

# Vaccinations in Pregnancy

**Australian Vaccinology Course**  
**August 28-30, 2025**

Professor Michelle Giles OAM

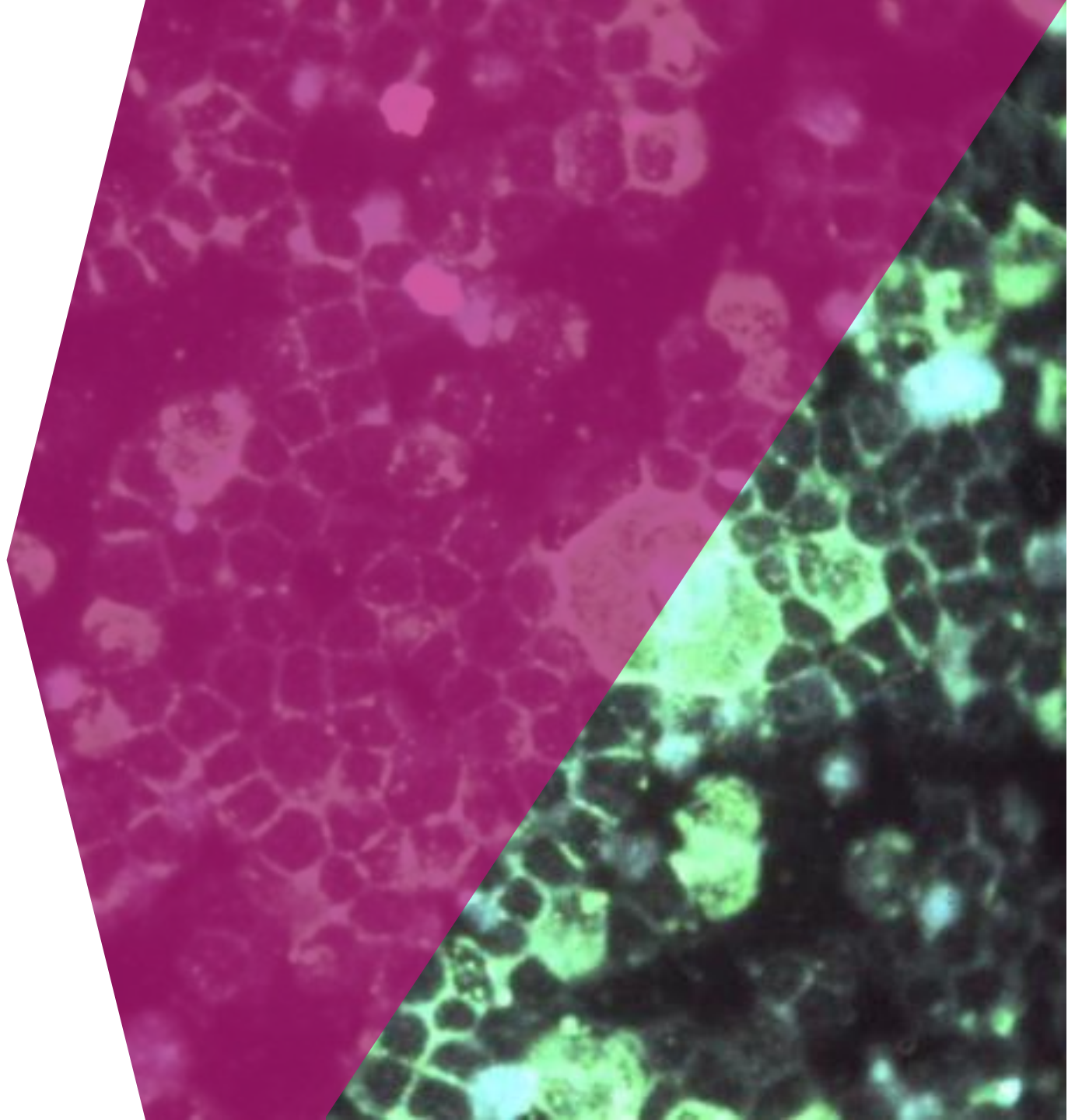
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Gynaecology, Monash University

Department of Infectious Diseases,  
University of Melbourne



# • Declarations of Interest

- 
- Head, Vaccine Research Group  
Doherty Institute
  - Principal investigator on vaccine trials sponsored by Sanofi, Novavax, Moderna, GSK
  - Past member of ATAGI (2016-2025)
  - Views expressed during this presentation are in my professional capacity not related to my other roles



# First principles

Pregnant women are more susceptible to severe disease

Maternal vaccination reduces the vulnerable period in the infant leveraging unique immunological setting

'Two for One' deal

# Pregnant women are more susceptible to vaccine preventable diseases



Smallpox (higher case fatality rate in 19<sup>th</sup> century)<sup>1</sup>



Influenza  
(Pandemics 1918, 1957, 2009)<sup>3-5</sup>



Measles (Greenland 1951)<sup>2</sup>



SARS-CoV-2<sup>6</sup>

# Physiological changes during pregnancy can affect the recognition of and response to infection

## Cardiovascular

- Increased heart rate and stroke volume
- Increased oxygen consumption

## Respiratory

- Decreased lung capacity

## Immune

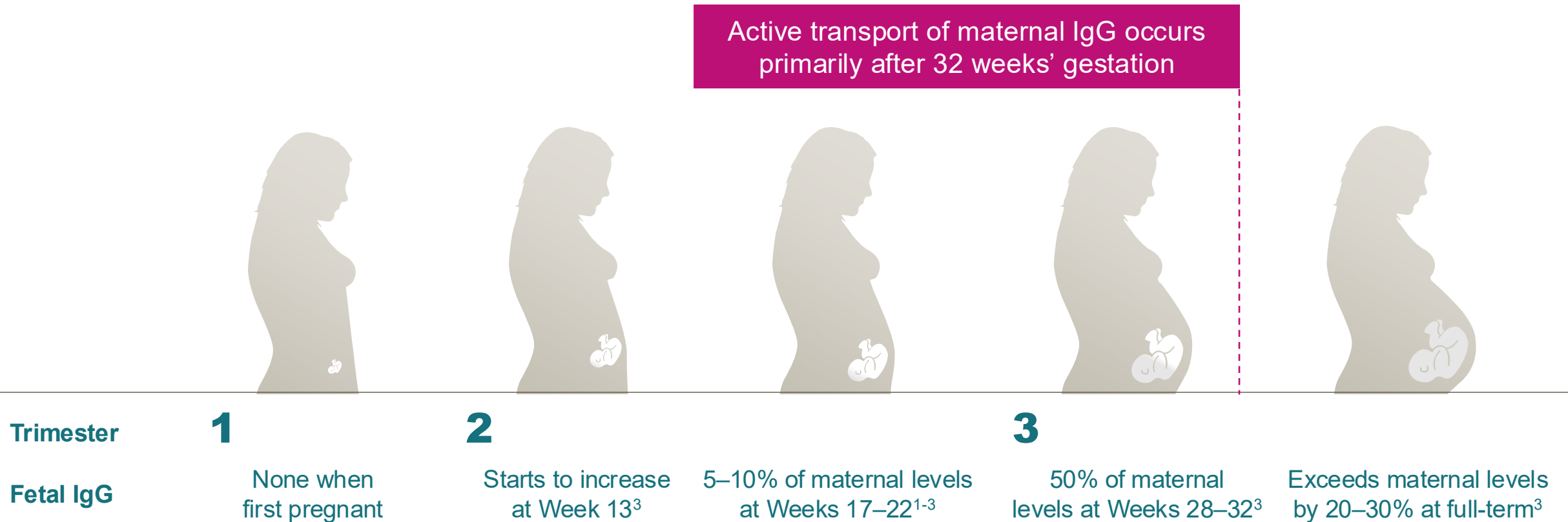
- Shift from cell-mediated to antibody-mediated immunity, may explain poorer response to some infections



**Lack of recognition of symptoms of infection, due to their similarity with changes occurring during pregnancy, can lead to reduced diagnosis and treatment, and an increased risk of complications**

# Maternal immunisation can optimise the amount of pathogen-specific IgG at birth

Placental transfer of IgG is generally linear, with the largest amount transferred in the third trimester



IgG, immunoglobulin G

1. Abu Raya B *et al.* *Vaccine* 2014;32:5787–5793; 2. Naidu MA *et al.* *Am J Obstet Gynecol* 2016;215:237.e1–6; 3. Palmeira P *et al.* *Clin Dev Immunol* 2012;2012:985646; 4. Chu HY, Englund JA. *Clin Infect Dis* 2014;59:560–568

# Infants are particularly vulnerable to infectious diseases in the first 6 months of life

Maternal immunisation helps protect pregnant women and addresses this vulnerability in young infants

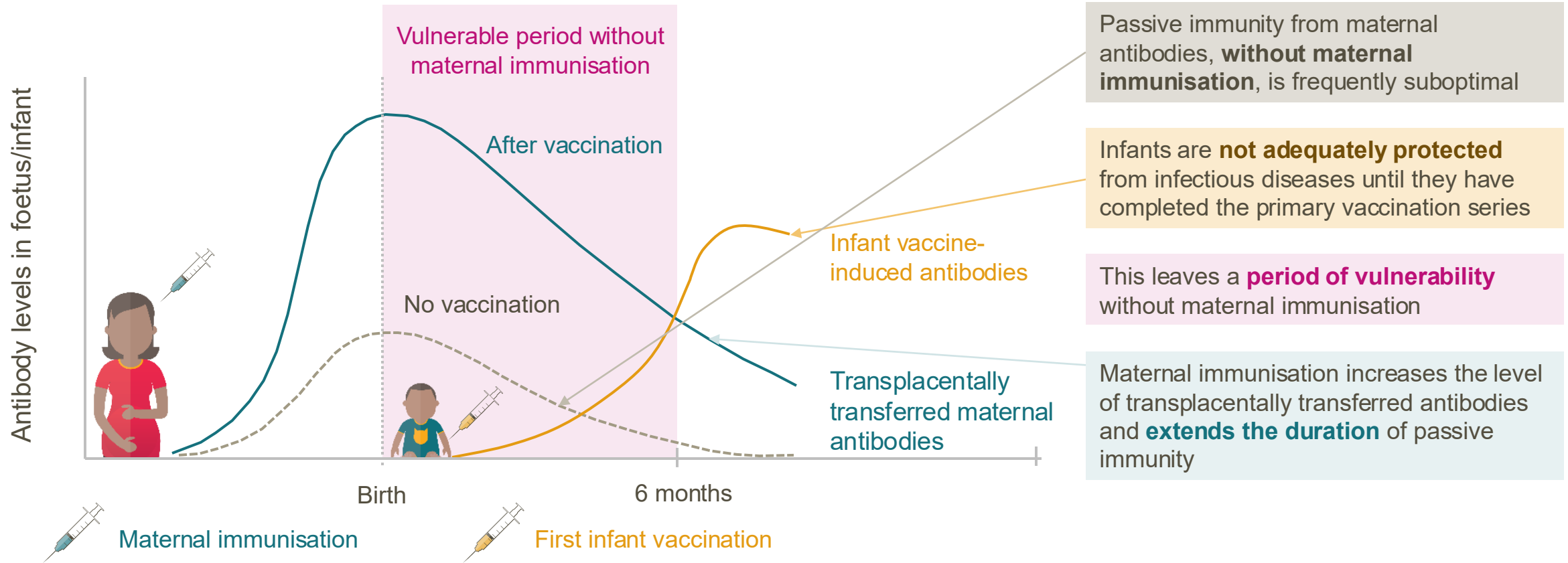


Figure adapted from Mukherjee P *et al. Eur Gynecol Obstet* 2021;3:2–12 with permission from the editors of European Gynecology & Obstetrics

# The “Two for One” Deal



- **To protect the pregnant woman** from infections that are potentially severe for herself (influenza, tetanus, COVID-19)

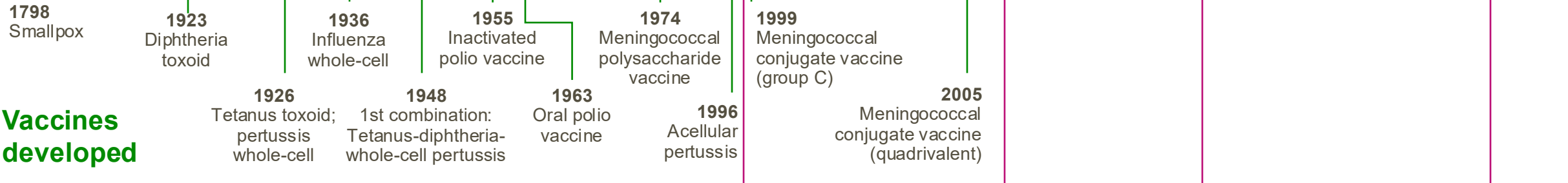


- **To protect the infant in the first 6 months of life:**  
Passive immunity via transfer of vaccine-specific antibodies via the placenta to protect the baby in first months of life (influenza, pertussis, tetanus)

# Maternal immunisation is not a new strategy

The history of maternal immunisation

## Outbreaks



## Vaccines developed

## WHO recommendations

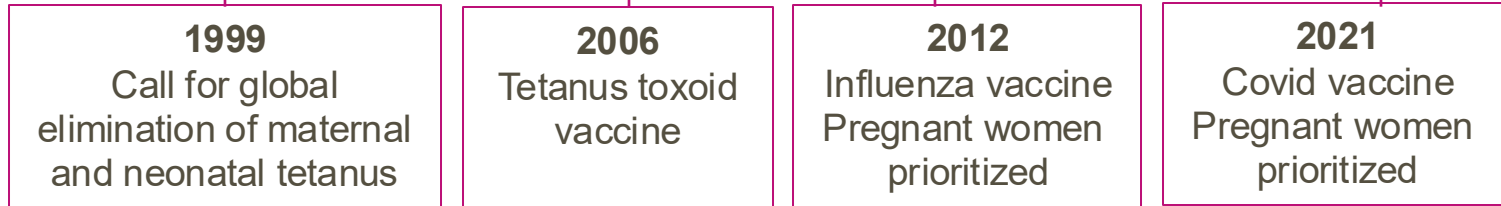


Figure adapted from Maternal Immunization. Elsevier Inc 2019

# Maternal immunisation is not new. We can build on this experience.

## Vaccine

Widespread/  
global use

- Tetanus

Use in limited  
(mostly higher  
income) markets

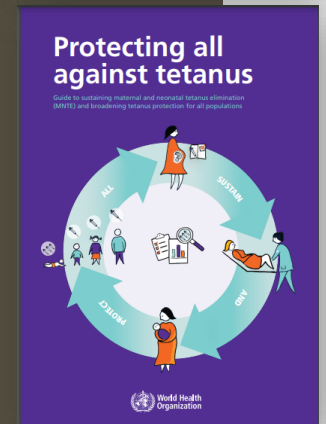
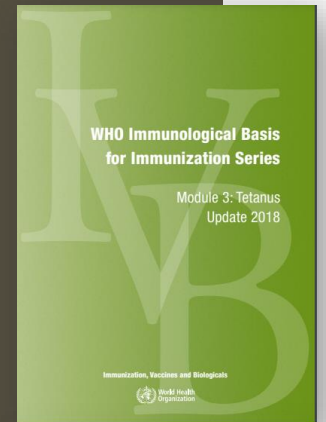
- Influenza
- Pertussis
- COVID-19

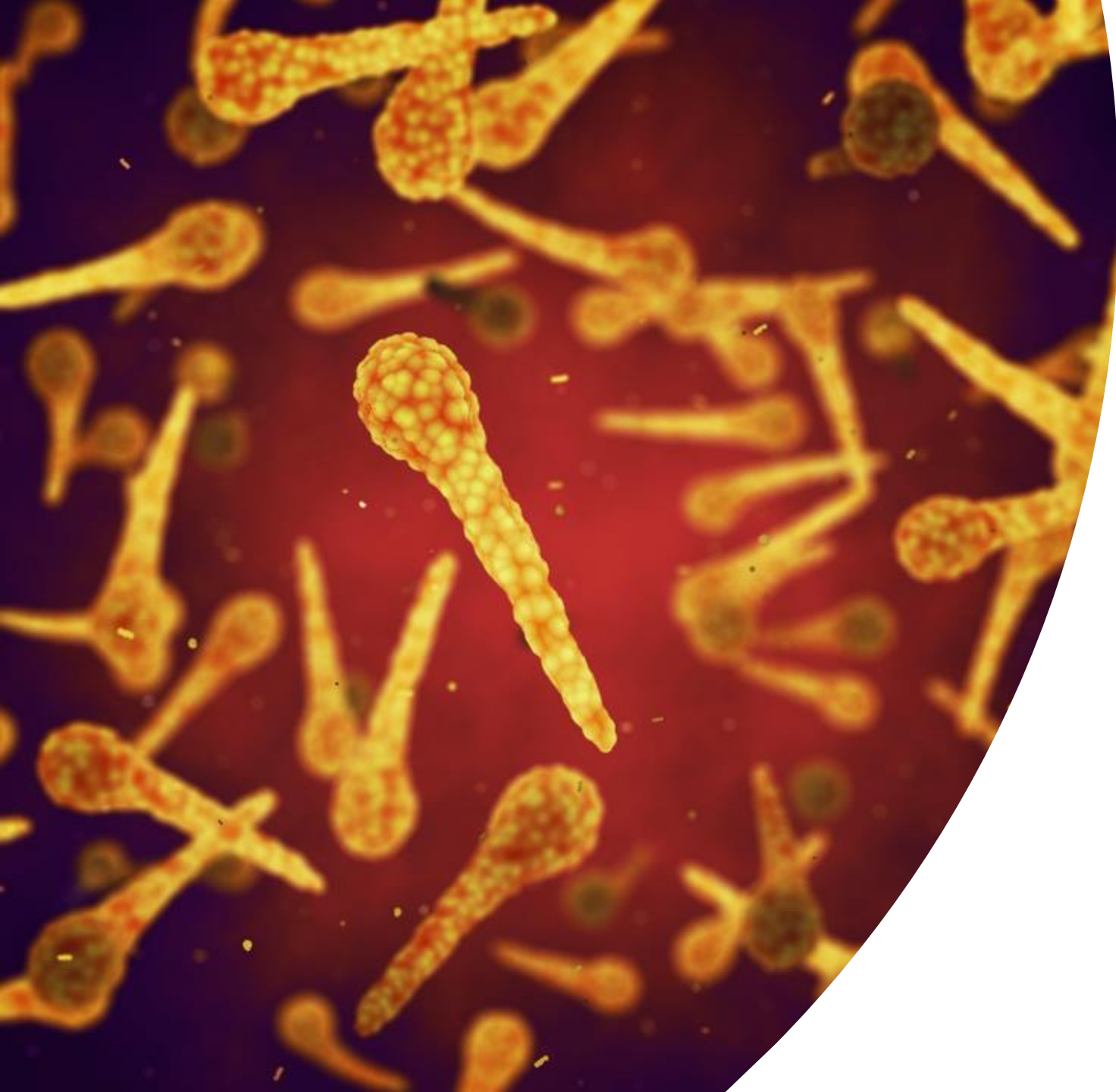
New and emerging  
opportunities

- RSV
- Group B  
*Streptococcus* (GBS)
- Hepatitis E

## Maternal and neonatal tetanus (MNT) elimination

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



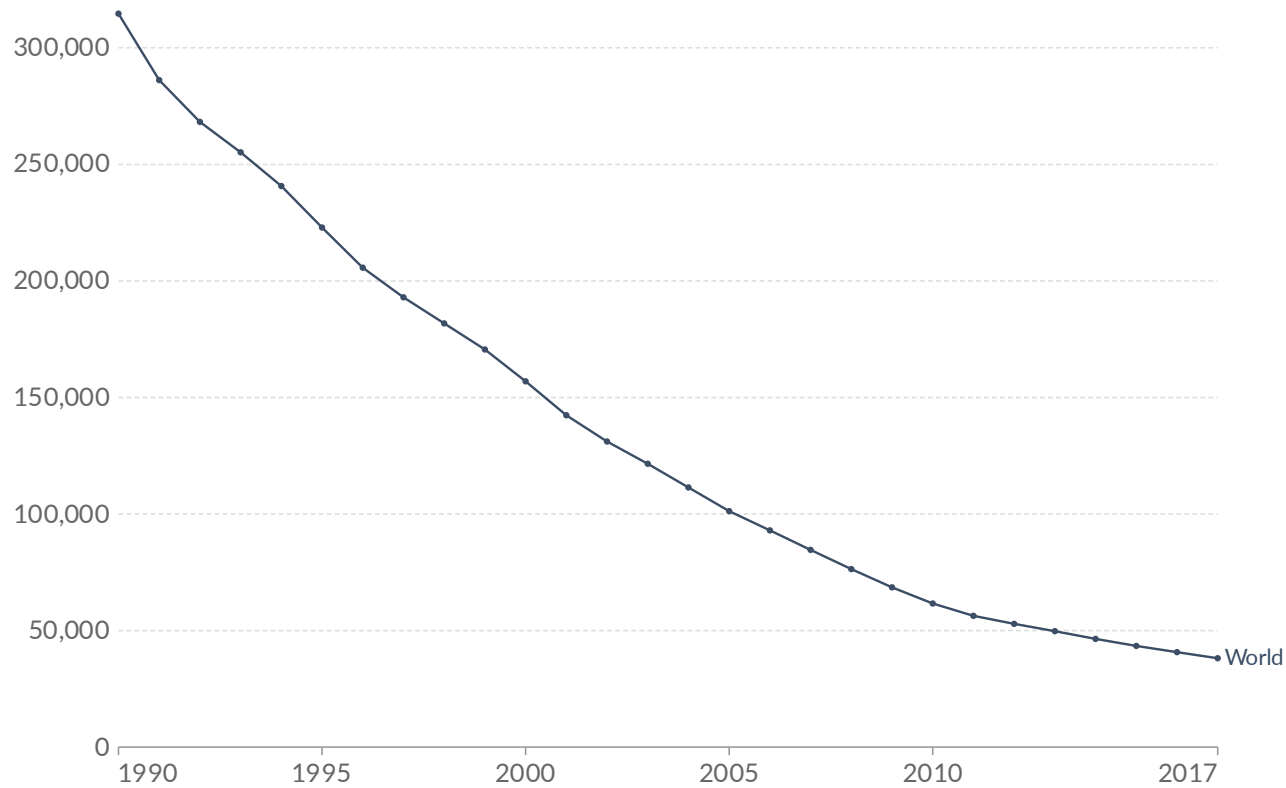


# Tetanus

# Since 1990, the number of deaths from tetanus has fallen by 89%

Number of deaths from tetanus, 1990 to 2017

Our World  
in Data



Source: IHME, Global Burden of Disease

CC BY



Tetanus neonatorum

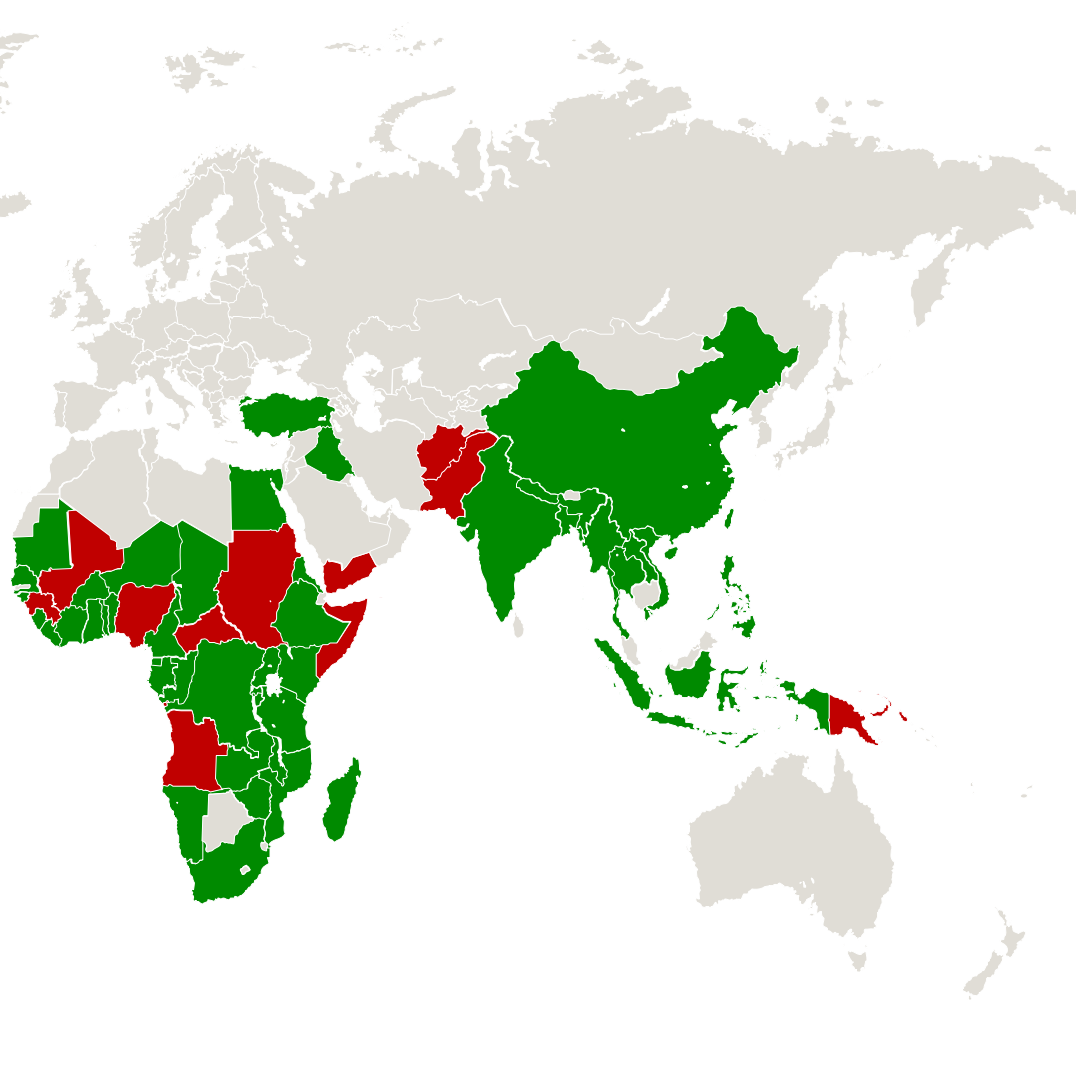


Child tetanus

# What can we achieve?

1999: call for global elimination of maternal and neonatal tetanus

Afghanistan  
Angola  
Central African Republic  
Nigeria  
Pakistan  
PNG  
Somalia  
Sudan  
South Sudan  
Yemen



49 countries eliminated maternal and neonatal tetanus after 2000

As of 2024, 10 countries have not yet eliminated MNT



**Influenza**

# Cobram flu victim and first-time mum Sarah Hawthorn discharged from Melbourne hospital

A Cobram flu victim who woke from a three-month coma unaware she'd given birth has been discharged from hospital in Melbourne. *The Border Mail* understands the bubbly first-time mum, who contracted Influenza A in the later stages of pregnancy, is recovering at home and undergoing rehabilitation after spending months in intensive care.



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HEALTH

## Top doctor warns pregnant women over deadly flu

“ At some point the U of gun control. | More >

## Canberra mother dies from influenza complications amid 'one of worst flu seasons on record'

Updated 26 Sep 2017, 1:44pm

A Canberra mother of two has died of complications from influenza in what health authorities say is "one of the worst flu seasons on record" in Australia.

Jennifer Thew, from Gungahlin in Canberra's north, died over the weekend after contracting influenza.

STATE OF THE AUSTRALIAN

SEAT PREDICTION THE CHAMBER

If an election

Acting chief health officer Dr Andrew Pengilly said to his knowledge the "fit, young" woman was the only young adult in the country who had died from influenza this year.



# Influenza infection causes harm to the pregnant woman, the fetus and the newborn infant



## For the pregnant woman

- Increased morbidity
- Hospitalisation
- Increased risk of death

## For the fetus

- Fetal growth restriction
- Fetal distress
- Fetal mortality
- Preterm delivery
- Caesarean delivery

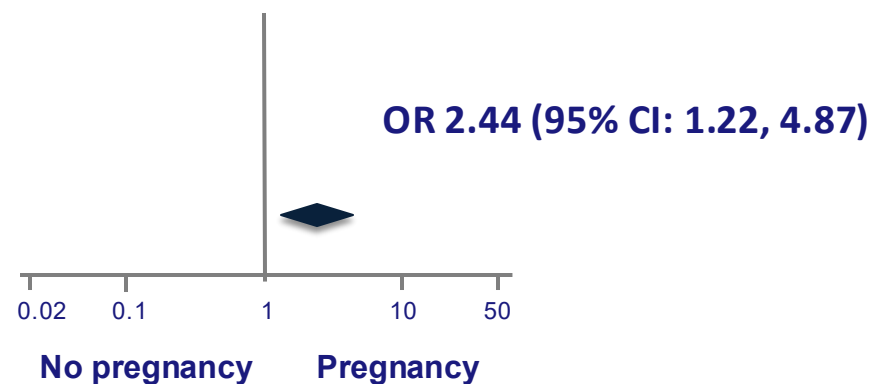


## For the newborn

- Low birth weight
- Paediatric intensive care
- Neonatal death
- Hospital admission for the infant

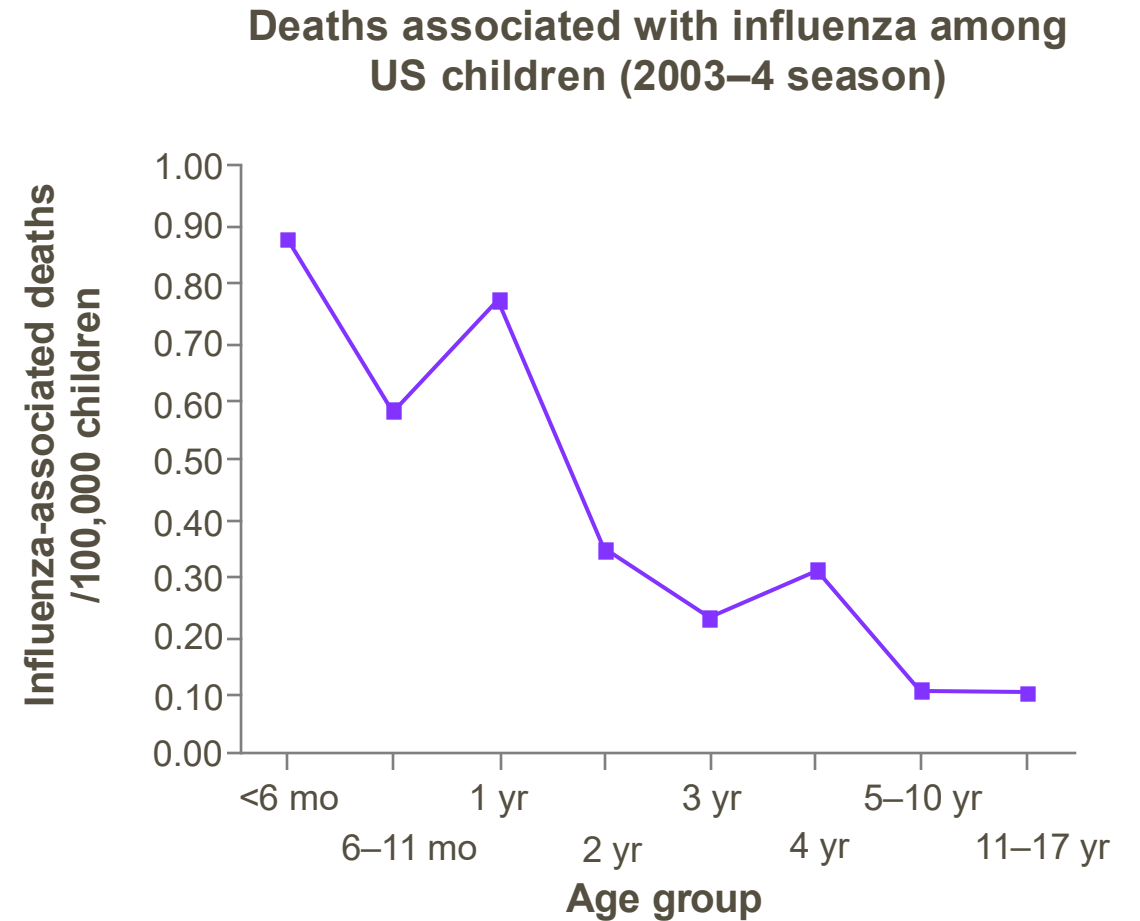
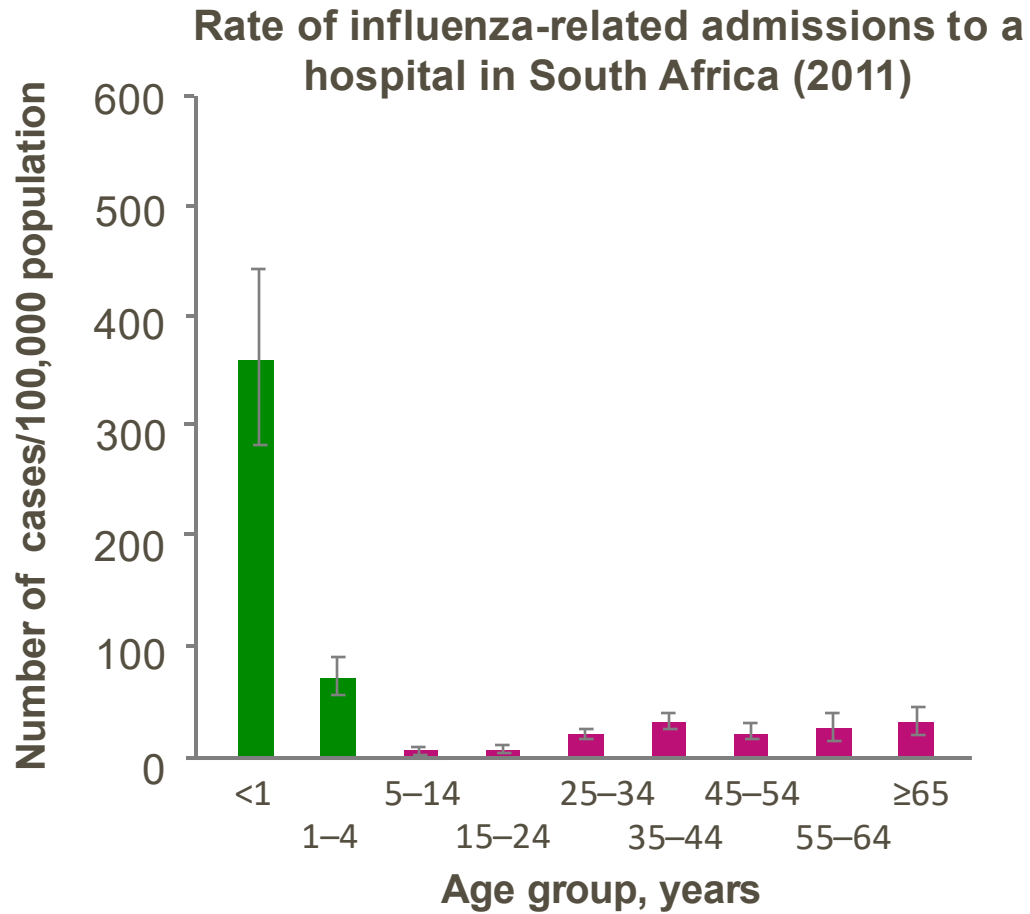
Pregnant women were more than twice as likely to be admitted to hospital with influenza than non-pregnant women

## Odds of being admitted to hospital with influenza



Review of 152 observational studies  
(most conducted during the 2009 flu pandemic)

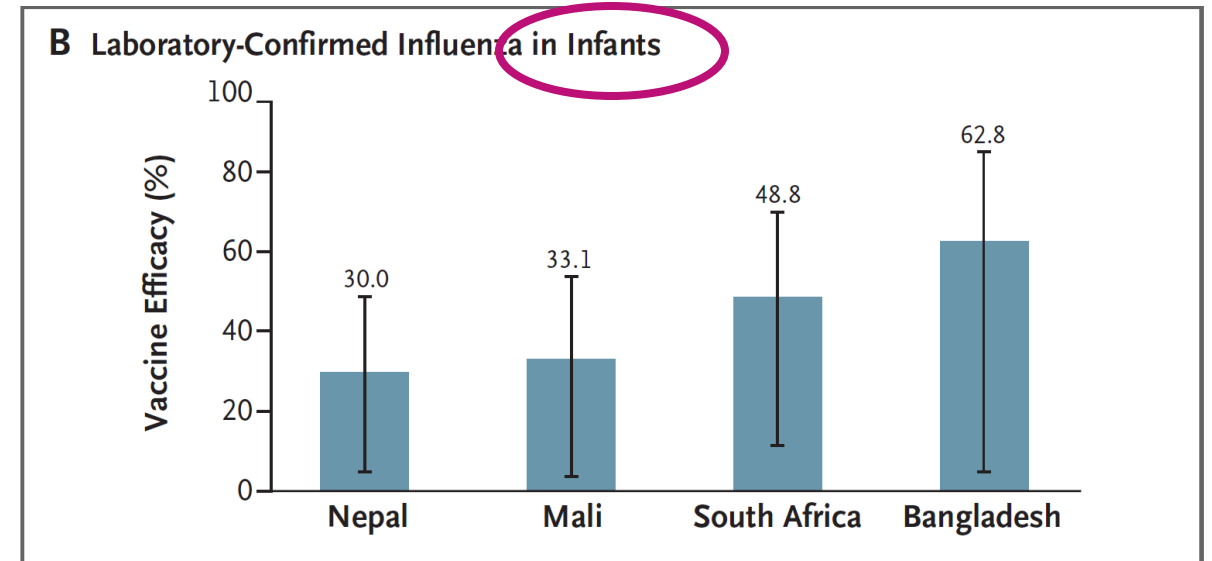
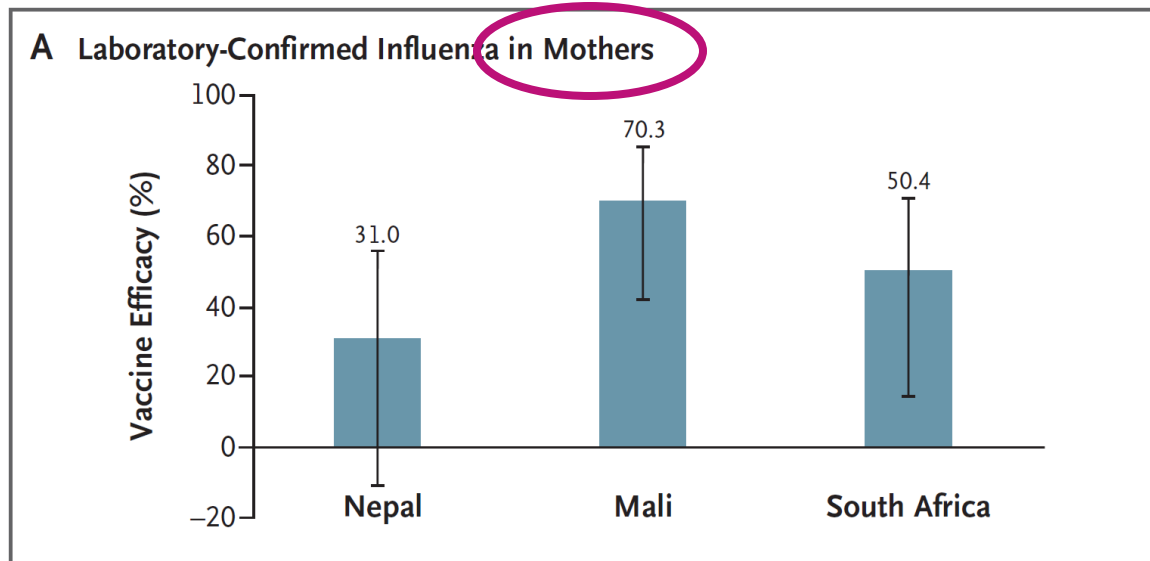
# Infants aged <1 year are more likely to need hospitalisation or to die from complications of influenza



# Efficacy of influenza vaccination during pregnancy

Results from four RCTs show that maternal immunisation is efficacious

Estimated efficacy of influenza vaccination during pregnancy for preventing laboratory-confirmed influenza in infants and mothers

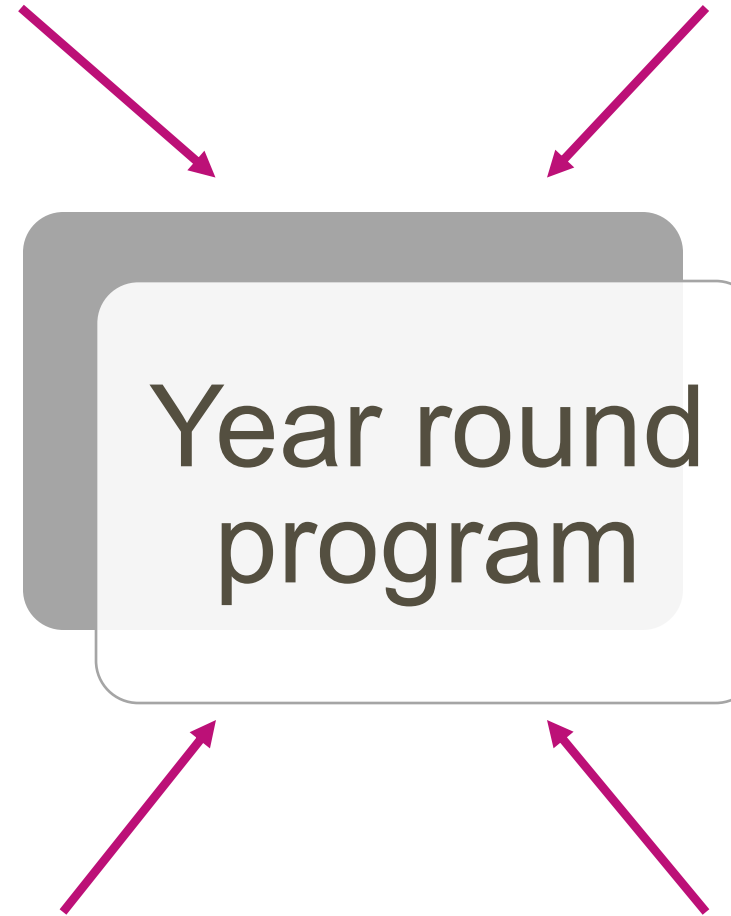


# Influenza Recommendations

Any time in pregnancy

Every pregnancy

Year round program





# Pertussis

# The burden of pertussis impacts infants

In children aged <1 year with pertussis disease in the USA:

**~50%**

require hospital treatment



Hospitalisation rates are highest in those aged **<3 months**, followed by those aged **3–6 months**

Complications include:



Apnoea  
**61%**



Pneumonia  
**23%**



Convulsions  
**~1%**



Encephalopathy  
**0.3%**

**1 in 100**

might die



# Three infant deaths from pertussis reported in 2023 in New Zealand

## Pertussis deaths in New Zealand without community transmission—an infant immunity gap?

Peter B. McIntyre,<sup>a,\*</sup> Emma Best,<sup>b</sup> Catherine A. Byrnes,<sup>b</sup> Owen Sindair,<sup>c</sup> Adrian Trenholme,<sup>b</sup> and Cameron C. Grant<sup>b</sup>

<sup>a</sup>Dunedin School of Medicine, University of Otago, New Zealand

<sup>b</sup>Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

<sup>c</sup>Te Whatu Ora Health New Zealand Waitemata, New Zealand

Attention was first drawn to development of a post-COVID “immunity debt” in children in late 2021, attributed to reduced community exposure to pathogens transmitted by the respiratory route.<sup>1</sup> Subsequent evidence from multiple European countries has supported this concept for both viruses (especially respiratory syncytial virus (RSV)) and bacteria (especially invasive disease due to Group A Streptococcus), supported by no increase in invasive bacterial diseases not transmitted by

Organization in 2014—the historical New Zealand rate of 10.1 was higher than Australia, Canada, Denmark, and Sweden (3.7–4.2) but comparable to Israel, Portugal and England and Wales (7.4–8.8).<sup>6</sup> A cluster of 14 deaths in 2012 in England and Wales (19.1 per million live births),<sup>6</sup> prompted a precedent-setting emergency maternal pertussis vaccination programme but occurred in the context of large increases in notified pertussis, especially among adolescents.<sup>7</sup>



The Lancet Regional  
Health - Western Pacific  
2023;37: 100850

Published Online 20 July  
2023  
<https://doi.org/10.1016/j.lanwpc.2023.100850>

# Effectiveness of pertussis vaccination during pregnancy

Results from two studies in England show maternal vaccination is effective

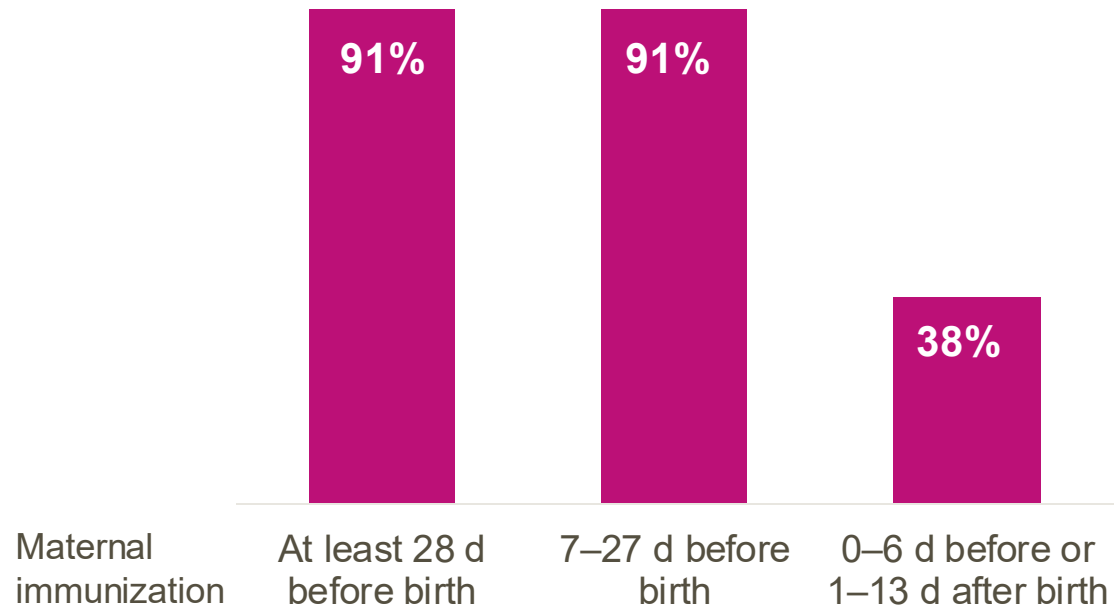
Effectiveness of maternal pertussis vaccination in England: an observational study

*Gayatri Amirthalingam, Nick Andrews, Helen Campbell, Sonia Ribeiro, Edna Kara, Katherine Donegan, Norman K Fry, Elizabeth Miller, Mary Ramsay*

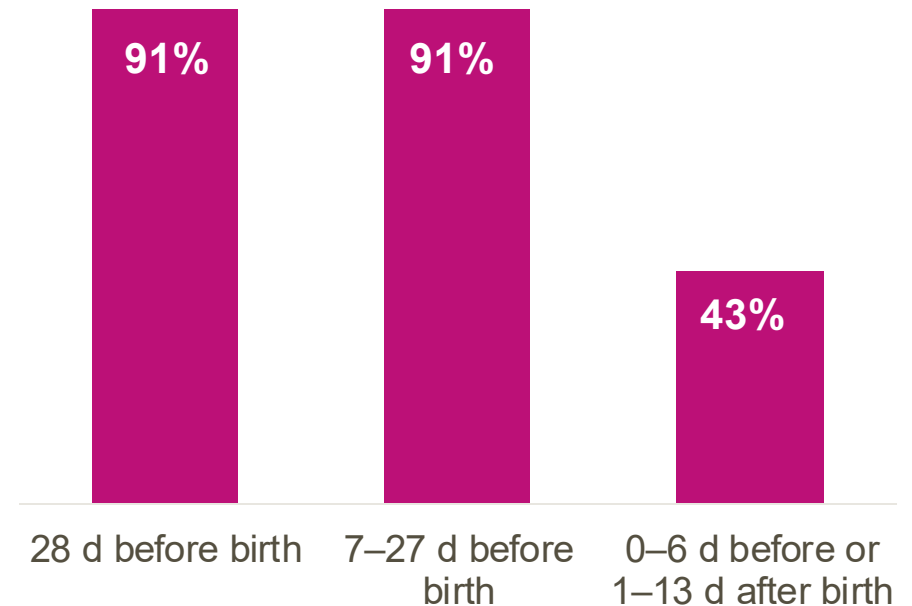
Sustained effectiveness of the maternal pertussis immunization program in England 3 years following introduction

*Gayatri Amirthalingam, Helen Campbell, Sonia Ribeiro, Norman K Fry, Mary Ramsay, Elizabeth Miller, Nick Andrews*

## Vaccine effectiveness in infants <3 months of age



## Vaccine effectiveness

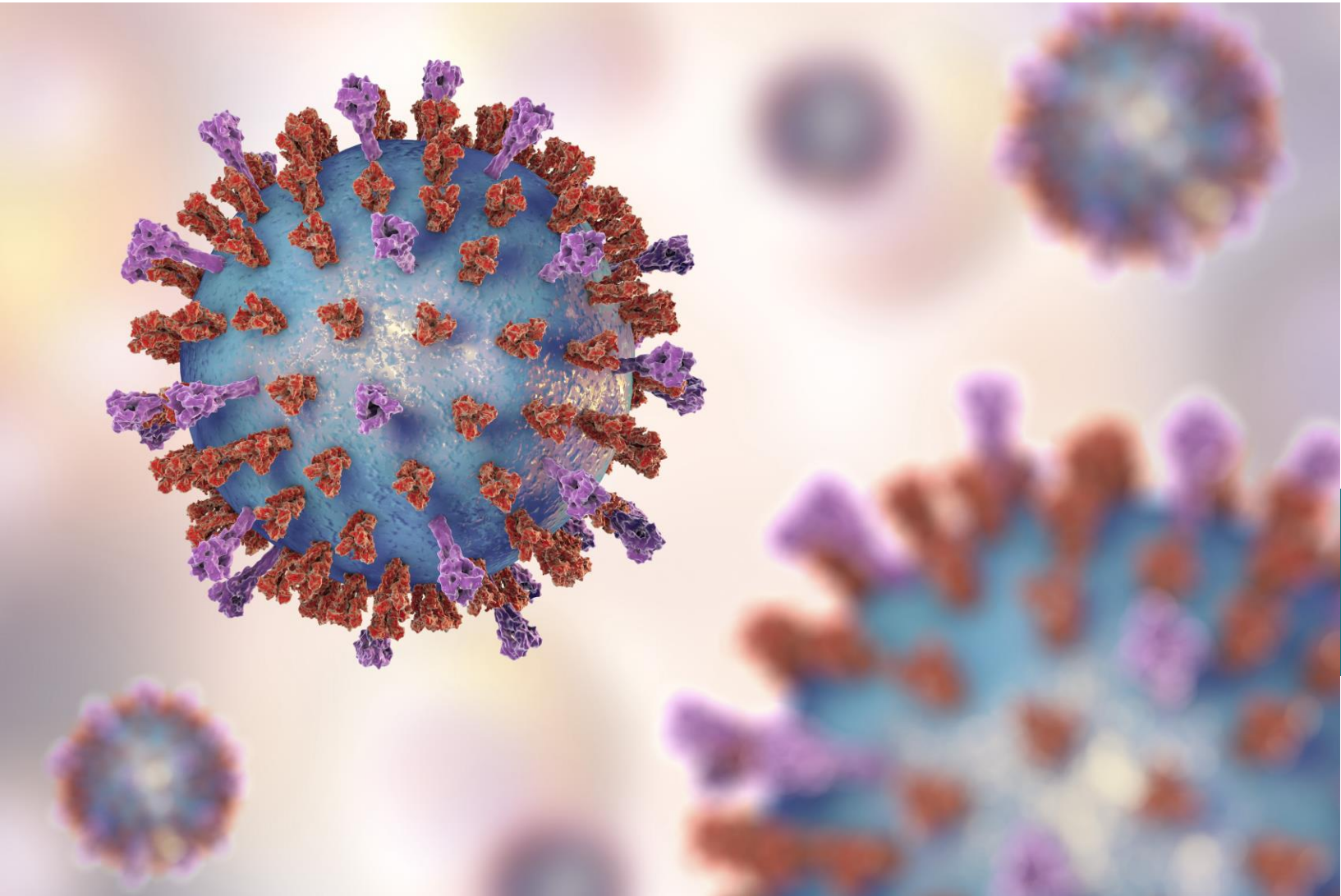


## Pertussis Recommendations

From 20  
weeks

Every  
pregnancy

Year round  
program

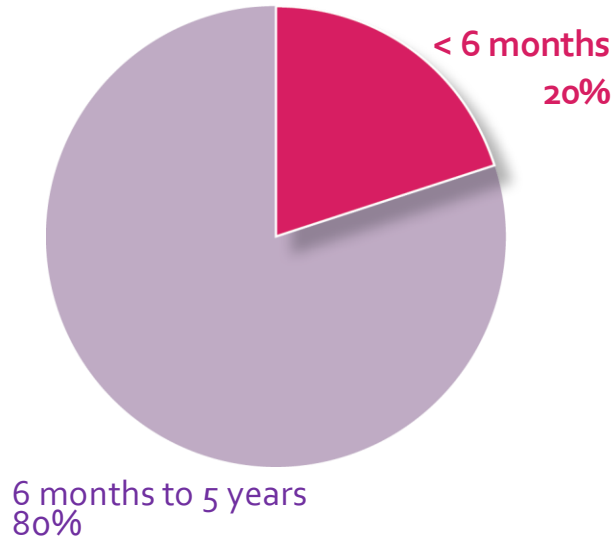


**RSV**

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

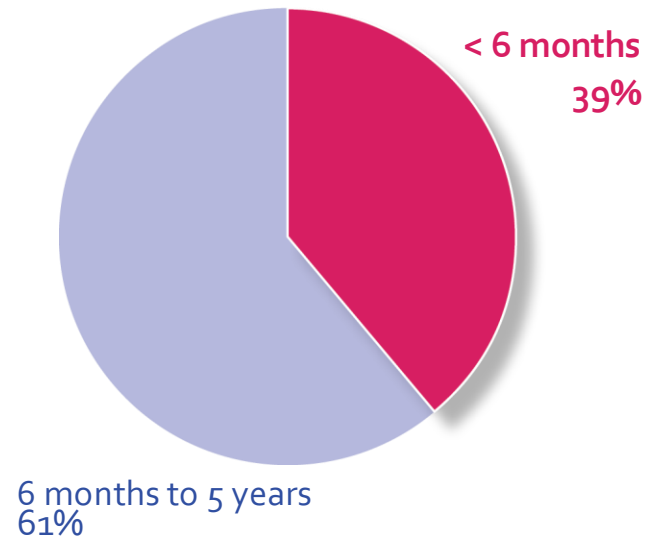
LEADING CAUSE OF SEVERE RESPIRATORY INFECTION

**33,000,000**  
episodes



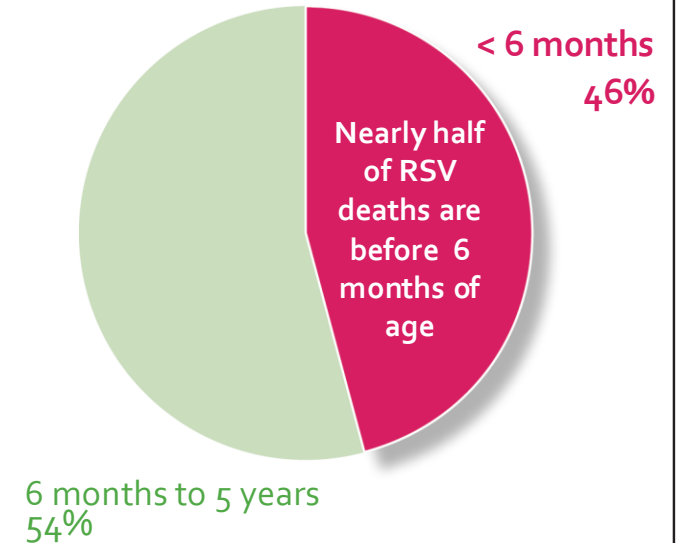
LEADING CAUSE OF PEDIATRIC HOSPITALIZATION

**3.6 million**  
hospitalizations



IMPORTANT CAUSE OF PEDIATRIC MORTALITY

**101,000**  
deaths



TOTAL GLOBAL CHILD MORTALITY DUE TO RSV

**3.6%**  
< 6 MONTHS

**2.3%**  
< 5 YEARS

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

In fact, most global RSV deaths occur



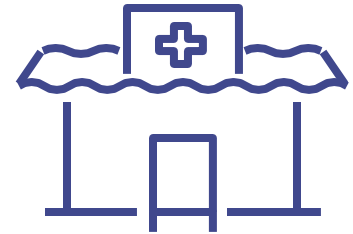
in infants born  
**full term**



**before 3 months**  
of age



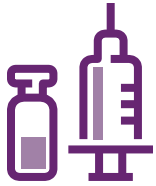
in **low- and**  
**middle-income**  
areas



**outside the**  
healthcare system

# Phase 3 clinical study evidence

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



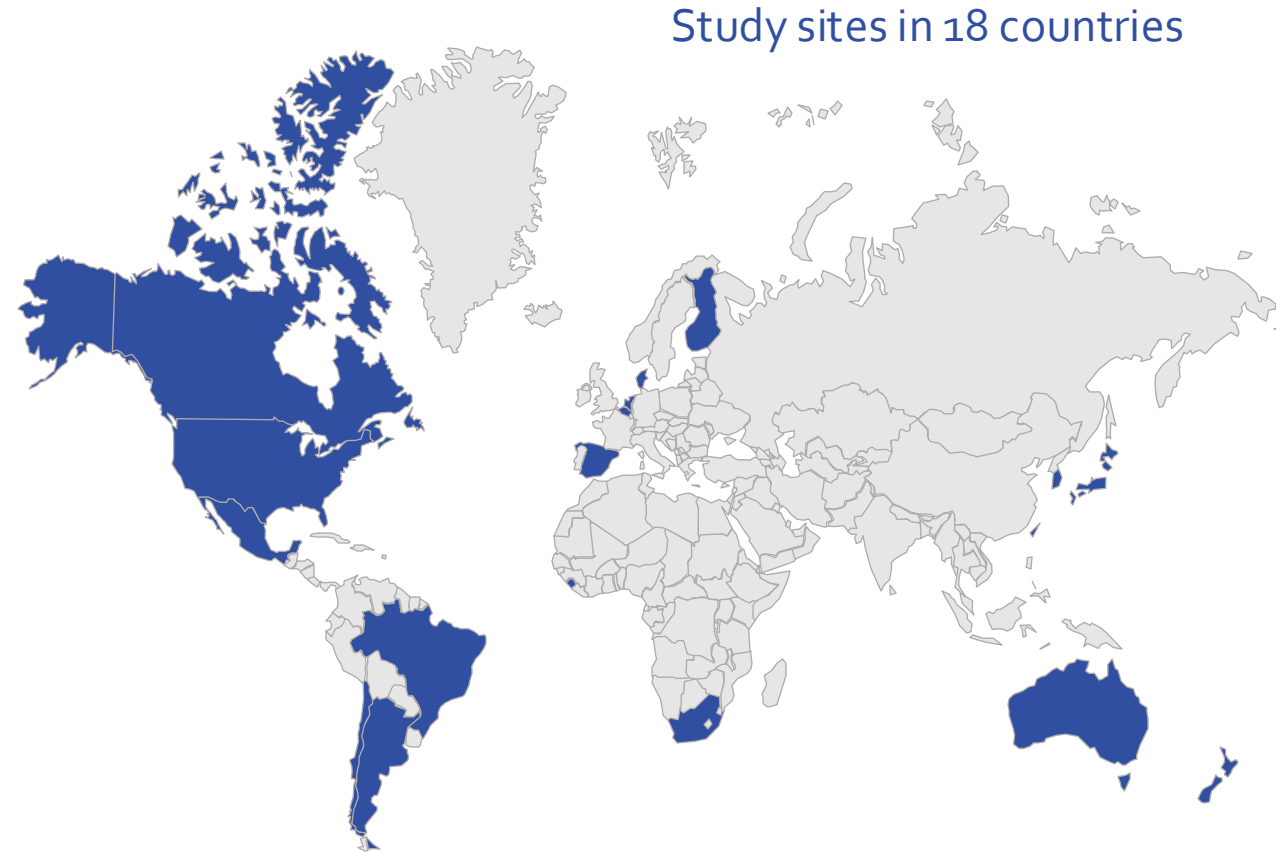
Study product: Abrysvo™



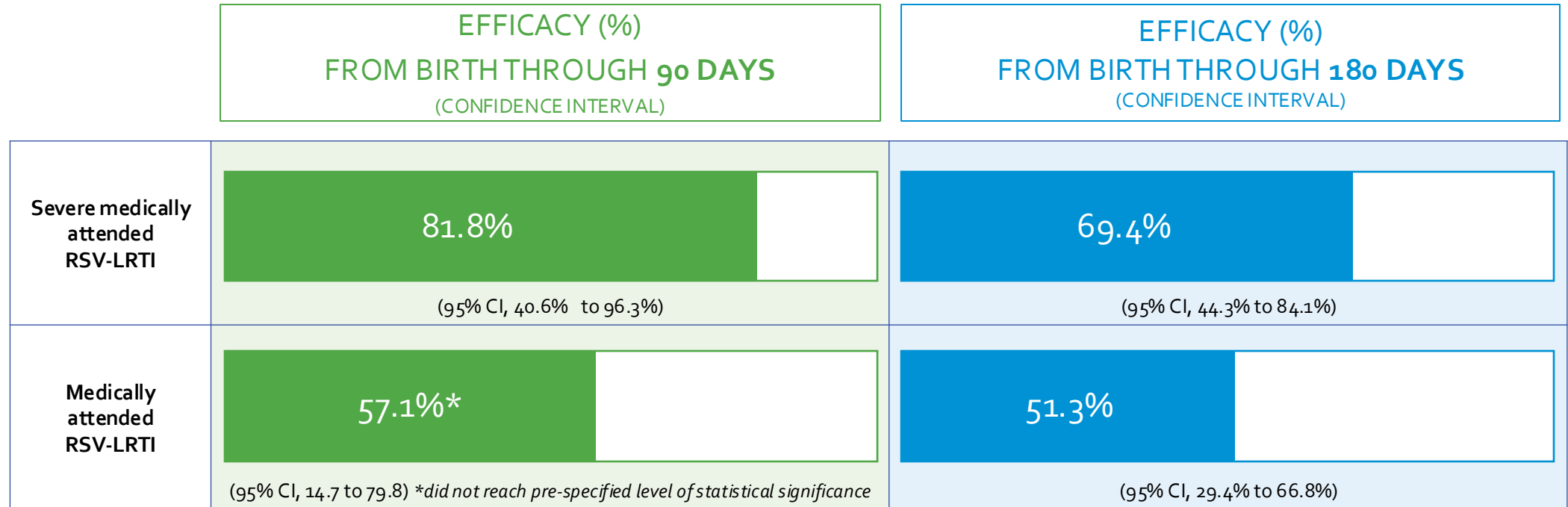
7,392 pregnant participants  
≤49 years between ≥ 24 and ≤ 36  
weeks gestation



7,128 infants enrolled



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

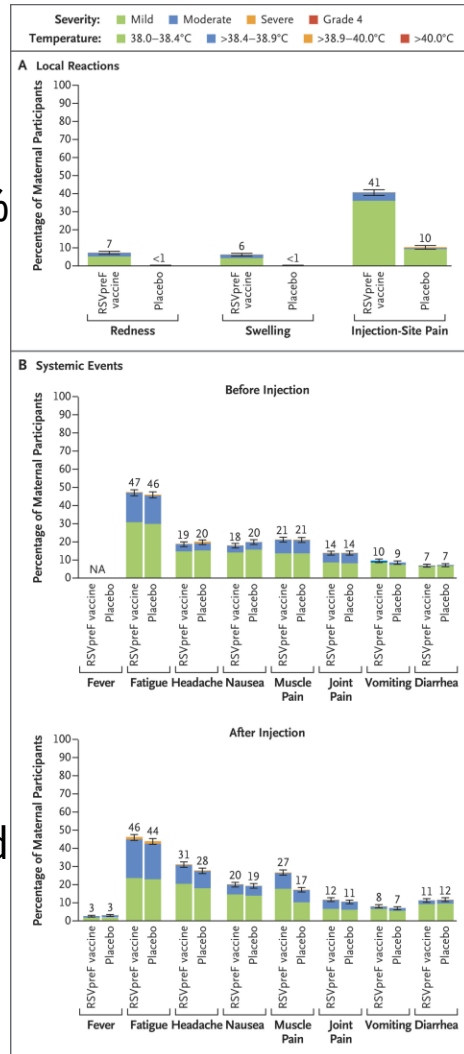


**Efficacy remains high through first, most critical 6 months after birth—  
when infants are at greatest risk.**

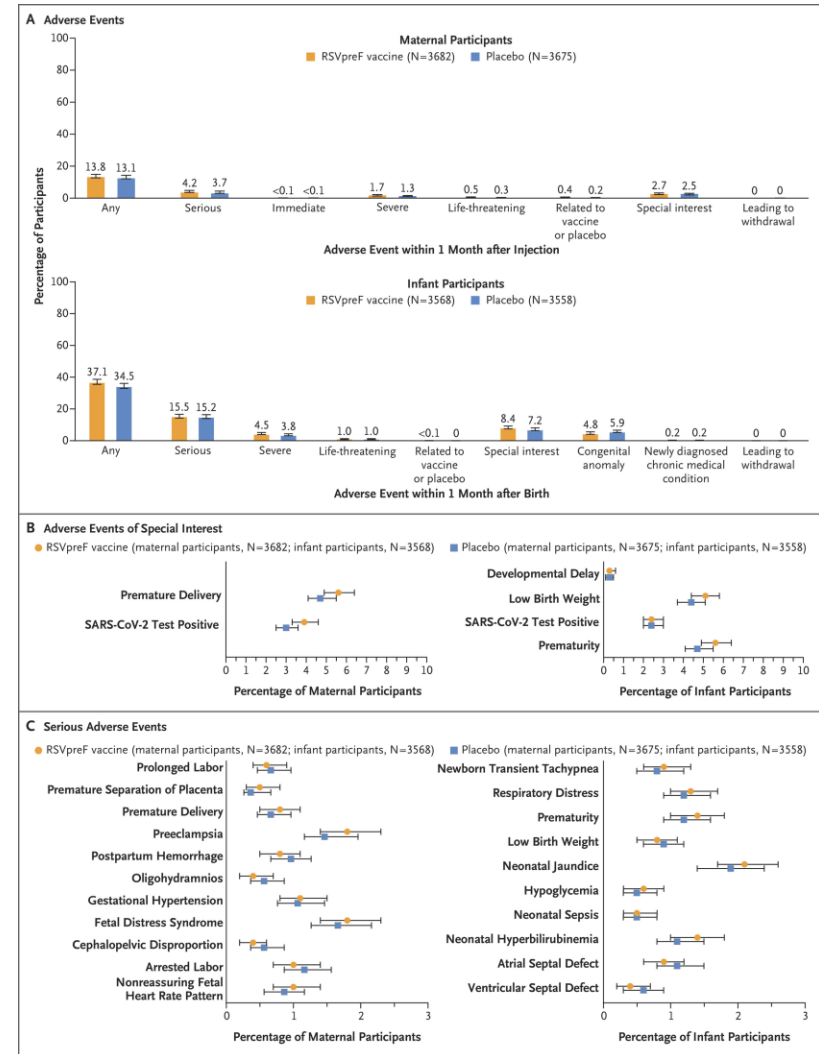
# Safety

Local reactions  
Injection site pain  
higher approx. 40%

Systemic mild-mod  
Low rates fever  
Myalgia 27%



## Adverse events



## AESI- PTB

## SAEs- maternal and infant



# Gestational age and AESI of pre-term birth

## Context

Trial of a similar maternal RSV vaccine was halted due to an imbalance of neonatal deaths due to preterm births

## Preterm birth and low birth weight outcomes in Abrysvo vaccine phase 3 trial data

	Abrysvo vaccine group N=3,568	Placebo group N=3,558
Preterm birth (<37 weeks)	5.7% (95% CI: 4.9%, 6.5%)	4.7% (95% CI: 4.1%, 5.5%)
Late preterm birth (≥34 to 37 weeks)	5.0% (CI not reported)	4.4% (CI not reported)
Infant deaths (all-cause) through 24 months of age	5 (0.1%)*	12 (0.3%)
*1 death was in an infant with extreme prematurity (27 weeks) and prematurity-related complications, and FDA was unable to exclude possibility of relationship to investigational product		



# Gestational age and AESI of pre-term birth

## Time from vaccination to birth among preterm and term births: Abrysvo vaccine phase 3 trial data

Days from Vaccination to Birth	RSVpreF 120 µg (N=3568) n (%)	Placebo (N=3558) n (%)	Total (N=7126) n (%)
<b>Preterm deliveries</b>	201	169	370
≤7 days <sup>a</sup>	11 (5.5)	13 (7.7)	24 (6.5)
>7 days to ≤30 days <sup>a</sup>	69 (34.3)	58 (34.3)	127 (34.3)
>30 days <sup>a</sup>	121 (60.2)	98 (58.0)	219 (59.2)
<b>At term deliveries</b>	3364	3386	6750
≤7 days <sup>a</sup>	1 (<0.1)	2 (<0.1)	3 (<0.1)
>7 days to ≤30 days <sup>a</sup>	516 (15.3)	498 (14.7)	1014 (15.0)
>30 days <sup>a</sup>	2847 (84.6)	2886 (85.2)	5733 (84.9)

Source: Pfizer CSR 1008  
 Abbreviations: N=number of participants having birth date in the specified vaccine group. This value is the denominator for the percentage calculations; n = Number of participants in the specified category.  
 Note: Six participants have missing gestational age at birth in database, so are not included in counts above. Preterm/at term deliveries are determined based on gestational age at birth. Preterm=gestational age at birth less than 37 weeks. At term=gestational age at birth of 37 weeks or more. Number of days between vaccination and birth is calculated as birth date - vaccination date.  
 a. Percentages for this row are based on the number of preterm/at term deliveries, respectively.

## Subgroup analysis of gestational age at birth among live births by country income level: Abrysvo vaccine phase 3 trial data

Country / Gestational Age at Birth	RSVpreF N=3568 n (%)	Placebo N=3558 n (%)
<b>High income</b>	2494	2484
≥24 weeks to <28 weeks	0	1 (<0.1)
≥28 weeks to <34 weeks	13 (0.5)	7 (0.3)
≥34 weeks to <37 weeks	113 (4.5)	118 (4.8)
≥37 weeks to <42 weeks	2360 (94.6)	2351 (94.6)
≥42 weeks	6 (0.2)	5 (0.2)
<b>Upper middle income</b>	964	961
≥24 weeks to <28 weeks	1 (0.1)	0
≥28 weeks to <34 weeks	7 (0.7)	4 (0.4)
≥34 weeks to <37 weeks	64 (6.6)	35 (3.5)
≥37 weeks to <42 weeks	882 (91.5)	906 (94.3)
≥42 weeks	9 (0.9)	15 (1.6)

In high-income countries, preterm birth rate was 5.1% in Abrysvo recipients vs 5.1% placebo recipients.

Imbalance was most prominent in upper middle-income countries: 7.5% in Abrysvo recipients vs. 4.1% (39/961) in placebo recipients

Median gestational age at vaccination in trial was 31 weeks

Majority of preterm births occur >30 days from vaccination

# RSVpreF Vaccine, Preterm Birth, and Small for Gestational Age at Birth Preliminary Results from The Vaccine Safety Datalink

Malini DeSilva, MD, MPH

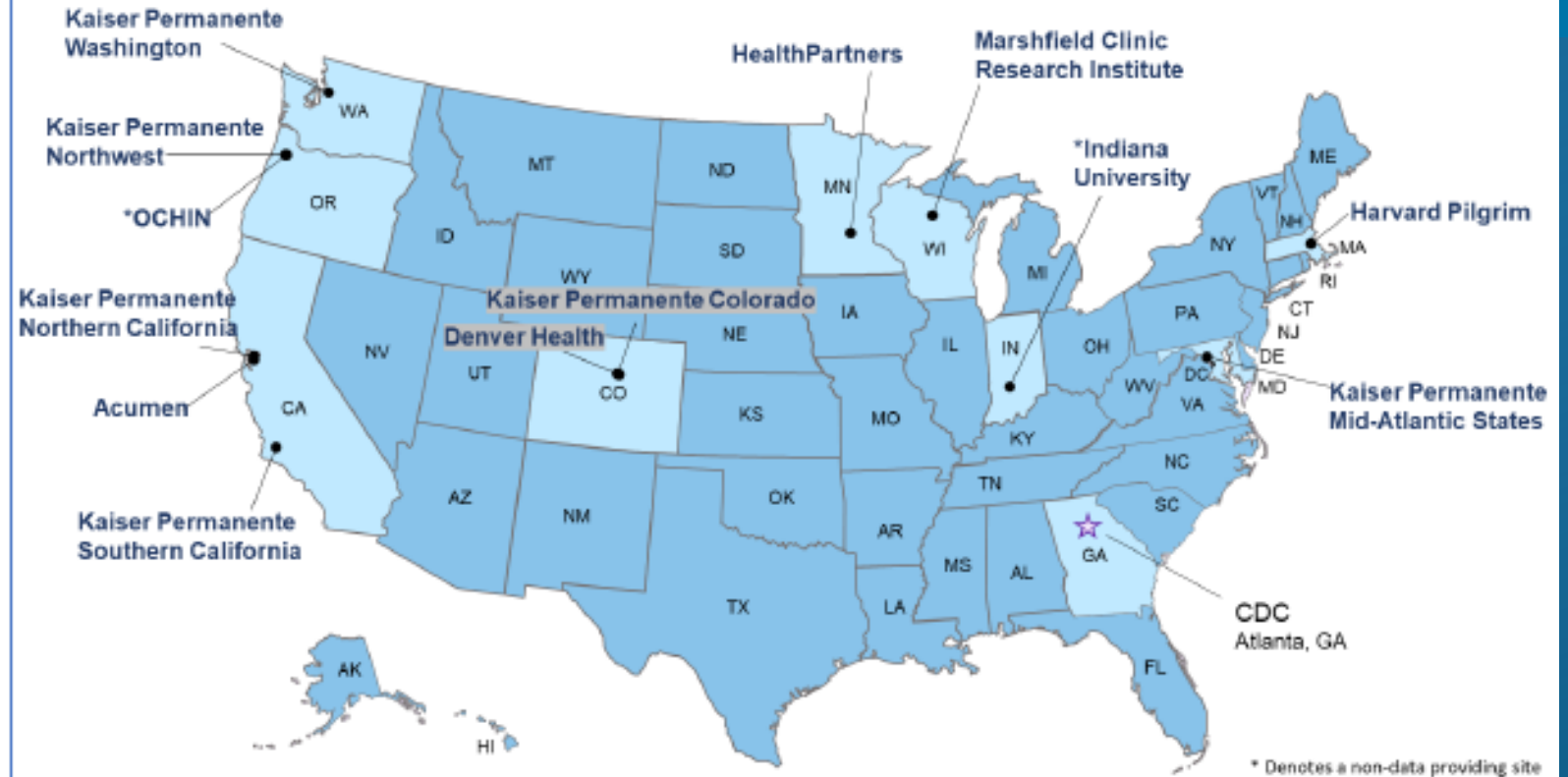
ACIP

October 23, 2024



# Vaccine Safety Datalink, 2024

- Collaborative project between CDC and 13 integrated healthcare organizations
- Monitors safety of vaccines used in the U.S., primarily through observational multisite studies of rare and serious events following vaccination
- Includes data on ~15.5 million individuals across all sites annually (~3-4% of U.S. population)
- Annual birth Cohort ~ 115,000
- Data is organized using a common data dictionary with standardized coding systems



# Matched analysis methods

- Pregnant persons 16–49 years with gestational age 30–<37 weeks during 9/22/2023–1/31/24 (2/29/24 for two sites)
- Target trial emulation design to compare vaccinated and unvaccinated persons at each gestational week
  - Pregnant persons exposed to RSVpreF vaccine matched 1:1 on VSD site and propensity to be vaccinated to unvaccinated pregnant persons during same gestational week
  - Unvaccinated index date = gestational day of vaccine
  - Matched pair censored if unvaccinated person later vaccinated
- Propensity to be vaccinated calculated individually for 2 sites and for all other sites combined
  - Maternal age at pregnancy start, calendar week at pregnancy start, number of weeks with prenatal care encounters, race/ethnicity, comorbidities (hypertension, diabetes mellitus, gestational hypertension, gestational diabetes, obesity, substance use), history of preterm labor, poor fetal growth, supervision of high-risk pregnancy, enrollment, and VSD site

## Preterm birth<sup>a</sup> risk among pregnant persons receiving RSV vaccine and unvaccinated matches, 30–36 weeks GA

	Matched pairs, N	RSV vaccinated		Unvaccinated match		Risk Ratio (95% CI)
		N events*	Preterm birth %	N events*	Preterm birth %	
Overall <sup>b</sup>	14,099	571	4.0	637	4.5	0.90 (0.80–1.00)
32–36 weeks	13,965	563	4.0	628	4.5	0.90 (0.80–1.00)

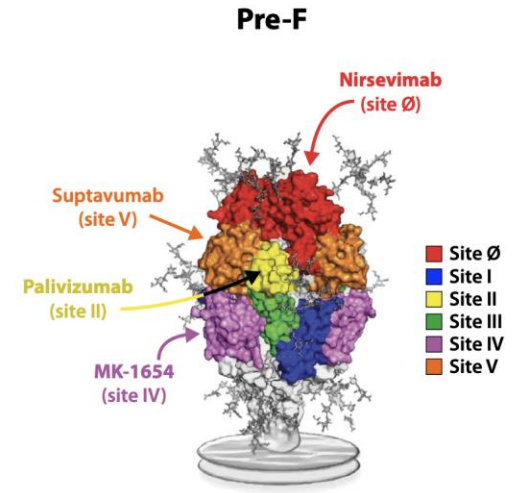
GA = gestational age

<sup>a</sup>Preterm birth = birth <37 weeks gestational age

<sup>b</sup>N RSV vaccines administered <32 weeks = 134 (0.95%)

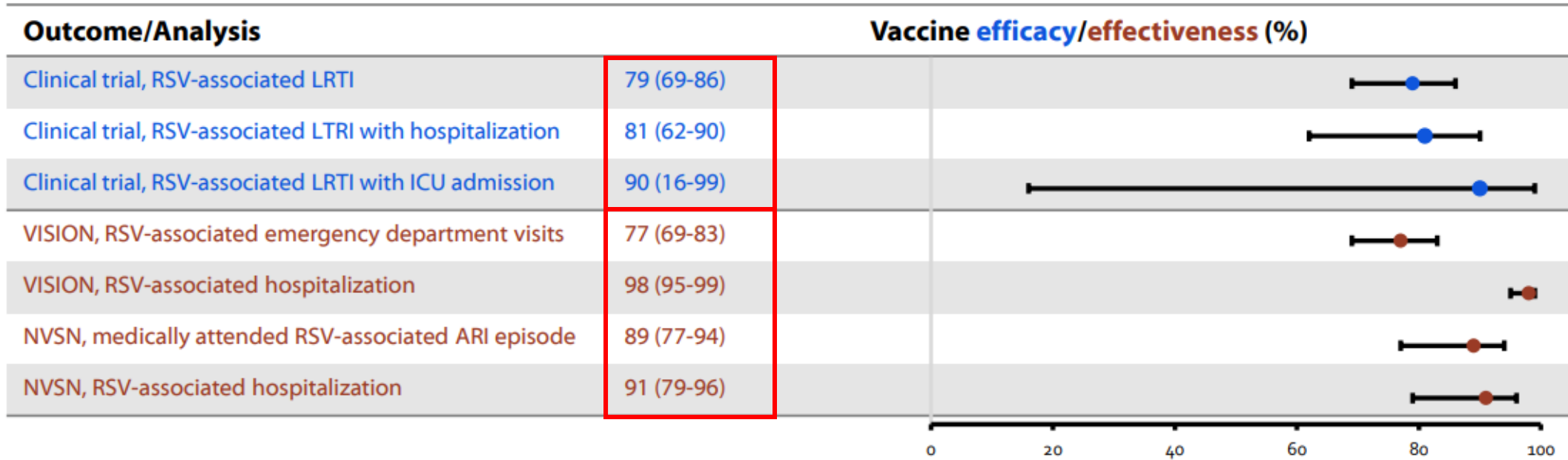
\*Events only included through date of censoring when unvaccinated pair crosses over to vaccinated

# Nirsevimab (BEYFORTUS)



- Nirsevimab is a human immunoglobulin G1 kappa (IgG1 $\kappa$ ) monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology
- It binds to a highly conserved epitope in antigenic site on the prefusion (F) protein for RSV subtype A and B strains
- Nirsevimab has an extended half-life of **@ least 5-months**

# Observational data indicate nirsevimab is working as expected (vs. RCT results) during the first RSV season after approval among infants in their first RSV season



Results may not be comparable across studies due to differences in outcome definitions, timing, and other factors.

<https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm>  
 RCT = randomized clinical trial | ARI = acute respiratory illness

# Both products protect infants via passive immunization, but have differences



## Maternal vaccine



## Long-acting mAb

### PROTECTION

Maternal antibodies protect infant in the first 6 months **after birth**.

mAbs protect for at least 5 months **after administration**, whenever given.

### HOW IT WORKS

- Given to pregnant women
- Induces antibodies against **multiple** neutralizing sites on the Fusion protein in the mother and passed to infant.
- Much less likely that a virus mutation would render induced antibodies ineffective.

- Given to infants at birth or as soon as possible
- Antibodies against a **single** potent neutralizing site on the Fusion protein.
- A virus mutation could render the antibody ineffective.

### COST

- Gavi plans to support a maternal RSV vaccine for eligible countries.\*
- A pricing agreement\*\* on multidose vial can make RSV maternal vaccine more accessible for GAVI-eligible countries.

Gavi plans to support a long-acting mAb when an affordable product is available for eligible countries.\*

### AVAILABILITY

Earliest availability in low- and middle-income settings likely in **2025**.

Uncertain timing of availability in low- and middle-income settings due to price and supply barriers.

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

\*\* Media center announcement accessed at:

<https://www.gatesfoundation.org/ideas/media-center/press-releases/2022/09/gates-foundation-announces-grants-to-reduce-infant-mortality>

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

# ATAGI Recommendations

Pregnant women are recommended to receive a vaccine from 28 weeks

Abrysvo is the only RSV vaccine approved for use in pregnancy NOT Arexvy

Reduces risk of disease by around 70% in infants <6 months of age

Advice on repeat vaccination will be provided when data available

Need 2 weeks post vaccination for adequate protection

If inadvertently vaccinated <28 weeks a repeat dose not indicated

# Victorian Government funded infant program - nirsevimab



## Neonate program

**DOB: 1 April 2025 - 30 September 2025**

### Infants born to:

- mothers who **did not receive** Abrysvo® RSV vaccine during pregnancy **or**
- Abrysvo® RSV vaccine was administered <2 weeks before birth,
- high risk infants\* regardless of maternal vaccination status

\*[Australian Immunisation Handbook | RSV](#)



## Catch up - 1<sup>st</sup> season

**DOB: 1 October 2024 - 31 March 2025**  
(up to 8 months of age)

### Infants born to:

- mothers who **did not receive** maternal Abrysvo® RSV vaccine during pregnancy **or**
- Abrysvo® RSV vaccine was administered <2 weeks before birth,
- high risk infants\* regardless of maternal vaccination status

\*[Australian Immunisation Handbook | RSV](#), age limit not applicable



## Catch up - 2<sup>nd</sup> RSV season

**DOB: on or after 1 October 2023**

### Children vulnerable to severe RSV:

- Aboriginal Torres Strait Islander children
- young children with conditions associated with increased risk of severe RSV disease\*\*

\*\*[Conditions associated with increased risk](#)

## 2025 RSV season



**Starts 1 April 2025**

**Ends 30 September 2025**

# PRACTICAL SUGGESTIONS FOR IMPLEMENTATION



INFLUENZA, PERTUSSIS, RSV, COVID  
CAN BE CO-ADMINISTERED



ONLY CONTRAINDICATIONS TO RSV  
VACCINES AND IMMUNIZATION  
PRODUCTS ARE ANAPHYLAXIS AFTER  
A PREVIOUS DOSE OF THE SAME  
PRODUCT OR ANY COMPONENT OF  
AN RSV VACCINE



CHECK AIR BEFORE ADMINISTERING  
AN RSV VACCINE OR IMMUNIZATION  
PRODUCT



NO RSV VACCINE IS FUNDED FOR  
OLDER ADULTS AND MEDICALLY AT  
RISK INDIVIDUALS

# Common barriers to vaccination in pregnancy

## Pregnant women

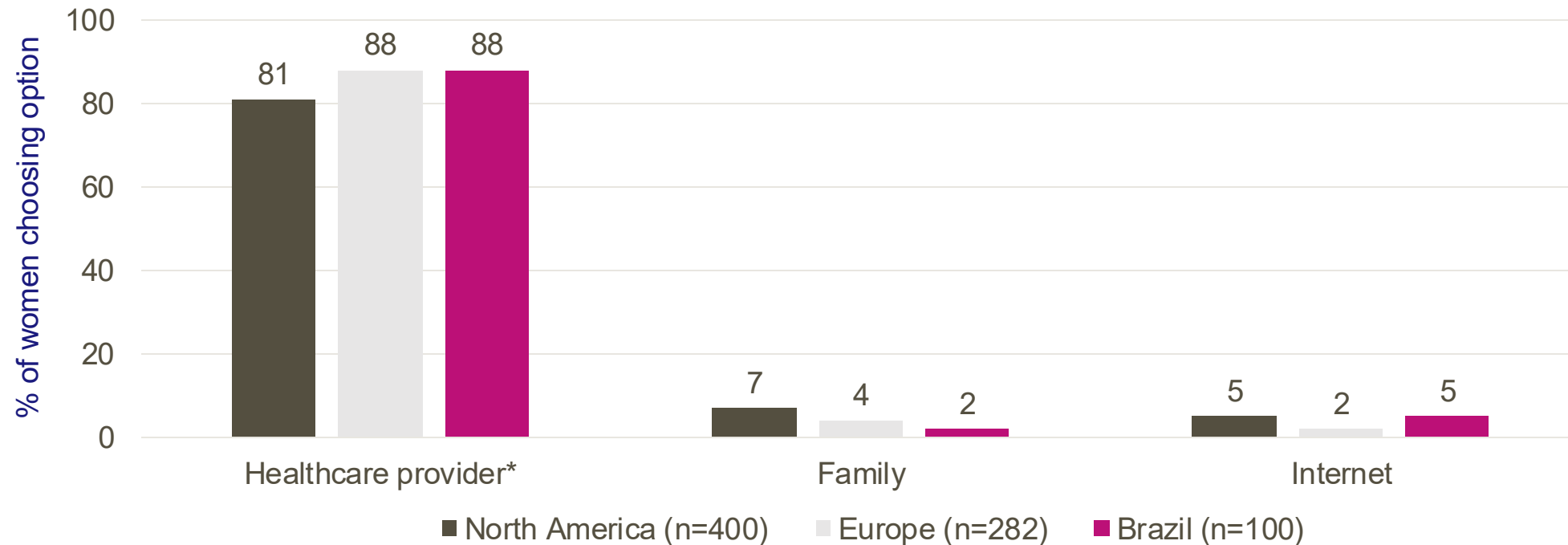
- Concerns about **safety/side effects/harm**
- Perceiving themselves **not to be at risk** of the disease
- Belief that the **disease is not serious**
- **Misconceptions** that the vaccine causes disease, illness, death or other negative outcomes
- **Fear of needles**
- **No provider recommendation**
  - Receipt of a healthcare provider's recommendation was the factor most frequently reported as a reason for vaccination among pregnant women

## Healthcare providers

- **Lack of knowledge/education**
- Considered vaccination **outside their remit**
- Not enough **time**
- **Concerns** about vaccine **safety and efficacy**
- Perceived low risk of disease
- Perceived **lack of clinical trial data** with vaccines in pregnant women
- Administrative difficulties (e.g., logistical issues around staff, obtaining the vaccine, financial concerns)

# Healthcare providers are regarded by women as the most credible source of information on vaccination in pregnancy

Online survey of 782 pregnant women from North America, Europe and Brazil  
*Who is the most credible source of information on vaccination in pregnancy?*



\*Physician or midwife/nurse practitioner.

Patwardhan M, Gonik B. J Womens Health Safety Res 2019;3:90-8.

# Understand the reasons for vaccine hesitancy and target these in discussions



HCP, healthcare professional.

MacDougall DM, et al. Hum Vaccin Immunother 2016;12:857–65.

# Implementation in the antenatal setting

Principles and  
considerations for adding  
a vaccine to a national  
immunization programme

FROM DECISION TO IMPLEMENTATION AND MONITORING



RESEARCH

# An evaluation of strategies to achieve greater than 90% coverage of maternal influenza and pertussis vaccines including an economic evaluation

Michelle L. Giles<sup>1,2\*</sup>, Kong Khai<sup>1,3</sup>, Sushena Krishnaswamy<sup>1,3</sup>, Karen Bellamy<sup>4</sup>, Margaret Angliss<sup>4</sup>, Christopher Smith<sup>5</sup>, Olivia Fay<sup>5</sup>, Paul Paddle<sup>6</sup> and Beverley Vollenhoven<sup>1,2</sup>

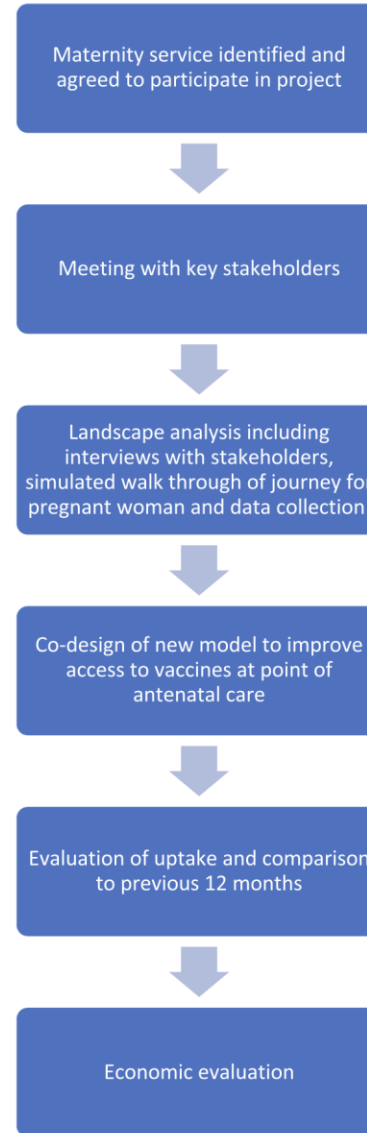


Fig. 1 An overview of the steps in the project

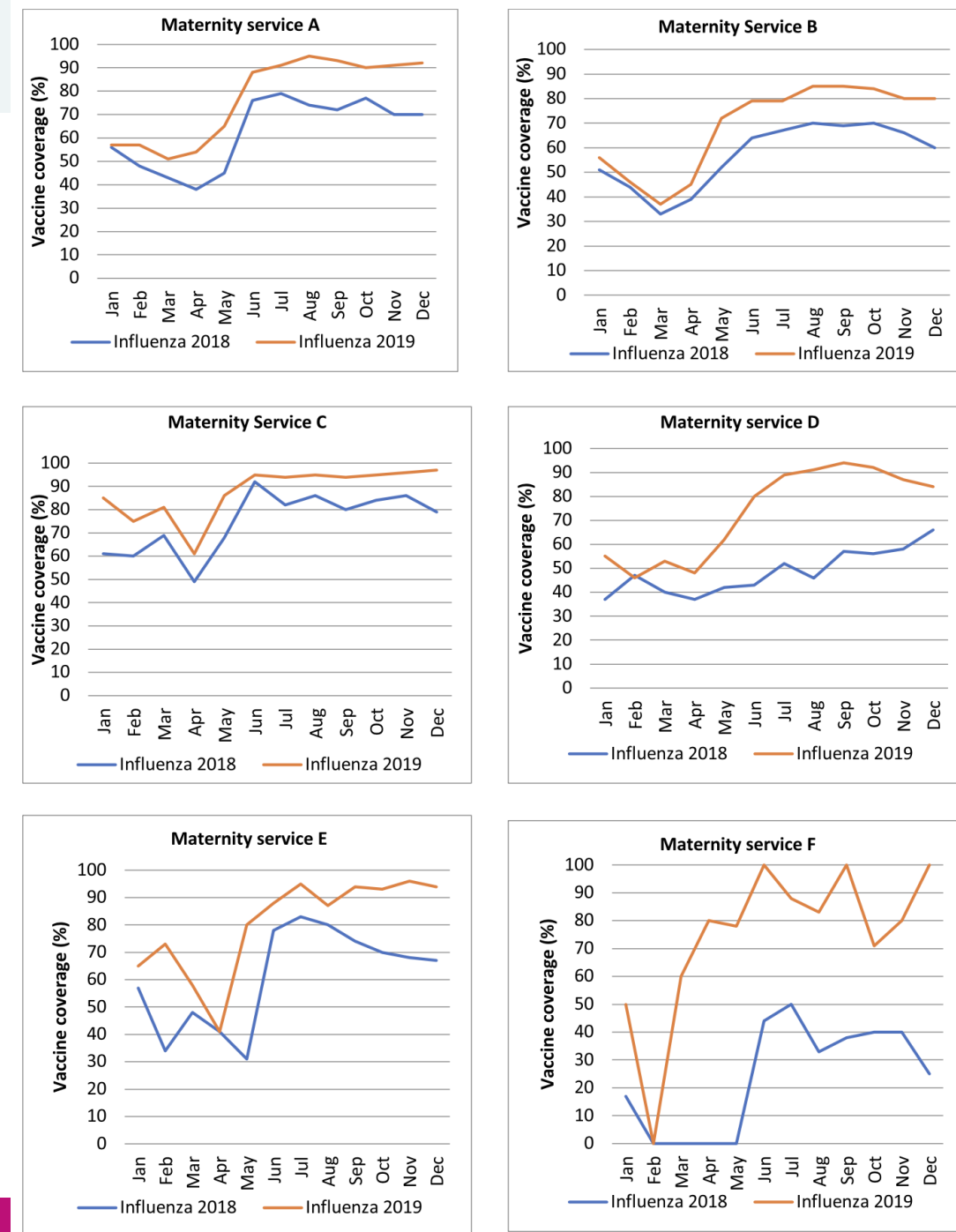
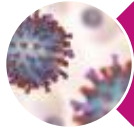


Fig. 2 Maternal influenza vaccine coverage per month (2018 compared to 2019) for each maternity service

## The future

Several vaccines are in development for use during pregnancy



HEV (hepatitis E virus)



GBS (group B streptococcus)



CMV (cytomegalovirus)



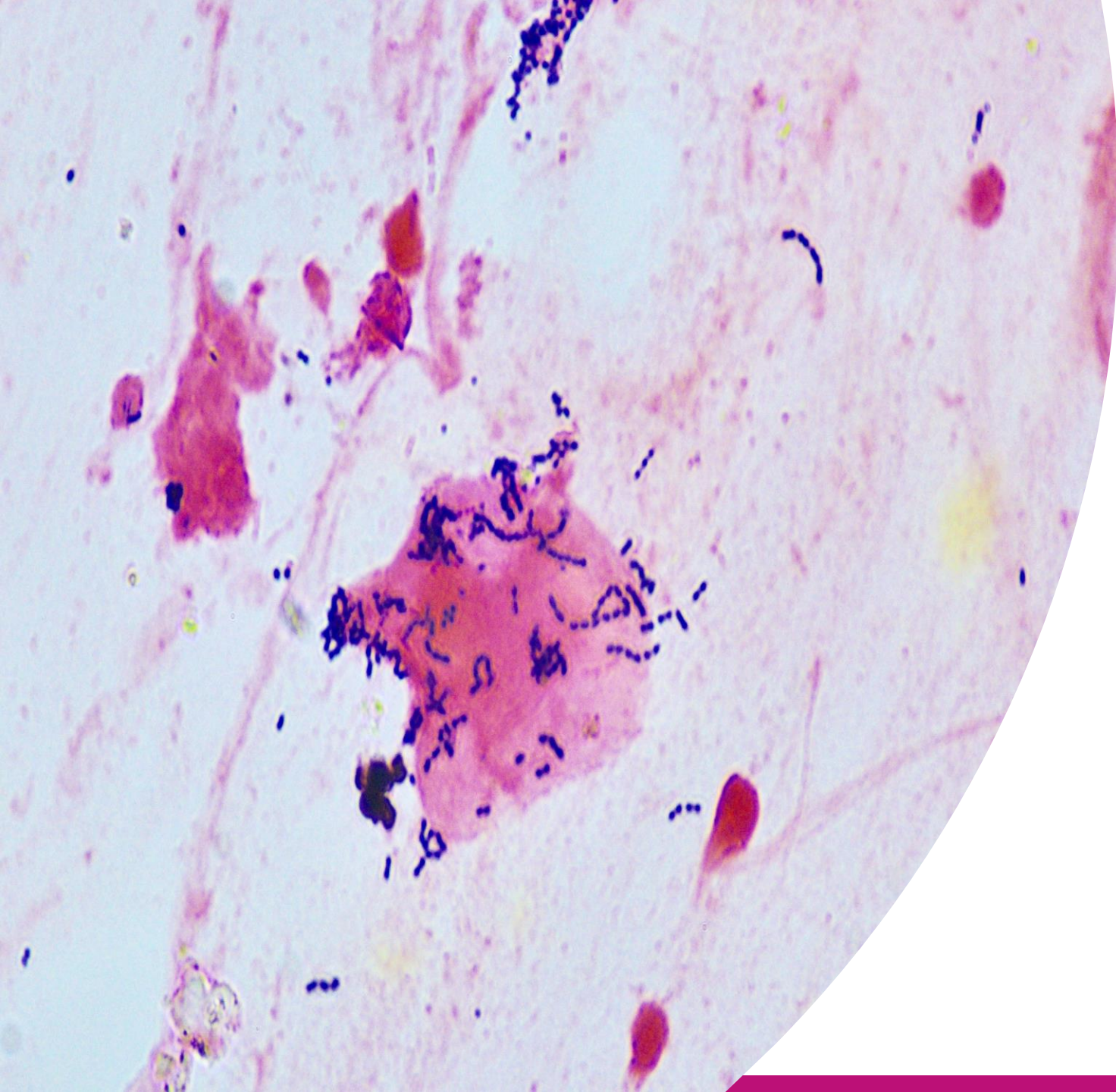
HSV (herpes simplex virus)



ZiV (Zika virus)



EBOV (Ebola virus)

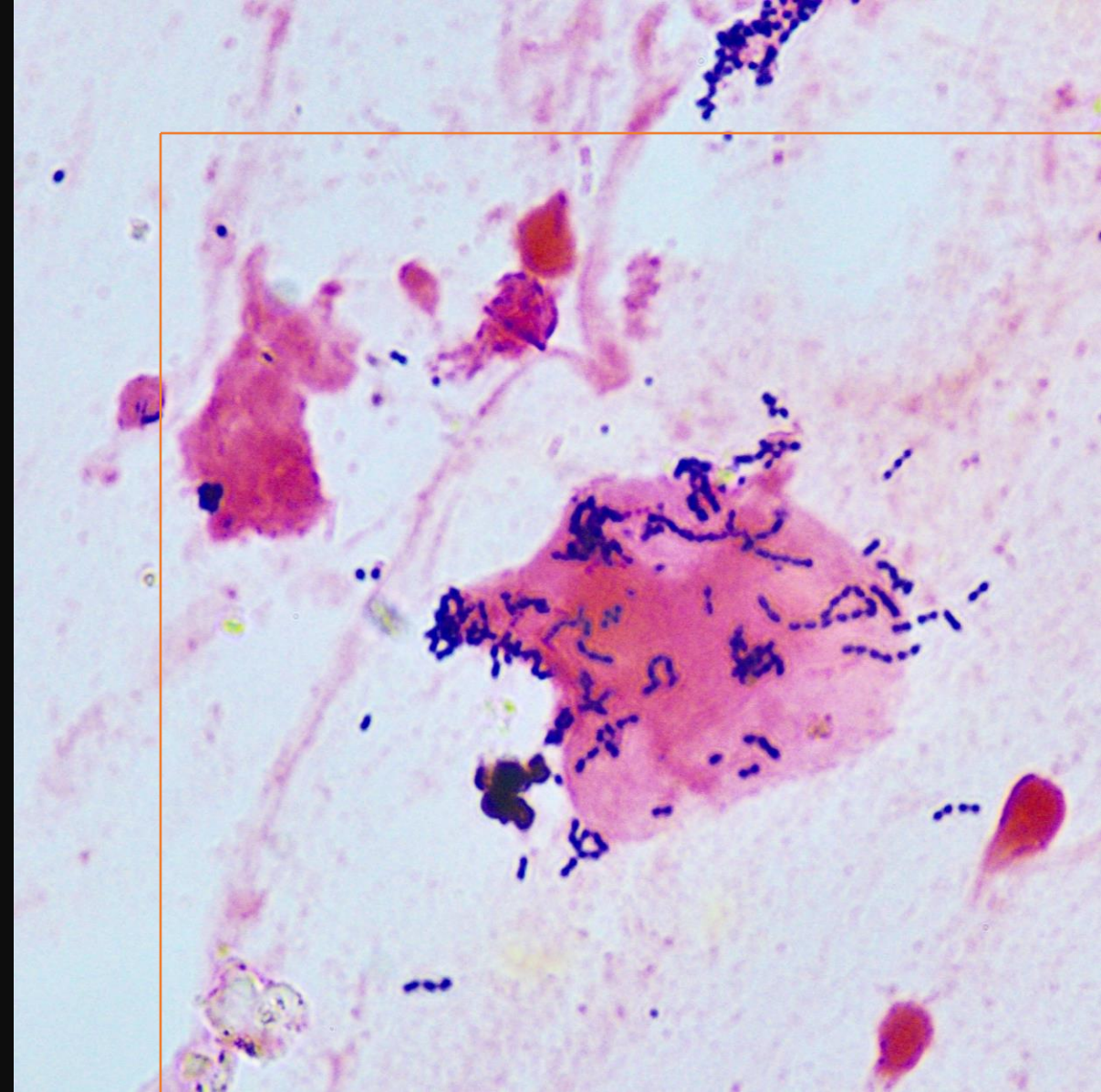


**Group B  
streptococcus**

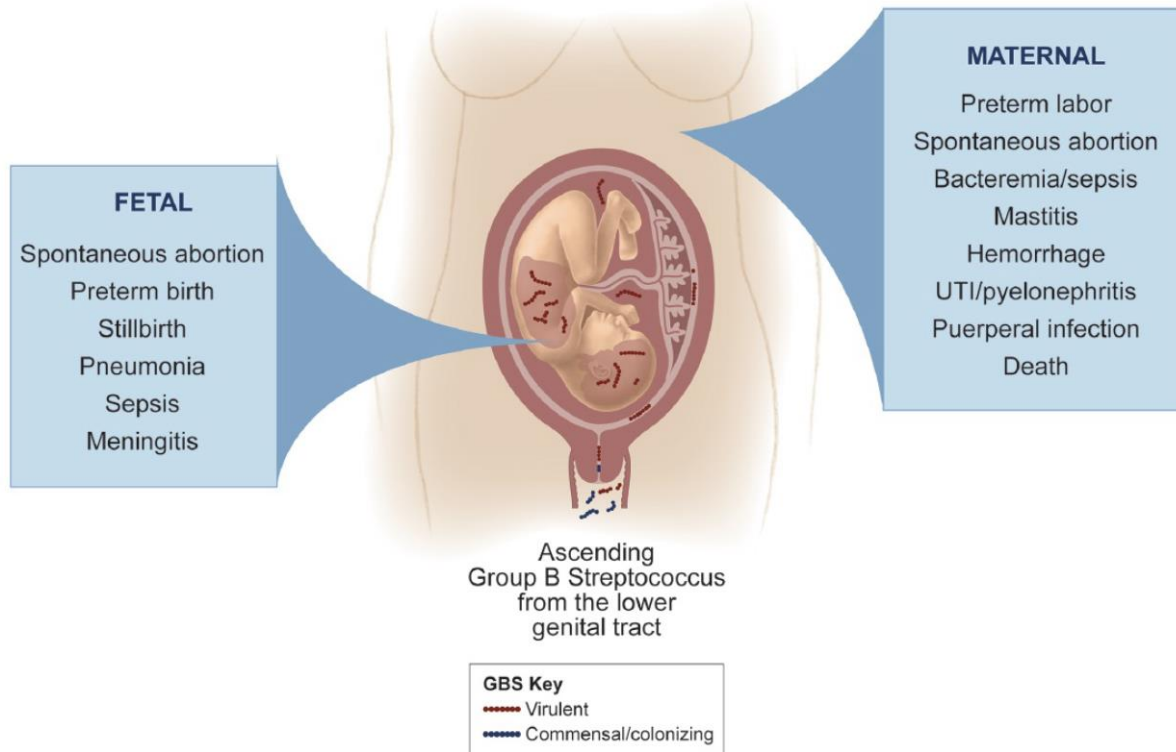
# Group B *Streptococcus*: the bacteria

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- Gram positive coccus
- Frequently colonizes the genital and GIT and URT in infants
- An important source of infection in 3 populations
  - Neonates
  - Pregnant individuals
  - Non pregnant adults

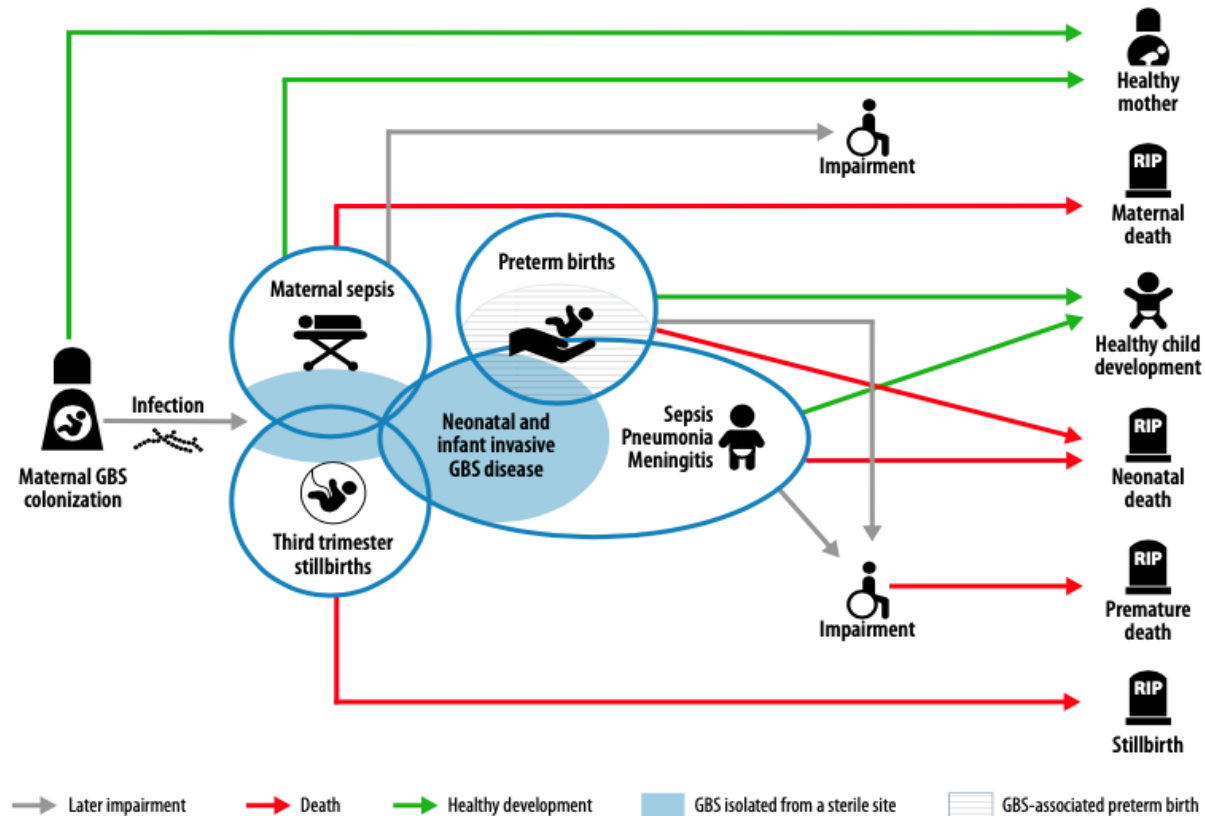


# STREPTOCOCCUS AGALACTIAE

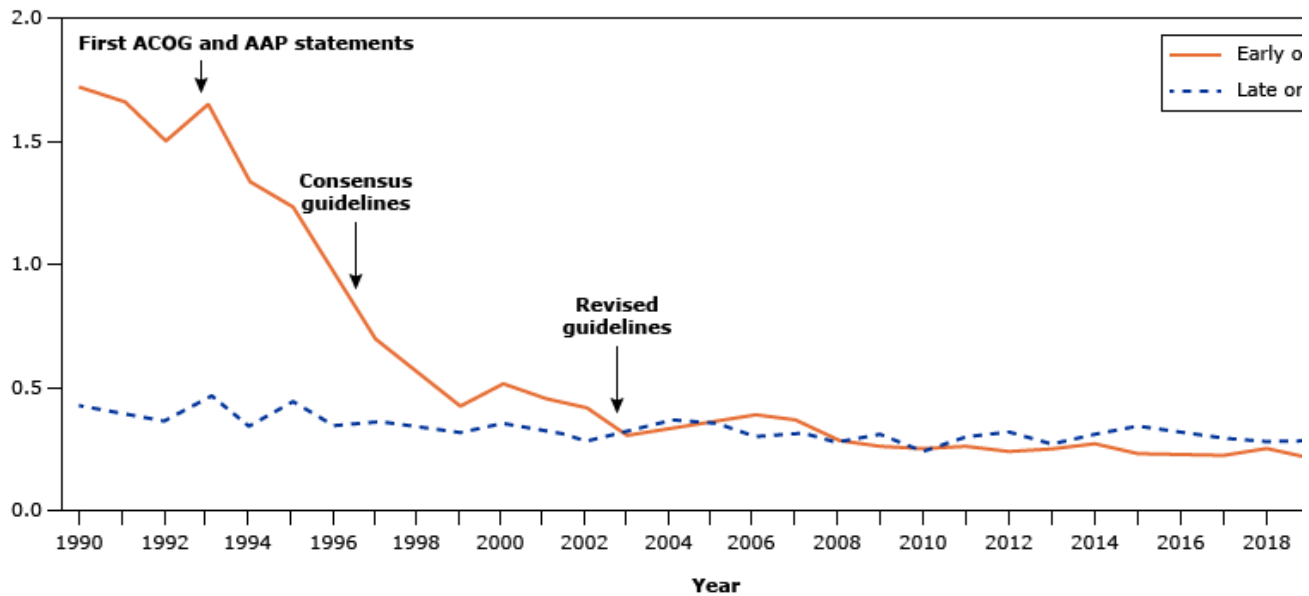


# Disease burden

Fig. 4. Group B streptococcus Natural History Model and case definitions\*



- 392,000 infants experience invasive GBS cases per year
  - 91,000 infant deaths
  - 40,000 neurodevelopmental impairment
  - 46,000 stillbirths
  - 518,000 preterm births
- Sub-Saharan Africa accounts for approximately 15% of the world's population but about half of the burden of GBS cases and deaths



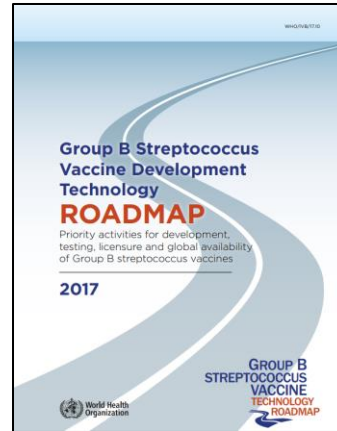
## Neonates

- EOGBS: usually within 24 hours to day 6 (sepsis, pneumonia, meningitis)
- LOGBS: day 7-89
- Late LOGBS: >3 months
- Estimated incidence 0.5/1000 live births
- Decline seen since introduction of IAP but not on extremely preterm infants and no impact on LOGBS

# GBS disease prevention is a priority at global level

1938

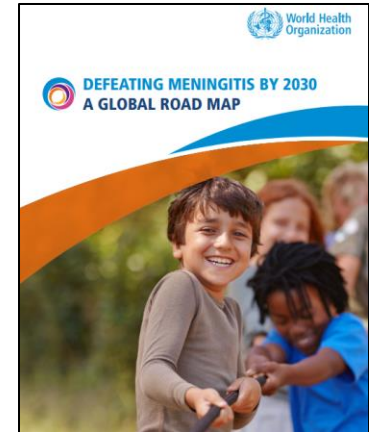
2016



2017



2021



GBS, first recognized as a cause of **puerperal sepsis**

GBS emerges as an important cause of **neonatal meningitis** and **sepsis**

Product Development for Vaccines Advisory Committee, identified **GBS vaccination of pregnant women in LMICs as a priority**

WHO publishes Global vaccine development roadmap and PPCs to support development of vaccines **suitable for LMIC settings**

**Defeating meningitis road map** milestone:

- By 2026, at least one **affordable** vaccine licensed and WHO-prequalified for maternal immunization
- By 2030, at least 10 countries introduce vaccine

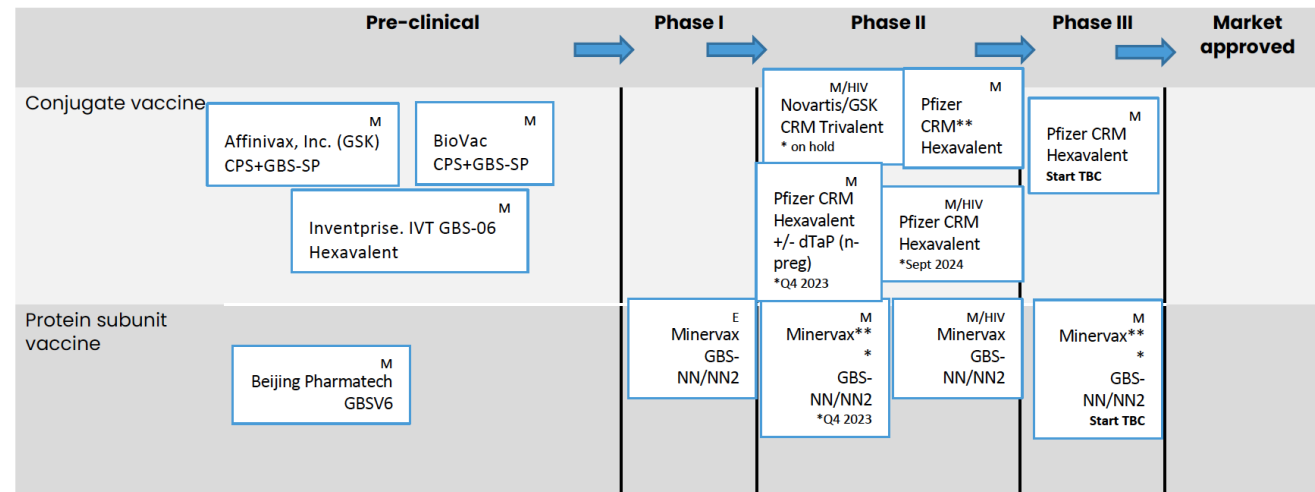
# Pre licensure efficacy study

- Conventional Phase 3 RCT
- Would need to occur in countries with high prevalence of EOD
- Assuming VE 75%
- Minimum of 28,000 participants required (assuming incidence of 3/1000 and upwards of 80,000 with incidence of 1/1000)
- Likely need >200 sites, cost \$\$\$, significant delay to vaccine

# Potential pathway to licensure

- Option 1: immunologic endpoint trial followed by a vaccine effectiveness study
- Option 2: immunologic endpoint trial embedded in a disease endpoint clinical trial
- Option 3: disease endpoint clinical trial

# GBS vaccine development pipeline



\*\*Pfizer: EMA PRIME: 22/04/2022; FDA Breakthrough Therapy Designation 7/09/2022

\*\*\*Minervax EMA PRIME: 15/09/2022

Target indications: M=maternal, E=elderly, HIV = HIV infection

Protein carrier: TT=tetanus toxoid, CRM=CRM 197, GBS-SP=GBS surface proteins

# Hepatitis E

- Affects world's poorest, most vulnerable populations particularly where access to clean water and sanitation is limited
- Pregnant women case fatality rate 25%
- Increases risk of miscarriage, stillbirth and neonatal death
- In 2011, HEV29 (recombinant protein subunit vaccine) was licensed
- Cluster randomized controlled trial in Bangladesh suggested an elevated risk of miscarriage (Zaman et al 2024)
- In March 2024, SAGE reviewed the evidence and concluded the benefits outweigh the risks in fragile, conflict-affected areas and vulnerable settings
- Concluded additional research is paramount
- Hecolin (HEV 239) registered in 2020 (Pakistan)
- NCT05808166 current Phase II RCT in Pakistan



**Questions?**

# Case study

- Kate
- G2P1
- EDD March 20, 2026
- Delivered at 36 weeks following PPRM last pregnancy
- Other medical problems: anxiety, iron deficiency
- Medication: iron, multivitamin, escitalopram

# Question 1

- Kate is seen for her first antenatal booking visit at 20 weeks (first week of November)
- What vaccines would you consider giving her at that visit?
  - - A. Influenza alone
  - - B Pertussis alone
  - - C Influenza and pertussis co-administered
  - - D RSV
  - - E. None yet: would discuss and vaccinate at a future visit

## Question 2

- Kate is next seen at 28 weeks following her oral glucose challenge test. She has not had any vaccines in pregnancy yet. What would you consider giving her now (December 24<sup>th</sup>)
- A. Influenza alone
- - B Pertussis alone
- - C Influenza and pertussis co-administered
- - D RSV alone
- - E. None yet: would discuss and vaccinate at a future visit
- - F. All 3 (Influenza, pertussis, RSV) co-administered

## Question 3

- Kate is next seen at 34 weeks.
- At 28 weeks she received influenza and pertussis coadministered.
- She receives RSV at 34 weeks.
- She then delivers her baby at 36 weeks.
- Would you recommend mAb for her baby?
  - A. Yes
  - B. No

A close-up photograph of a pregnant woman's hands resting on her belly. She is wearing a pink dress with white polka dots. The background is a solid, soft pink color. The text "Thank you" is overlaid in the center of the image.

Thank you