of preterm birth before 32 weeks of gestation, administer ABRYSVO to pregnant individuals at 32 through 36 weeks gestational age[1]

https://abrysvomaternal.pfizerpro.com/about-abrysvo/safety#tabpanel-tab1

Infant Safety

ABRYSVO®
Respiratory Syncytial Virus Vaccine

Incidence of adverse events in infants

Fetal/neonatal serious adverse events[1,3]

	ABRYSVO n=3,568 (%)	Placebo n=3,558 (%)
Congenital abnormalities	5.0%	6.2%
Fetal deaths	0.3%	0.2%

This study revealed no evidence for a vaccine-associated increase in the risk of congenital anomalies or fetal deaths[1]

- Any adverse events in infants from birth to 1 month of age were observed in 37.1% in the ABRYSVO group compared to 34.5% in the placebo group[1]
- Safety was monitored for a median duration of 8.9 months at time of data evaluation[1]

https://abrysvomaternal.pfizerpro.com/about-abrysvo/safety#tabpanel-tab1

Cochrane Database of Systematic Reviews | Review - Intervention

Respiratory syncytial virus vaccination during pregnancy for improving infant outcomes

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Selection criteria: We included randomised controlled trials (RCTs) comparing maternal RSV vaccination with placebo or no intervention in pregnant women of any age. The primary outcomes were hospitalisation with clinically confirmed or laboratory-confirmed RSV disease in infants. The secondary outcomes covered adverse pregnancy outcomes (intrauterine growth restriction, stillbirth, and maternal death) and adverse infant outcomes (preterm birth, congenital abnormalities, and infant death).

RSV disease. Maternal RSV vaccination compared with placebo has little or no effect on the risk of congenital abnormalities (RR 0.96, 95% CI 0.88 to 1.04; 140 per 1000 with placebo, 5 fewer per 1000 with RSV vaccination (17 fewer to 6 more); 4 RCTs, 12,304 infants; high-certainty evidence). Maternal RSV vaccination likely has little or no effect on the risk of intrauterine growth restriction (RR 1.32, 95% CI 0.75 to 2.33; 3 per 1000 with placebo, 1 more per 1000 with RSV vaccination (1 fewer to 4 more); 4 RCTs, 12,545 pregnant women; moderate-certainty evidence). Maternal RSV vaccination may have little or no effect on the risk of stillbirth (RR 0.81, 95% CI 0.38 to 1.72; 3 per 1000 with placebo, no difference with RSV vaccination (2 fewer to 3 more); 5 RCTs, 12,652 pregnant women). There may be a safety signal warranting further investigation related to preterm birth. This outcome may be more likely with maternal RSV vaccination, although the 95% CI

Vaccinazione contro il virus respiratorio sinciziale in gravidanza

POSITION PAPER, 2024

Vaccinazione contro il virus respiratorio sinciziale in gravidanza

POSITION PAPER, 2024

1. Dose singola di del vaccino per VRS (Abrysvo) alle donne gravide tra la **24a e la 36a settimana di gestazione**
2. I **maggiori benefici per il neonato**, anche relativamente agli ipotetici rischi di parto prematuro, sono attesi dalla vaccinazione in gravide dalla **28a settimana in poi** e nei periodi di maggiore stagionalità (da settembre a marzo).
3. **La maggior parte dei neonati, la cui madre è stata vaccinata in gravidanza, non necessiteranno della somministrazione di anticorpi monoclonali.**
4. Tuttavia, sono necessari almeno **14 giorni dal momento della vaccinazione materna per lo sviluppo e il trasferimento transplacentare** degli anticorpi materni per proteggere il neonato/bambino.
5. Il vaccino fornisce **protezione contro la grave malattia da VRS** nel neonato/bambino della ricevente **fino a sei mesi dopo la nascita**.
6. Sarebbe auspicabile che **la somministrazione del vaccino per VRS** avvenisse **in concomitanza con gli altri vaccini raccomandati**, come quelli contro tetano, difterite e pertosse (Tdap), influenza e COVID-19.
7. Si suggerisce **un intervallo minimo di due settimane** tra la somministrazione di Abrysvo e vaccino difterite, tetano e pertosse acellulare (dTap).

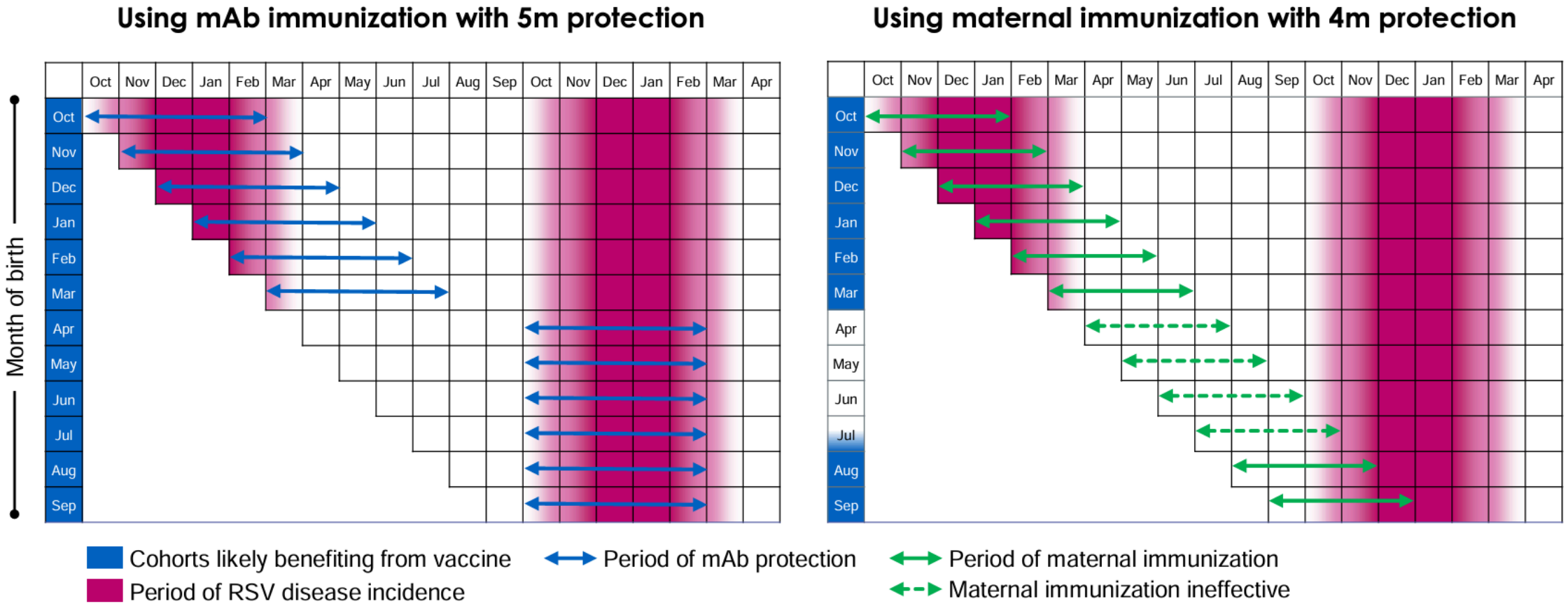
Overview of passive immunization approaches

	Palivizumab (marketed)	Nirsevimab (target profile)	Maternal immunization (development project)
Recommended population (% of birth cohort)	**<2%** CHD/CLD & ≤29wGA	**100%** Pre- and full-term Born in- and out-season	**~40-60%**[1] Full-term only Born in-season only
Achievable immunization (% of birth cohort)	**<2%**[2] Pediatric vaccination	**~90-100%**[2] Pediatric immunization	**~20-40%**[3] Maternal vaccination
Observed efficacy (risk reduction of RSV hospitalization)	**45-55%**[4] Label (Trial 1: N=1,502; Trial 2: N=1,287)	**78%** Phase 2b (N=1,453)	
Treatment burden	**Up to 5 injections** Monthly doses in RSV season	**Single injection** Covering full first season	**Single injection** Covering only part of season

Griffin et al N Engl J Med 383;5 July 30, 2020

Nirsevimab prophylaxis would benefit all infants, regardless of when they are born

Modelling the period of potential protection from RSV infection in a temperate country



Janet, Broad, Snape, Human Vaccines & Immunotherapeutic, 2017

Pricey or priceless: cost-effectiveness of respiratory syncytial virus (RSV) prevention in infants

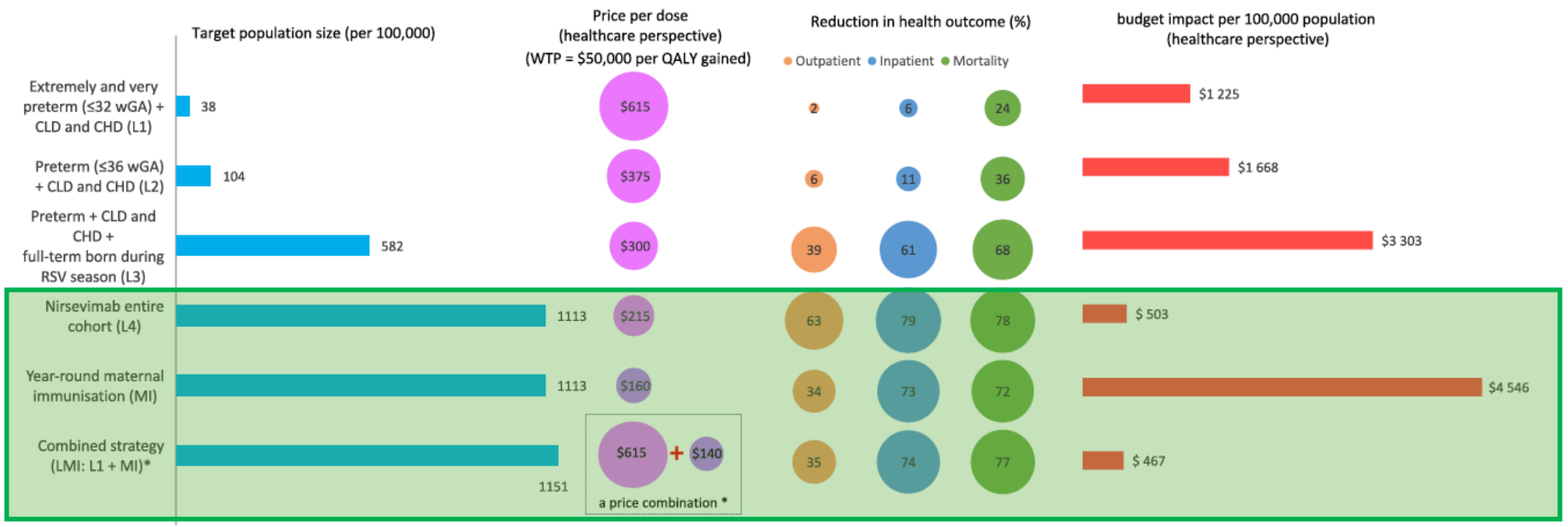


Fig. 1: Key findings: the cost-effectiveness analysis of RSV prevention strategies in Canada (Shoukat et al., 2023). The price-per-dose is estimated from the healthcare perspective under the willingness-to-pay threshold of CAD $50,000 per QALY gained. This Figure visually presents the data from the original publication Tables 3 and 5 and Figs. 2 and 3 with sigmoidal vaccine efficacy profiles (100% coverage). Abbreviation: wGA: weeks of gestational age; CLD: chronic lung disease, CHD: congenital heart disease, RSV: respiratory syncytial virus, MI: maternal immunisation, WTP: willingness-to-pay, QALY: quality-adjusted life-year, L: passive immunisation with nirsevimab, LMI: year-round maternal immunisation (MI) followed by nirsevimab to infants at high risk of severe RSV disease during RSV season (L1). *Various price combinations of combined strategy (LMI) were reported in the Shoukat et al., 2023, this figure only shows one combination with the lowest budget impact from the Canadian healthcare perspective.

- La gravidanza: un’opportunità REALE per le vaccinazioni del neonato

- La gravidanza: un’opportunità **FUTURA** per le vaccinazioni del neonato

Maternal Vaccination for the Prevention of Infantile RSV Disease: An Overview of the Authorized, In-Progress, and Rejected Vaccine Candidates

Vaccine	Registration Number	Phase	Population	Results
RSV MAT (GSK)	NCT04126213	II (2019–2021)	pregnant female participants (28th–33rd gestational week)	- pregnancy and peripartum abnormalities in similar rates between groups, more cases of hypertension and preeclampsia in the active group without exceeding the general pregnant population rates - elevated titers of antibodies for mothers and their infants [26]
ResVax (Novavax)	NCT02247726	II (2014–2016)	pregnant female participants (33rd–35th gestational week)	- protection against severe disease for both mothers and their infants, with high antibody titers for the infants - no significant safety issues [31]
Currently ongoing clinical trials				
mRNA-1345	NCT04528719	I (2020–2024)	young adults including female participants	- promising outcomes for further development as a maternal candidate with elevated antibody titers within a 6-month period [32]
	NCT06143046	II (2023–2026)	pregnant female participants (28th–36th gestational week)	-
ABRYSVO	MORISOTNCT06325657	III (2024–2026)	pregnant female participants living with HIV (24th–36th gestational week)	-
RSV MAT	NCT05705440	IIIb (2023–2025)	participants from all previous trials	- safety monitoring

Papazisis G et al. Vaccines 2024

The urgent need to recognize and properly address prenatal-onset group B *Streptococcus* disease

INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

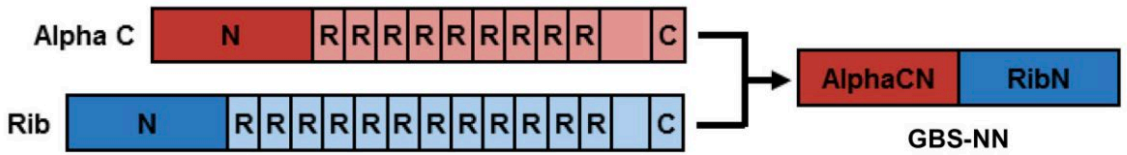
	Prenatal-Onset GBS Disease	Early-Onset GBS Disease	Late-Onset GBS Disease
Timing	Before birth	Up to 7 days after birth	7 to 90 days after birth
Transmission	*In utero* acquisition	Vertical intrapartum acquisition	Horizontal postpartum acquisition
Main Clinical manifestations	Stillbirths, Preterm birth and Miscarriage	Pneumonia	Meningitis
Prevention	No prevention guidelines	Intrapartum Antibiotic Prophyaxis	No prevention guidelines

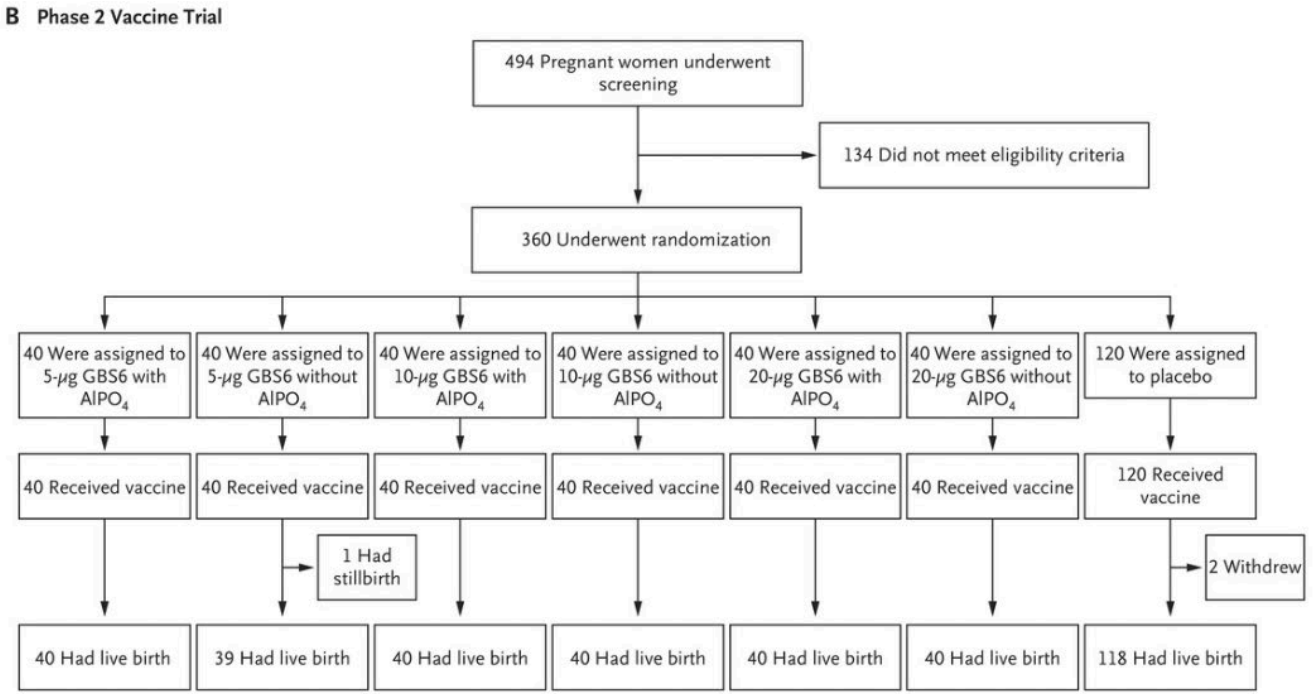
Costa NS Int J Inf Dis et al. 2022

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Potential for Maternally Administered Vaccine for Infant Group B Streptococcus





Madhi SA et al. 2023

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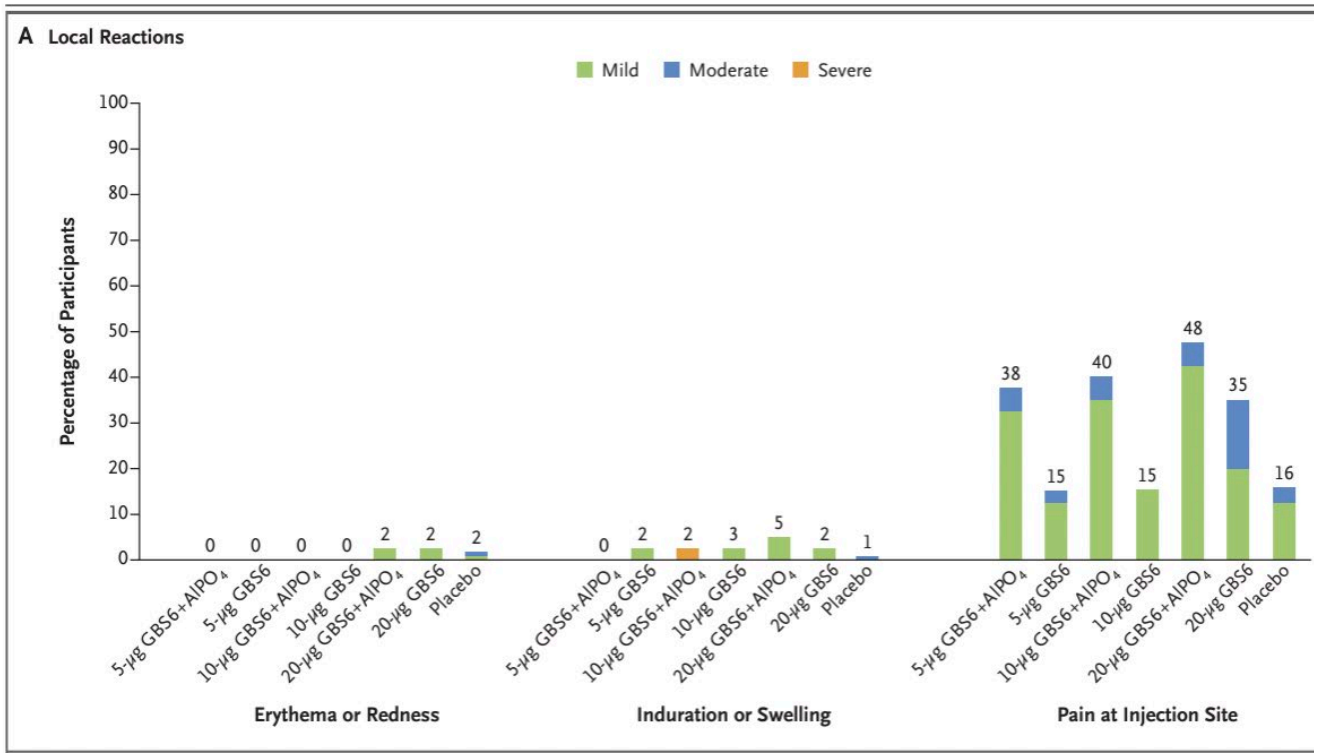
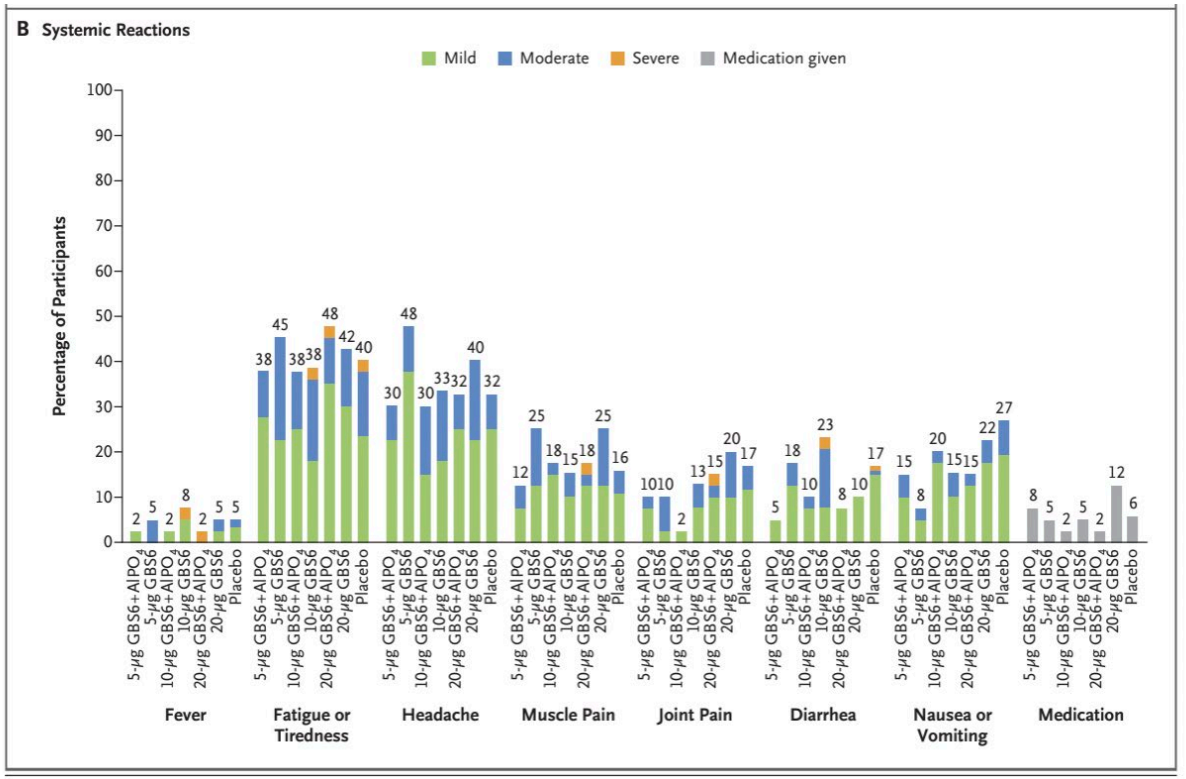




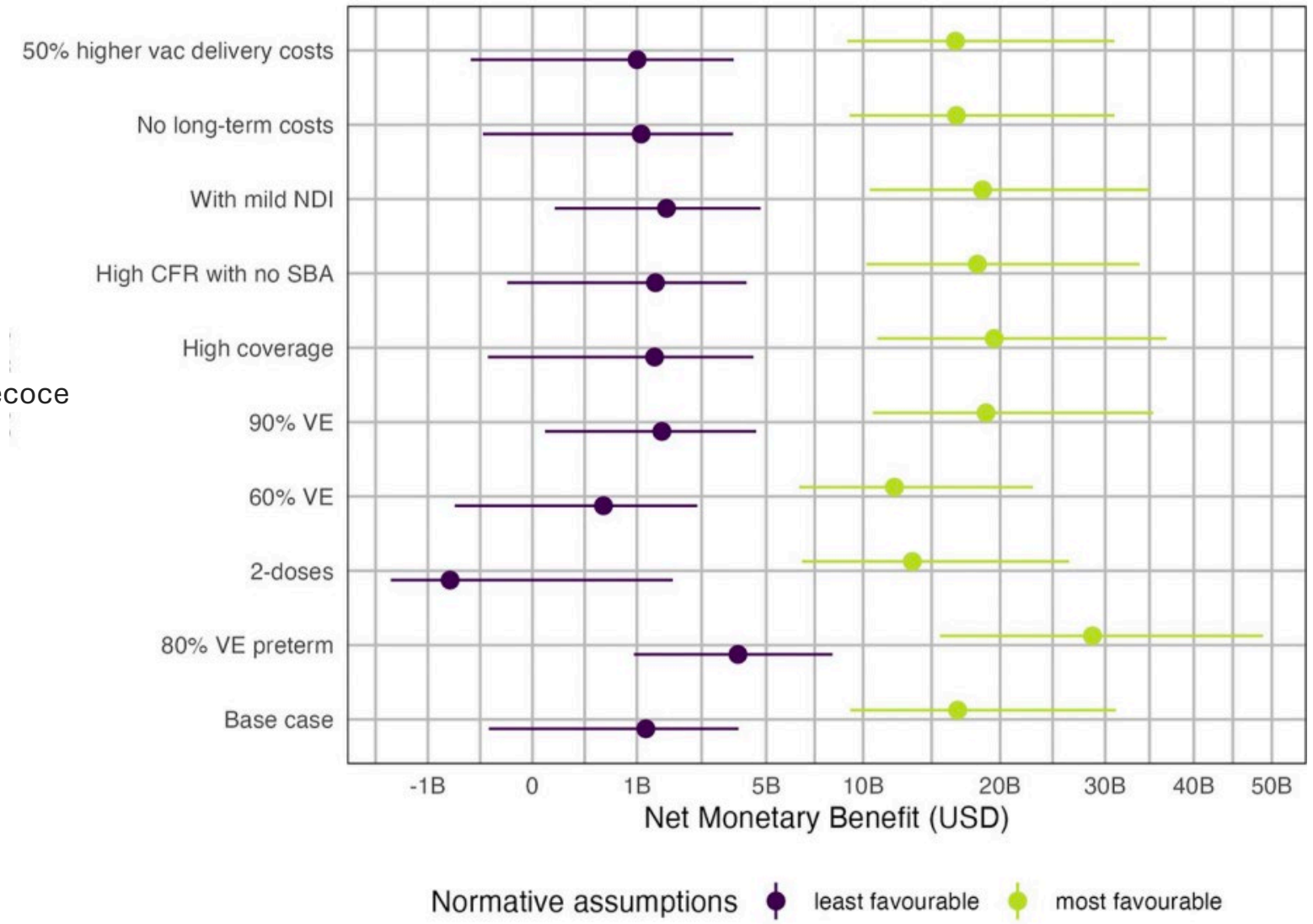
Madhi SA et al. 2023

PLOS MEDICINE

Maternal immunisation against Group B Streptococcus: A global analysis of health impact and cost-effectiveness

140 milioni di donne gravide
In 183 paesi nel 2020.

- ❑ - 80% di infezioni nelle donne vaccinate
- ❑ - 127.000 casi di infezione infantile a esordio precoce
- ❑ - 87.300 a esordio tardivo
- ❑ - 31.100 decessi
- ❑ - 17.900 casi di compromissione dello sviluppo neurologico moderato e grave
- ❑ - 23.000 nati morti



Procter SR et al. 2023

A Clinical Trial of a Cytomegalovirus (CMV) Vaccine in Healthy Women 16 to 40 Years of Age

This study is: Recruitment Complete

Moderna TX ID	Clinicaltrials.gov ID	EudraCT ID
mRNA-1647-P301	**NCT05085366**	**2020-006051-17**

Medical Condition	Phase	Enrollment	Product	Type	Trial Dates
Cytomegalovirus (CMV)	**3**	**7454**	**CMV vaccine**	**Interventional**	**Oct 2021 - Apr 2026**

Brief Summary

The main purpose of this study is to evaluate the efficacy of mRNA 1647 vaccine in CMV-seronegative female participants and to evaluate the safety and reactogenicity of mRNA-1647 vaccine in all participants. The purpose of the Phase 3 extension sub study is to extend the observation period of the main study and to evaluate the longer-term immune persistence of mRNA-1647 vaccine administered to CMV-seronegative females who complete mRNA-1647-P301 main study and to assess for CMV seroconversion in CMV-seronegative participants who did not seroconvert during mRNA-1647-P301 main study. No interventional vaccine will be administered in the extension study.

Study Start (Actual)

2021-10-26

Primary Completion (Estimated)

2026-04-06

Study Completion (Estimated)

2026-04-06

https://clinicaltrials.gov/study/NCT05085366

THE LANCET
Infectious Diseases

Safety and efficacy of PfSPZ Vaccine against malaria in healthy adults and women anticipating pregnancy in Mali: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials

Halimatou Diawara, Sara A Healy*, Agnes Mwakingwe-Omari, Djibrilla Issiaka, Aye Diallo, Seydou Traore, Ibrahim H Soumbounou, Santara Gaoussou, Irfan Zaidi, Almahamoudou Mahamar, Oumar Attaher, Michal Fried, Blair J Wylie, Rathy Mohan, Viyada Doan, Justin Y A Doritchamou, Amagana Dolo, Robert D Morrison, Jing Wang, Zonghui Hu, Kelly M Rausch, Amatigue Zeguime, Tooba Murshedkar, Natasha KC, B Kim Lee Sim, Peter F Billingsley, Thomas L Richie, Stephen L Hoffman†, Alassane Dicko†, Patrick E Duffy†, for the PfSPZ Vaccine Study Team‡*

August 2024

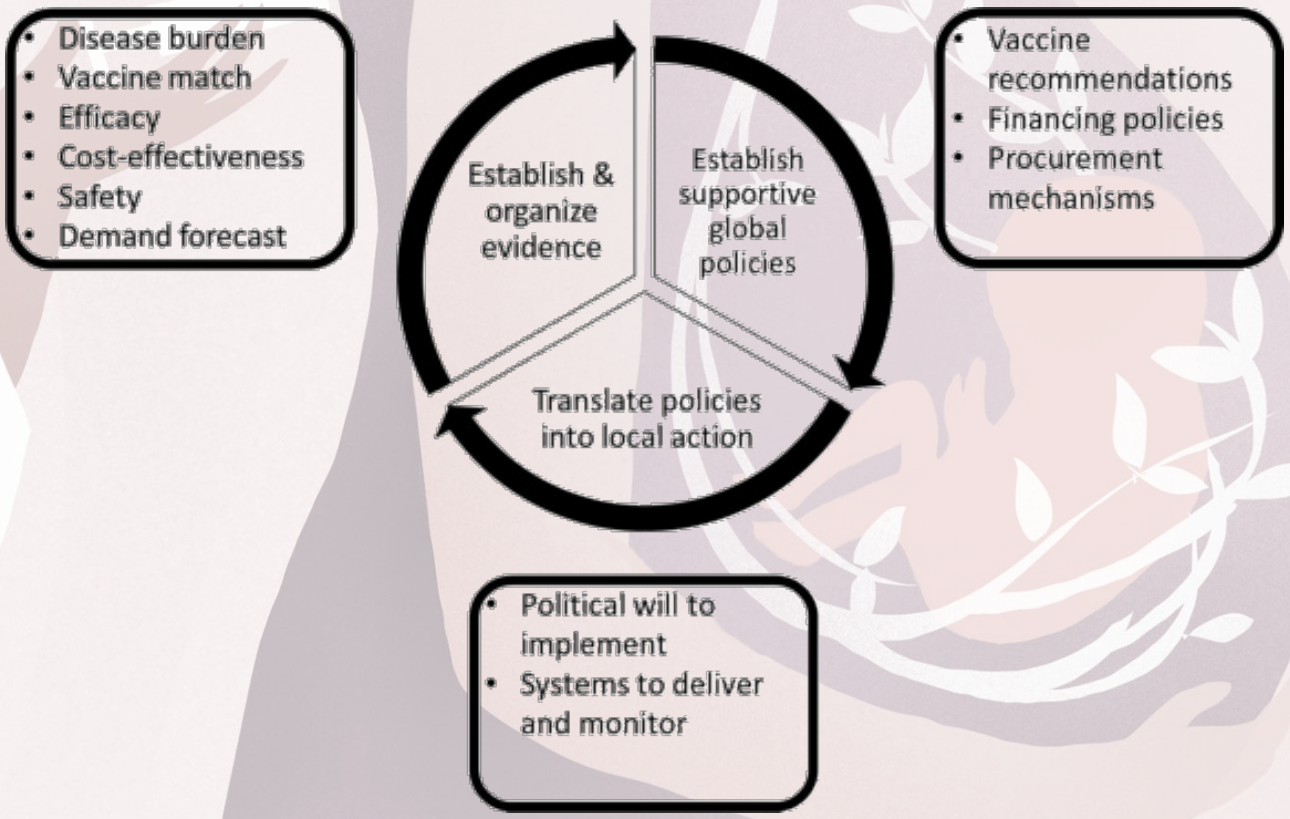
Vaccination during pregnancy: A golden opportunity toembrace

TABLE 2 Best time for the use of certain various vaccines among pregnant/postpartum individuals (source: original authorship).

	Pregnancy—recommended	Pregnancy—special situations	Postpartum/Interval	Pregnancy—under research
Tetanus	X			
Pertussis	X			
Influenza	X			
Pneumococcus		X		
Hepatitis B		X		
Meningococcus		X		
Yellow fever		X		
SARS-CoV-2		X		
MMR			X	
Varicella			X	
HPV			X	o
Dengue				o
Zika				o
RSV				o
HSV				o
GBS				o
CMV				o

Abbreviations: CMV, cytomegalovirus; GBS, Group B streptococcus; HSV, herpes simplex virus; MMR, measles-mumps-rubella; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

Amaral E et al. Int J Gynecol Obstet. 2023



https://www.cdc.gov/vaccines-pregnancy/hcp/vaccination-guidelines/index.html

Opportunities and challenges in conducting community-engaged dissemination/implementation research

Strategies
Providing education and ongoing training in maternal immunisation for all members of maternity care teams
Making maternal vaccination an integral part of routine antenatal care
Ensuring the consistency of the information resources used by maternal care providers (MCPs)
Introducing reminder/prompting systems to enhance the uptake of maternal immunisation
Improving immunisation registration and monitoring
Clearly defining vaccine-related responsibilities within maternity care teams
Providing written information in the official documentation given to pregnant women

Kochhar S et al. 2019; Vilca LM, Esposito S. Vaccine. 2018

Maternal awareness, acceptability and willingness towards RSV vaccination during pregnancy in Ireland

TABLE 1 Participant demographics.

Parameter	Median	Interquartile range (IQR)
Age	32 years	IQR (28–36)
Gestation	31 weeks	IQR (26–36)
Gravidity	1	IQR (1–3)

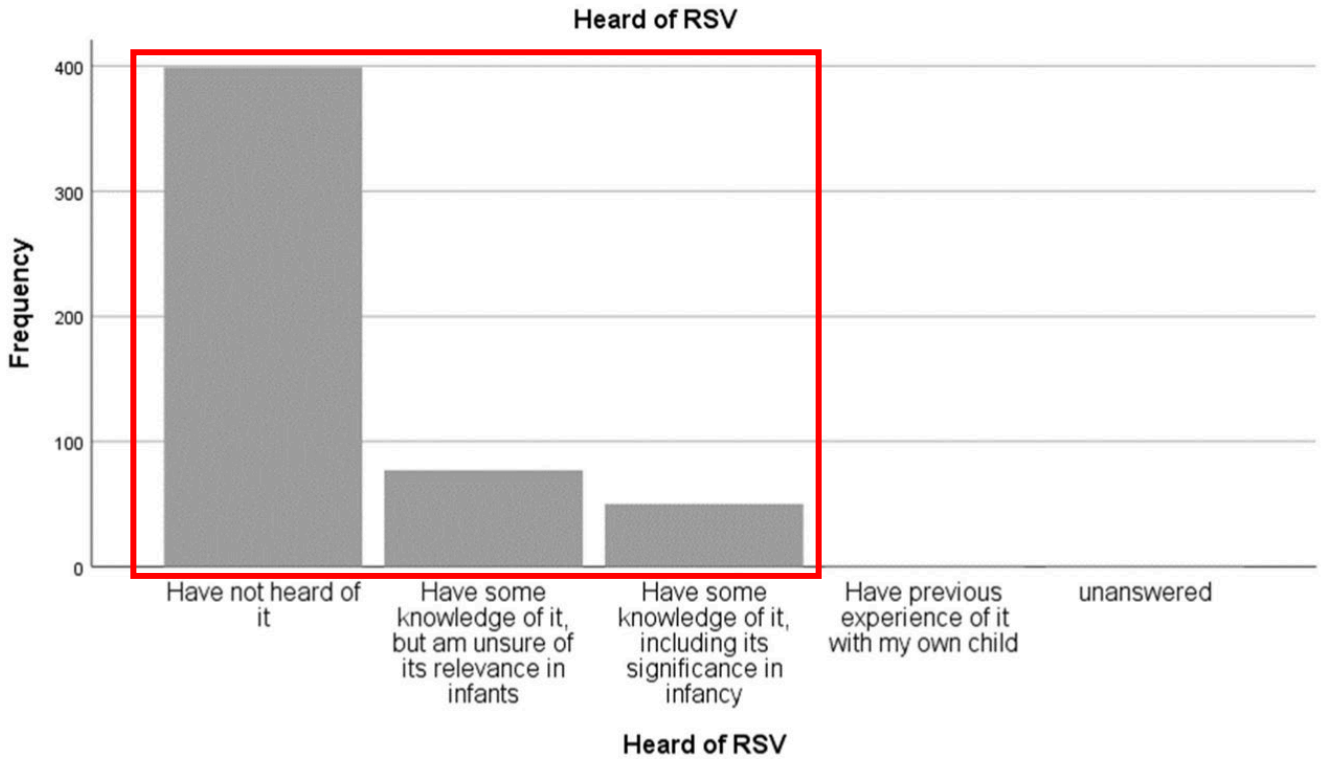


FIGURE 1 Pregnant women's awareness of respiratory syncytial virus (RSV).

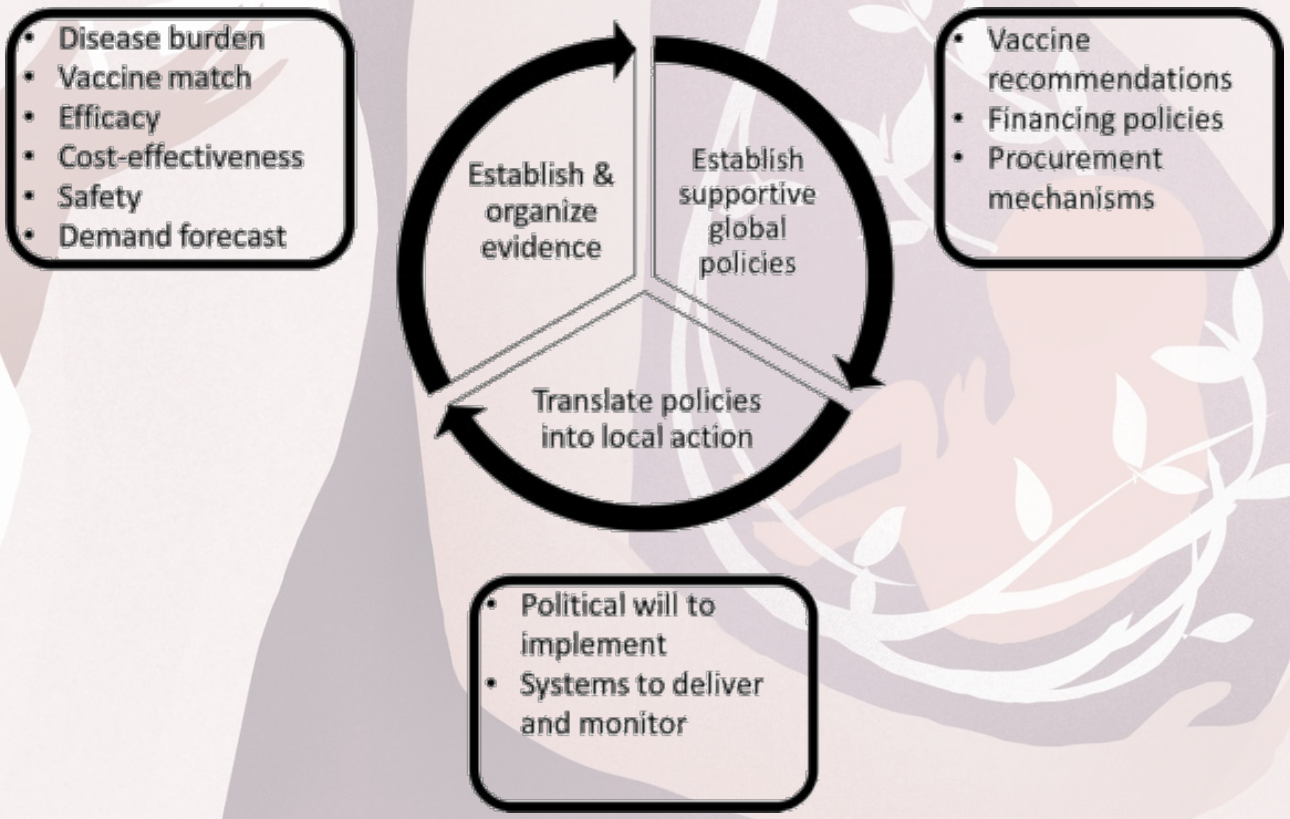
TABLE 2 Responses on acceptability of RSV vaccination.

Option selected	Response *n* (%)
Yes	256 (48.5)
Don't Know	242 (45.8)
No	28 (5.3)

TABLE 3 Attitudes towards vaccination.

Statements selected	*N* (%)
'I feel recommended vaccines will protect my baby from illness'.	356 (67.4)
'I feel confident in recommended vaccines'.	258 (48.9)
'I feel the vaccines could harm my baby'.	57 (10.8)
'I don't think my baby is at risk of infection'.	22 (4.2)
'I feel the vaccines could harm me'.	19 (3.6)
'I have no confidence in vaccines'.	15 (2.8)

McCormack S et al. Immun, Inflam, Dis. 2023



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