Protecting the future: what's new in antenatal vaccination

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Disclosures

CB was a member of ATAGI from 2012-2021

CB is a member of the COVID-19 Vaccines and Treatments for Australia Science and Industry Technical Advisory Group

CB is a member of the ATAGI Pneumococcal Working Group

CB is chair of the NHMRC Staying Health Advisory Group

CB has no conflicts of interest nor any financial disclosure to make

A long history

Bull. Org. mond. Santé
Bull. Wld Hlth Org. } 1966, **35**, 863-871

The Use of Toxoid for the Prevention of Tetanus Neonatorum

Final Report of a Double-blind Controlled Field Trial *

K. W. NEWELL,[1] A. DUEÑAS LEHMANN,[2] D. R. LEBLANC [3] & N. GARCES OSORIO [4]

With a view to determining the effectiveness of a method for the control of tetanus neonatorum which would be independent of medical examination or care, a double-blind field trial covering 1618 women was conducted between 1961 and 1966 in a rural area of Colombia with an estimated existing tetanus neonatorum death rate of 11.6 per 100 births. The study group was given 1-3 injections of 1 ml of an aluminium-phosphate-adsorbed tetanus toxoid more than 6 weeks apart, and the control group a similar number of injections of an influenza-virus vaccine.

There was no statistically significant difference between those in the two groups given one injection. Those in the control group given 2 or 3 injections had a tetanus neonatorum death rate of 7.8 deaths per 100 births, and the corresponding subjects in the study group had none. This difference is unlikely to have occurred by chance.

In Northern Europe or in Canada, tetanus neonatorum is a curiosity which generally occurs in conjunction with a series of unusual circumstances, and results in an insignificant number of illnesses and deaths. As one approaches the tropics and subtropics, its importance changes. The number of illnesses and deaths increases; in some areas the mortality may be as high as 10% of births (Jelliffe, 1950; Earle & Mellon, 1958; Schofield, Tucker & Westbrook, 1961; Newell et al., 1964), exceeding that from all other causes of death in the first 28 days of life and becoming one of the dominating health problems. In between these two extremes, mortalities of the order of 1% of births are met with in certain large populations.

The areas with the highest rates are generally those with unsophisticated obstetrical services and only a small proportion of institutional deliveries. It appears probable that neonatal tetanus infection is directly related to birth practices influencing the contamination of the umbilical cord when it is cut or dressed at the time of the delivery.

A number of possible methods of preventing the disease have been proposed. They have ranged from the provision of obstetrical services to the protection of newborn babies with tetanus antitoxin or antibiotics. The introduction or improvement of services has advantages additional to the prevention of tetanus neonatorum, but it is clear that even minimal services are unlikely to reach many high-risk populations in the near future.

A number of investigators have considered other methods of prevention. Most work has been directed towards the passive protection of the baby. Broeck & Bauer (1923) and Nathan-Larrier, Ramon & Grasset (1927) described the passage of tetanus antitoxin across the placenta and suggested that this antitoxin might protect the baby. Later Schofield, Tucker & Westbrook (1961) showed, in a field trial in New Guinea, that two or three injections of 1 ml of CSL formolized tetanus toxoid given at 6-week intervals to pregnant women appeared to result in a dramatically lowered tetanus neonatorum rate.

* Research study conducted by the International Center for Medical Research and Training, Cali, Colombia, and supported by Grant E-4178 of the National Institutes of Health, Public Health Service, US Department of Health, Education, and Welfare, under the authority of the International Health Research Act of 1960 (US Public Law 86-610).

[1] Professor of Epidemiology, Tulane University, New Orleans, La., USA. Director, International Center for Medical Research and Training, Cali, Colombia.

[2] Assistant Professor of Medicine, Universidad del Valle, Cali, Colombia.

[3] Assistant Professor of Epidemiology, Tulane University, New Orleans, La., USA.

[4] Field Co-ordinator, Epidemiology Unit, International Center for Medical Research and Training, Cali, Colombia.

BIRTHS, TETANUS AND NON-TETANUS MORTALITY RATES IN THE STUDY AND CONTROL GROUPS AFTER TWO OR THREE INJECTIONS

Interval from injection to birth (months)	Births	Tetanus mortality		Non-tetanus mortality	
		No.	%	No.	%
Control group					
0-3	44	2	4.5	2	4.5
4-12	80	7 [a]	8.8	5	6.3
13-24	109	10	9.2	5	4.6
25-36	83	6	7.2	3	3.6
37-54	31	2	6.5	4	12.9
Total	347	27	7.8 [b]	19	5.5
Study group					
0-3	58	0	0	1	1.7
4-12	88	0	0	7	8.0
13-24	98	0	0	4	4.1
25-36	74	0	0	2	2.7
37-54	23	0	0	0	0
Total	341	0	0 [b]	14	4.1

Summary

What's old? With some new bits	Influenza and pertussis
What's not so old?	COVID-19
What's new?	RSV
What are the challenges?	Vaccine coverage and equity
What does the future hold?	Group B streptococcus, CMV

Summary

What's old? With some new bits

What's not so old?

What's new?

What are the challenges?

What does the future hold?

Influenza and pertussis

COVID-19

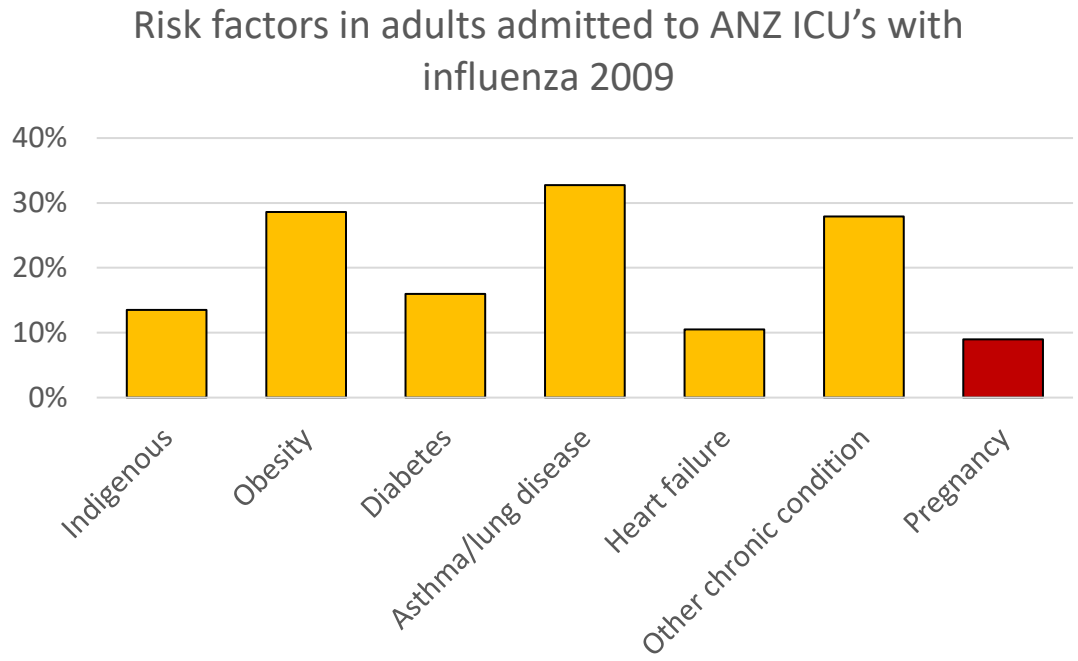
RSV

Vaccine coverage and equity

Group B streptococcus, CMV

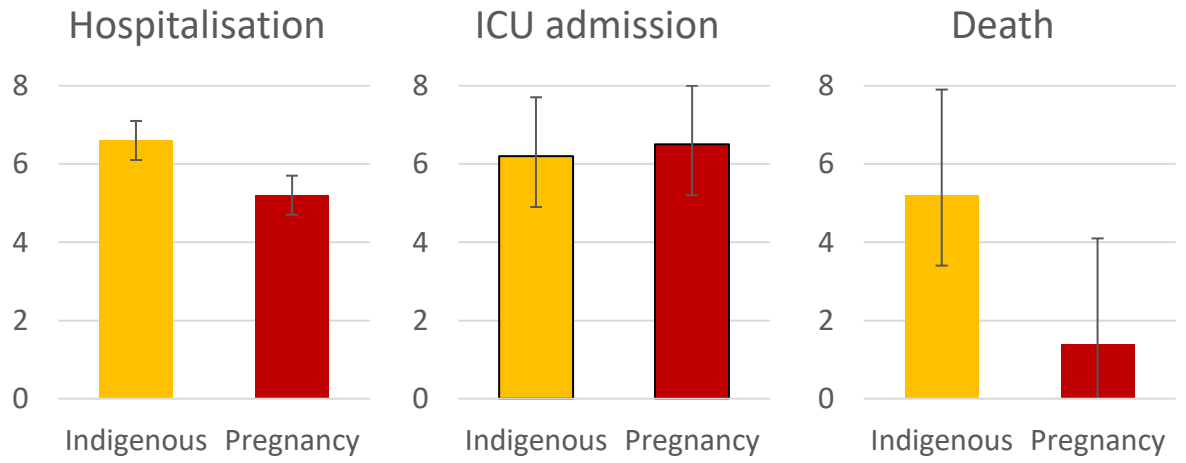
Influenza

1 in 10 influenza-associated admission to ICU were pregnancy



ANZIC Investigators, NEJM 2009

Pregnancy is an independent risk factor for severe disease

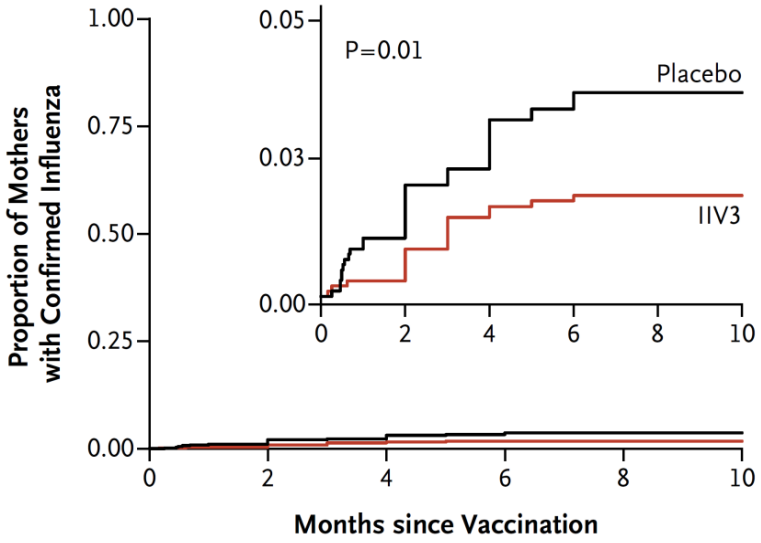


Kelly H et al Eurosurveillance 2009

Influenza

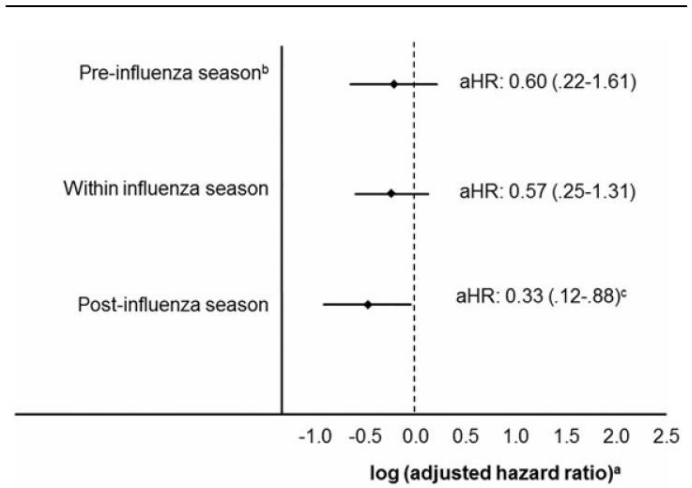
Influenza vaccine protects the mother, the fetus and the baby:

VE against maternal infection: 50% (15-71%)



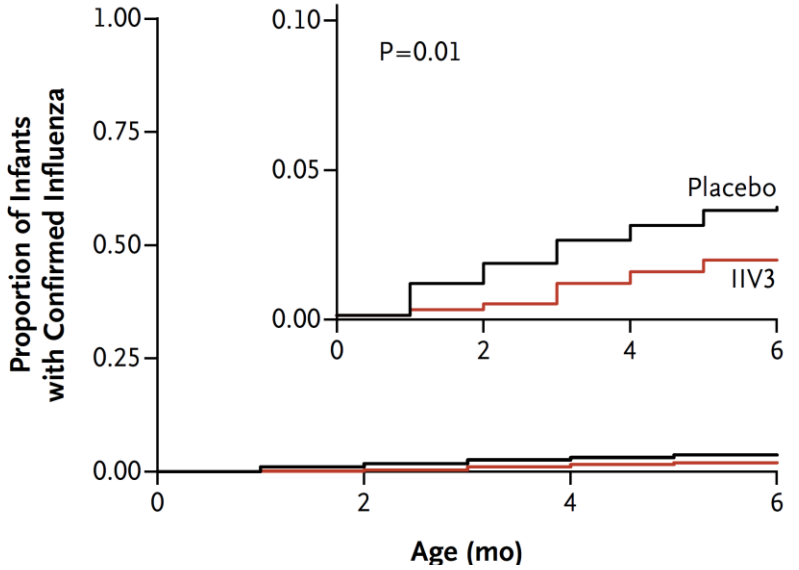
Mahdi S et al, NEJM 2014

VE against still-birth: 51% (16-71%)



Regan A et al, CID 2016

VE against infant infection: 48% (11-70%)

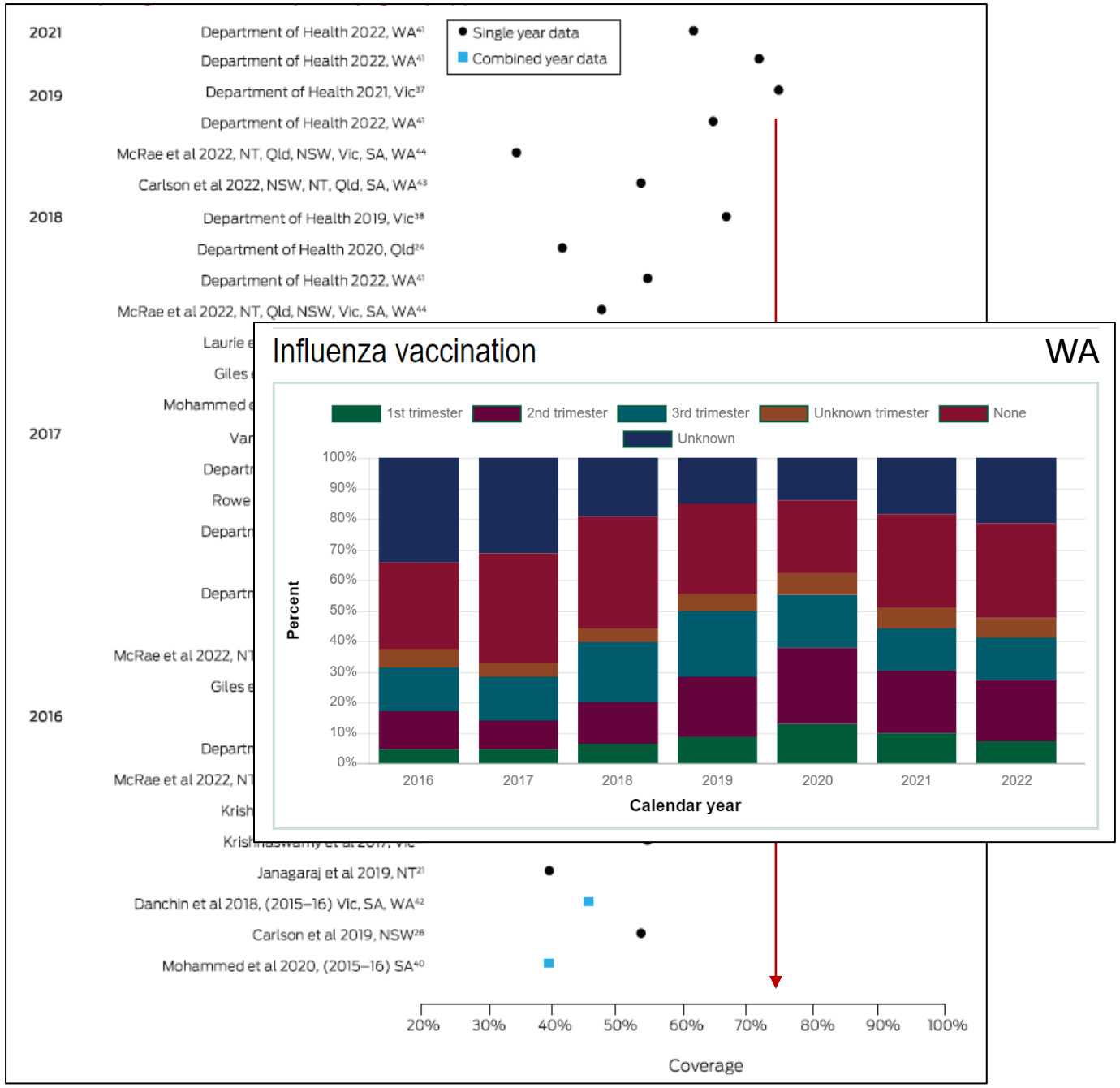


Mahdi S et al, NEJM 2014

Influenza

Coverage remains inadequate

- Recommended since 2000
- Funded since 2010



Influenza and pertussis vaccine coverage in pregnancy in Australia, 2016–2021

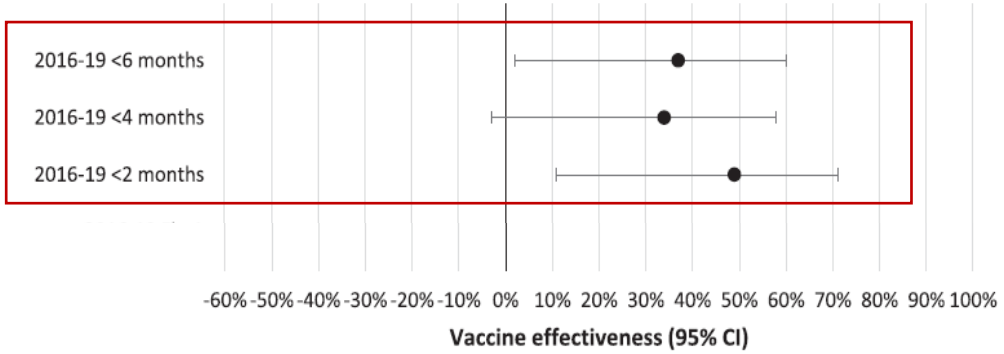
Jocelynne E McRae[1,2], Lisa McHugh[3], Catherine King[1,2], Frank H Beard[1,2], Christopher C Blyth[4,5], Margie H Danchin[6,7], Michelle L Giles[8,9], Hassen Mohammed[10,11], Nicholas Wood[2,12], Kristine Macartney[1,2]

McRae JE et al, MJA 2023

*Unknown vaccination status excluded

Influenza

Influenza vaccine protects the mother, the fetus and the baby, but waning is a problem



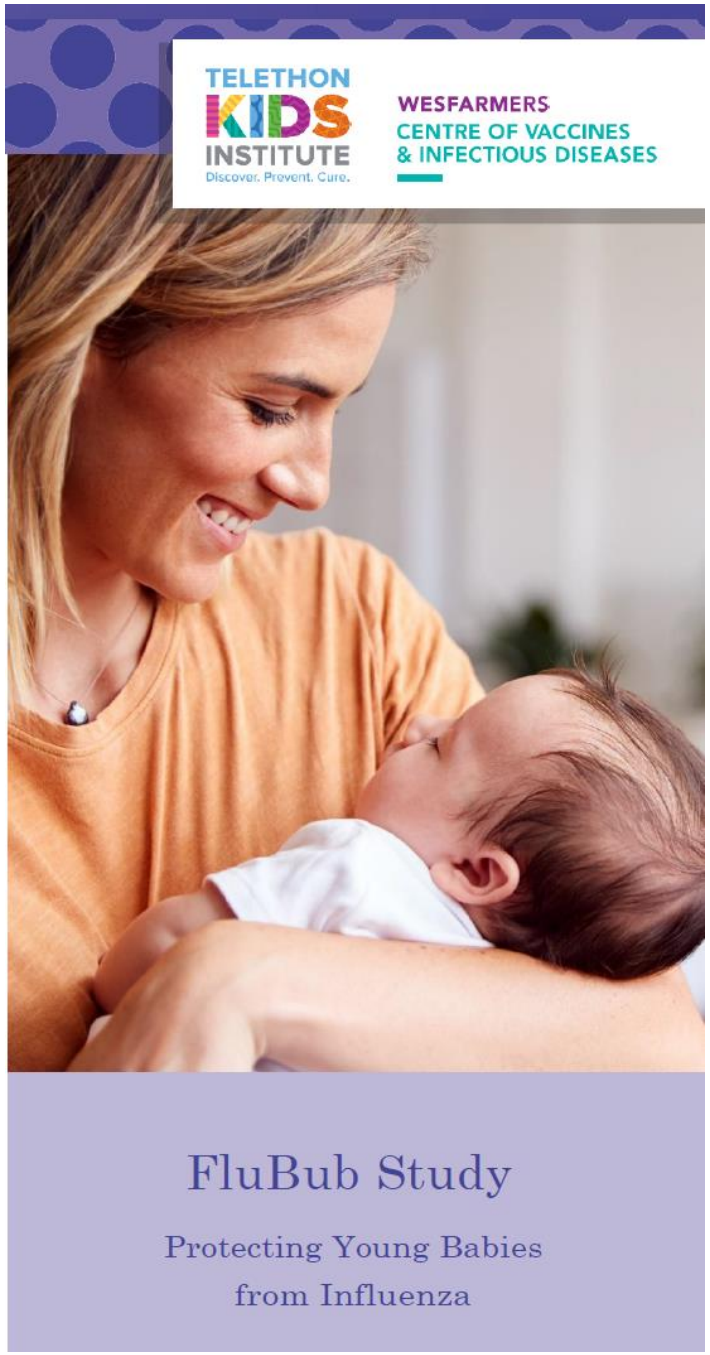
Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

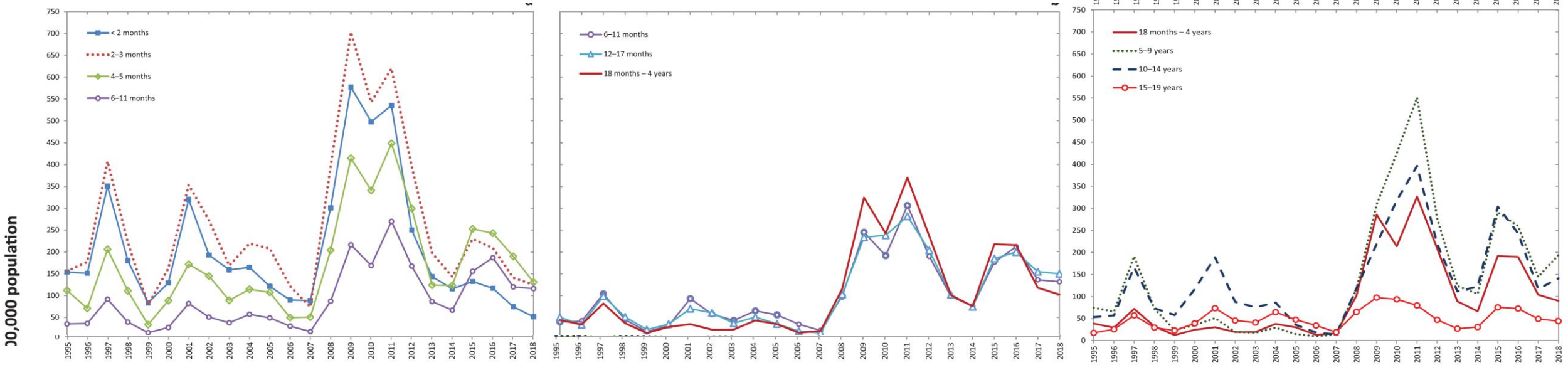
Preventing severe influenza in Australian infants: Maternal influenza vaccine effectiveness in the PAEDS-FluCAN networks using the test-negative design

J. McRae[a,b,c,*], C.C. Blyth[d,e,f,g], A.C. Cheng[h,i], H.E. Quinn[a,b], N. Wood[a,b,c], K.K. Macartney[a,b,c], on behalf of the PAEDS and FluCAN Network Investigators



Pertussis

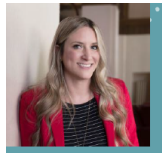
Pertussis remains an ever present risk



Marshall KS et al, CDI 2022

Pertussis

Maternal pertussis vaccine prevents infant disease and saves infant lives



Annette Regan/Hannah Moore #CDIC2023

Links2HealthierBubs: A Population-Based Linked Record Study Evaluating Potential 'Blunting' Effects of Maternal Pertussis Vaccination on Childhood Vaccine Effectiveness

Annette K Regan, Hannah C Moore, Michael Binks, Lisa McHugh, Christopher C Blyth, Gavin F Pereira, Karin Lust, Minda Sarna, Ross Andrews, Damien Foo, Paul Effler, Stephen Lambert, Paul Van Buynder

Curtin University · University of San Francisco · Telethon Kids Institute · menzies school of health research · The University of Queensland Australia · Government of Western Australia Department of Health · Queensland Government Queensland Health

Links-2-Healthier Bubs Cohort, 2014-2017

Includes 279,418 infants born to 252,444 mothers born between 2014/15 to 2017

Birth records

- Perinatal data
- Maternal immunization data

Infant health records

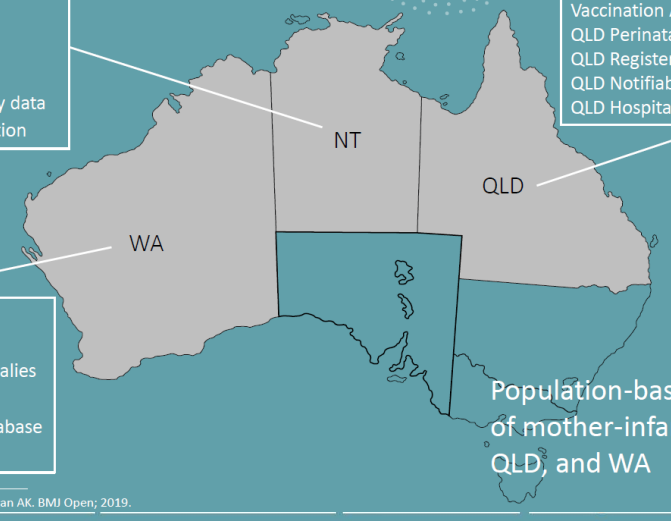
- Immunization register data (NT & Qld only)
- Notifiable disease data
- Hospital discharge data
- ED presentation data
- Death register data

SOURCE: Sarna M, Andrews R, Moore HC,... Regan AK. BMJ Open; 2019.

Links-2-Healthier Bubs Cohort, 2014-17

NT Births Registry
NT Deaths Registry
NT Perinatal Trends
NT Immunisation Register
NT Inpatient Activity
SA Pathology & RDH pathology data
NT Primary Health Care Collection

Vaccination Information and Vaccination Administration System
QLD Perinatal Data Collection
QLD Register of Births & Deaths
QLD Notifiable Conditions Database
QLD Hospital Admitted Patient Data



WA Antenatal Vaccination Database
Midwives Notification System
WA Register of Developmental Anomalies
Birth & Death Registrations
WA Notifiable Infectious Disease Database
Hospital Morbidity Data Collection

Population-based linked cohort of mother-infant pairs in NT, QLD, and WA

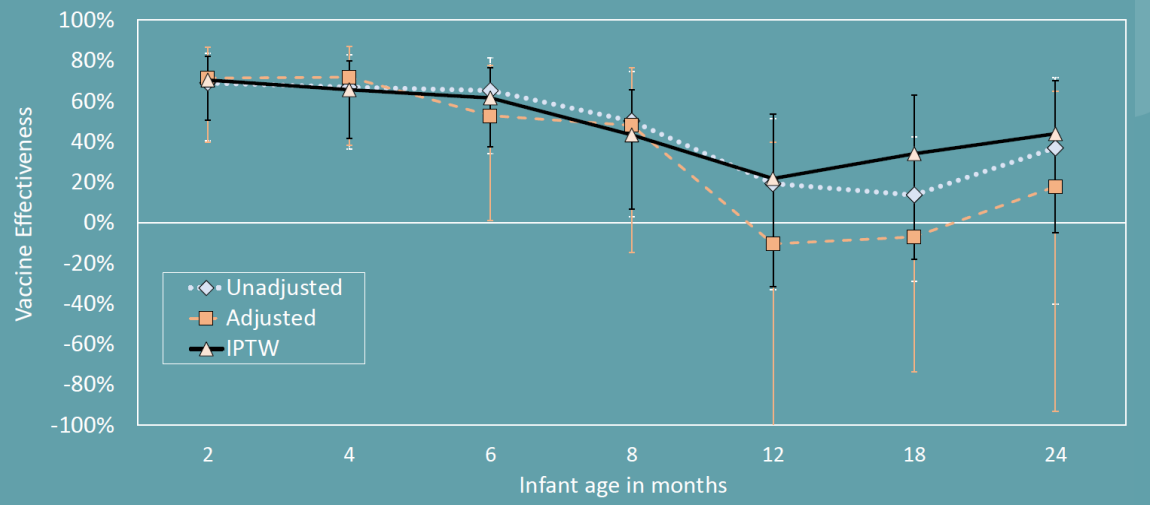
SOURCE: Sarna M, Andrews R, Moore HC,... Regan AK. BMJ Open; 2019.

Regan A et al. Pediatrics 2023 in press

Pertussis

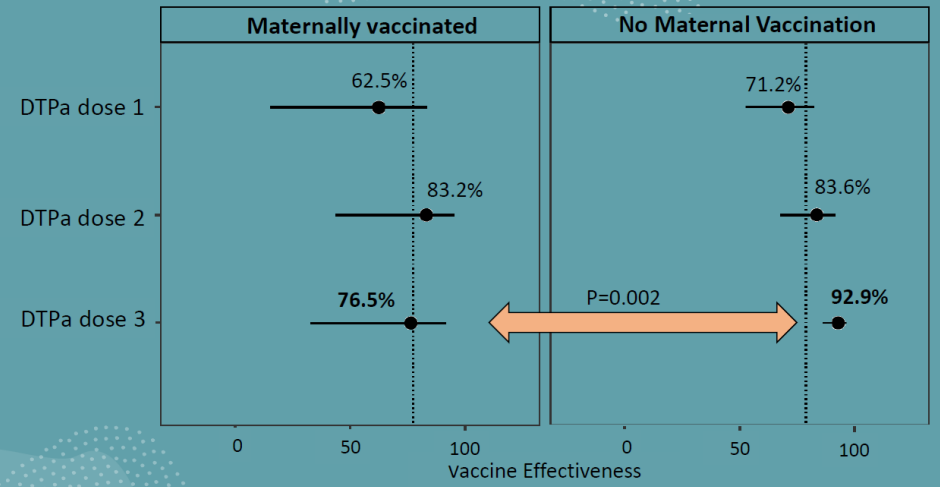
Maternal pertussis vaccine prevents infant disease and saves infant lives

Effectiveness of *maternal* pertussis vaccination against notified pertussis by infant age



SOURCE: Regan et al. Manuscript Under Review

Effectiveness of *infant* pertussis vaccination by maternal pertussis vaccination Status



UNPUBLISHED DATA – NOT FOR FURTHER DISTRIBUTION

Acknowledgements

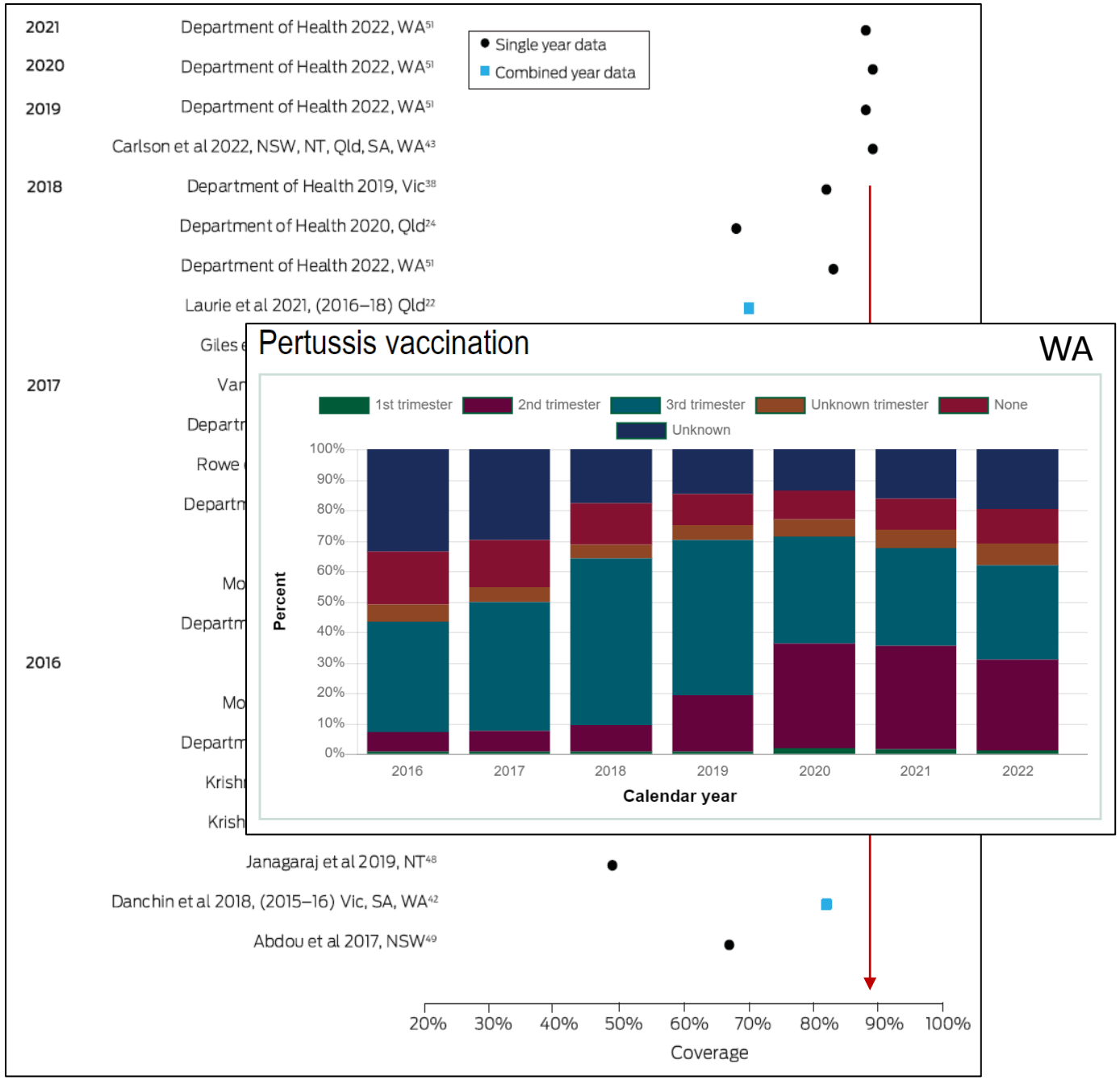
- Links2HealthierBubs Research Team
- Data Linkage Services: WA Department of Health Data Linkage Branch, SANT Datalink, QLD Health
- Data Custodians of the contributing datasets
- **Funding:** National Health & Medical Research Council (GNT1141510), Department of Health Western Australia, SANT Datalink, & QLD Health

Australian Government National Health and Medical Research Co | Government of Western Australia Department of Health | Queensland Government Queensland Health | SA·NT DataLink

Pertussis

Coverage better than flu

- Recommended since 2013
- Funded through state programs from 2015
- NIP program funded in 2018



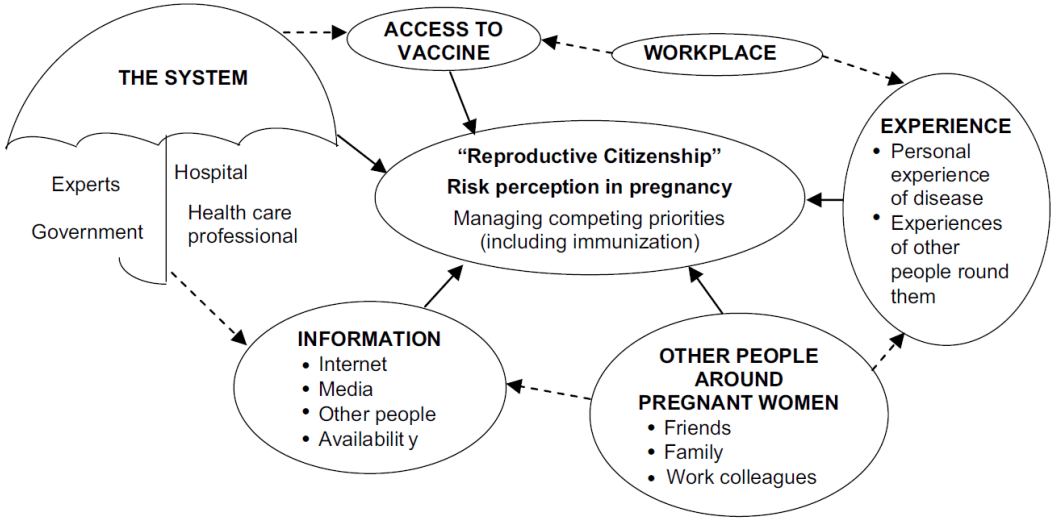
Influenza and pertussis vaccine coverage in pregnancy in Australia, 2016–2021

Jocelynne E McRae[1,2], Lisa McHugh[3], Catherine King[1,2], Frank H Beard[1,2], Christopher C Blyth[4,5], Margie H Danchin[6,7], Michelle L Giles[8,9], Hassen Mohammed[10,11], Nicholas Wood[2,12], Kristine Macartney[1,2]

McRae JE et al, MJA 2023

*Unknown vaccination status excluded

Pertussis vs influenza



Numerous reasons for variable coverage

- Seasonal versus year round program
- Differential perception of risk by the mother – to mother and infant
- Provider attitudes vary, impacting on vaccine promotion and delivery

No "one-size" fits all strategy

Strategies should be site specific, multifaceted, targeted at the existing barriers to maternal vaccine uptake, and heavily involve local stakeholders in the design and implementation of these strategies

McRae JE et al, MJA 2023
Wiley KE et al, Qual Health Research 2015
Giles M et al, BMV Pregnancy Childbirth

COVID-19

COVID-19 is associated with poor maternal and infant outcomes

(240 studies; 293,152 pregnant women vs 2,903,149 non-pregnant women)*

Compared with non-pregnant women with COVID-19			
Outcome	Pregnant women	Comparator	Odds ratio (95% CI)
Mortality	242/122,222	5,252/2,138,726	1.48 (0.62;3.49)
ICU admission	912/118,403	11,513/1,908,957	2.61 (1.84;3.71)
Invasive vent	310/116/458	3,607,1,772,716	2.41 (2.13;2.71)
ECMO	19/30,694	122/432/623	3.71 (0.71;19.41)

Compared with pregnant women without COVID-19			
Outcome	COVID+ve	COVID-ve	Odds ratio (95% CI)
Maternal mortality	47/11,362	37/411,126	6.09 (1.82;20.38)
ICU admission	447/12,957	1,962/459,359	5.41 (3.59; 8.14)
Preterm birth	1,306/12,076	26,068/436,964	1.57 (1.36; 1.81)
Still birth	76/9,338	1,397/414,139	1.81 (1.38; 2.37)
Neonatal death	16/3,153	28/9,263	2.35 (1.16; 4.76)
NICU admission	687/4,072	6,968/198,124	2.18 (1.46; 3.26)

*data predominantly from the pre-Omicron era

Allotey J et al. BMJ 2022

COVID-19

A booster primary course of COVID-19 vaccines reduces complications

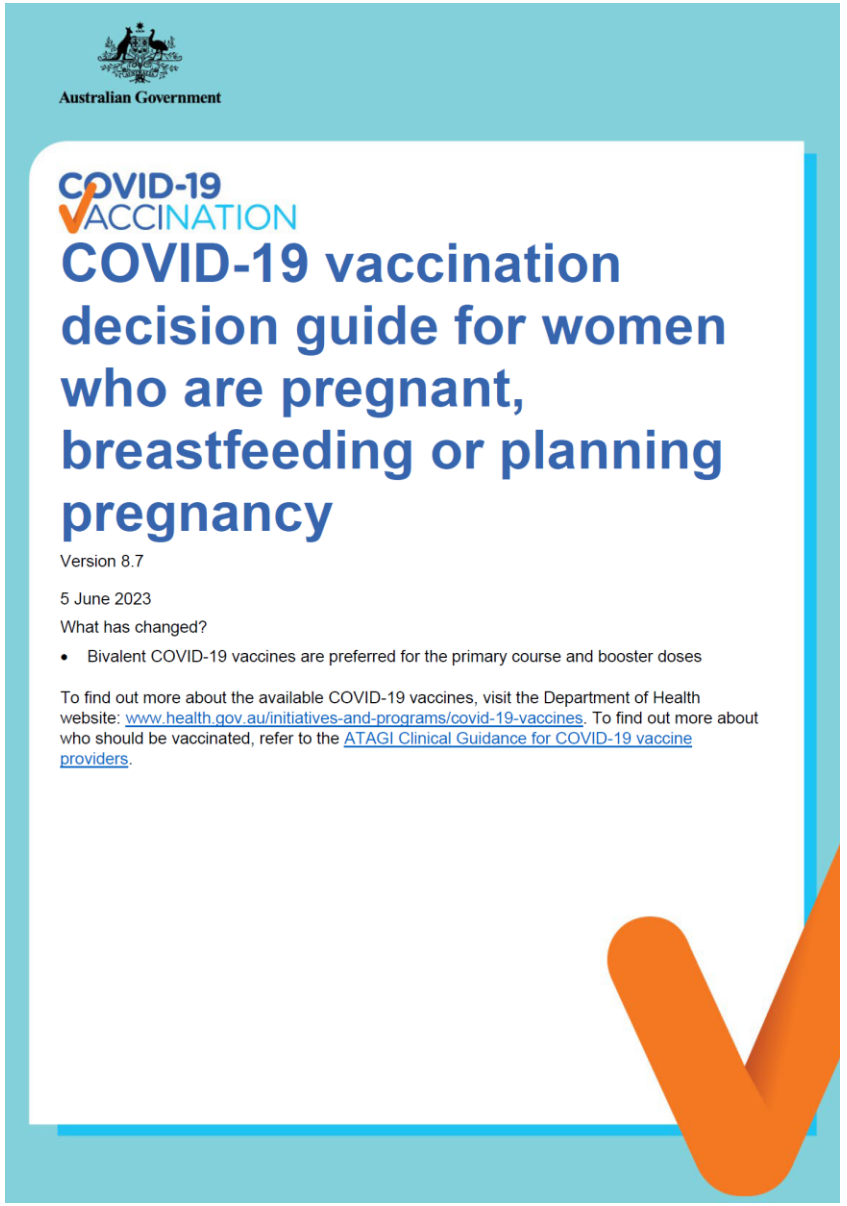
	All women: effectiveness against lab-confirmd COVID-19		All women: effectiveness against moderate COVID-19 symptoms		All women: effectiveness against severe COVID-19, ICU or death		Women with COVID-19: effectiveness against severe COVID-19, ICU or death	
Outcome	N	VE (95%CI)	N	VE (95%CI)	N	VE (95%CI)	N	VE (95%CI)
Unvaccinated	632	0 (ref)	213	0 (ref)	85	0 (ref)	65	0 (ref)
Partially vaccinated	145	5% (0; 18)	41	26% (0; 46)	13	35% (0; 64)	9	33% (0; 67)
Completely vaccinated	535	9% (0; 18)	171	20% (1; 34)	36	48% (22; 65)	10	74% (48; 87)
Boostered vaccination	233	30% (19-39)	71	48% (32; 61)	7	76% (47; 89)	2	91% (65; 98)

Villar J et al, Lancet 2023

COVID-19

Severe COVID is rare in fully vaccinated pregnant women

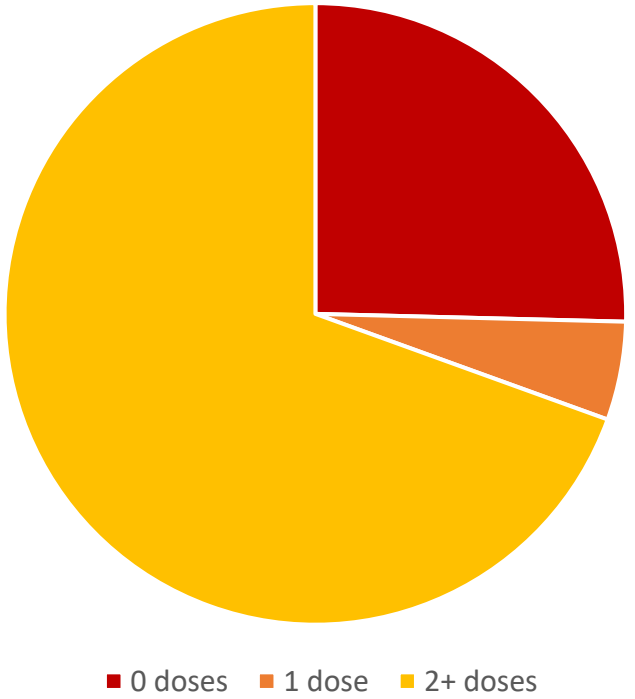
Country	Period covered	Number of women admitted to hospital with covid	Number admitted to critical care (% of those admitted to hospital)	Number admitted to critical care who are unvaccinated (% of those admitted to critical care)	Estimated proportion of pregnant population who have received at least one vaccine dose
UK	16/05/21-31/10/21	1436 (symptomatic only)	230 (16)	225 (98)	22% (England, August 2021) 43% (Scotland, October 21)
Netherlands	01/05/21-06/12/21	220 (symptomatic only)	52 (24)	47 (90) Unknown: 5 (10) Vaccinated: 0 (0)	30-50%
Norway	15/07/21-15/12/21	28[a] (symptomatic only)	8 (29)	8 (100)	80%[b]
Finland (Helsinki Region)	01/07/21-15/12/21	11 [a](symptomatic only)	5 (45)	5 (100)	60%[c]
Denmark	01/06/21-30/11/21	N/A	8 (N/A)	8 (100)	56% (November 2021)
Italy (Lombardy Region)	01/05/21-15/12/21	506[d]	15 (3)	12 (80) received one dose: 3 (20)	20 % (May-October 2021)



Engjom H et al, Lancet Regional Health – Europe 202

COVID-19

COVID vaccine coverage in pregnancy (2022)



Summary

What's old? With some new bits

What's not so old?

What's new?

What are the challenges?

What does the future hold?

Influenza and pertussis

COVID-19

RSV

Vaccine coverage and equity

Group B streptococcus, CMV

RSV

The most common reason post-delivery to interact with the hospital system

Immunisation Foundation of Australia: RSV and Me campaign

RSV

RSV Symposium at #CDIC2023. 18th July 2023

Summary

What's old? With some new bits	Influenza and pertussis
What's not so old?	COVID-19
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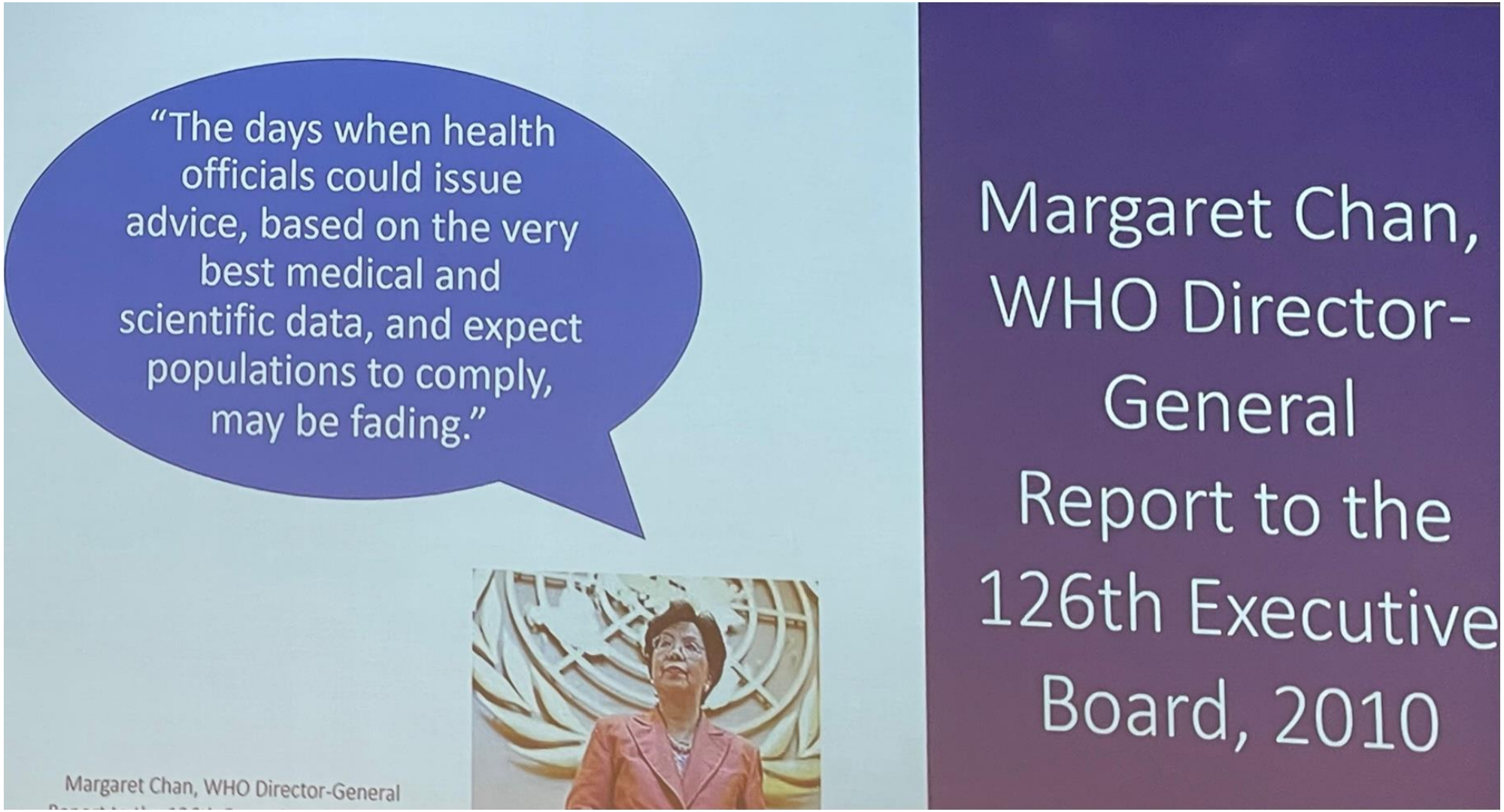
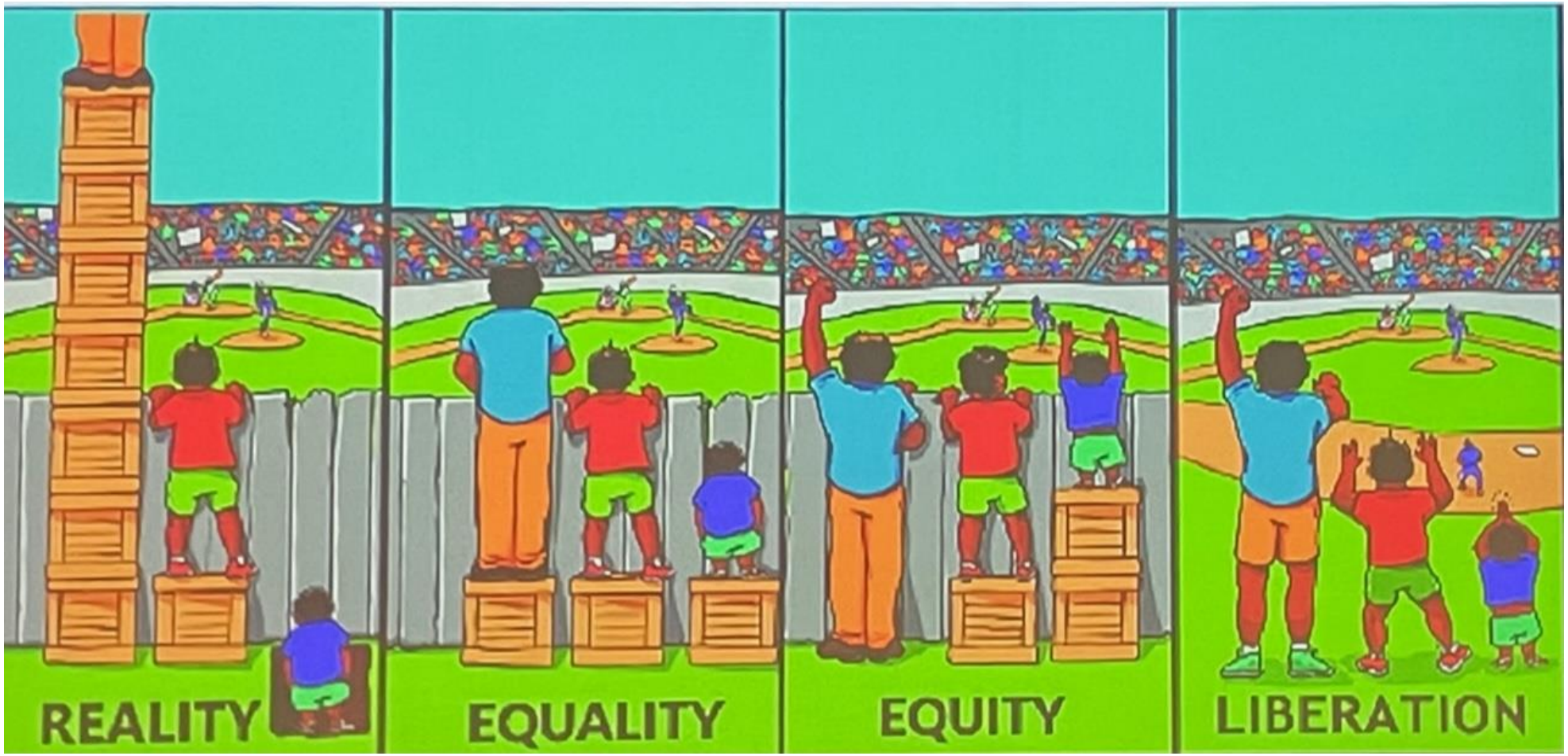
What are the challenges?	Vaccine coverage and equity
What does the future hold?	Group B streptococcus, CMV

Vaccine coverage and equity



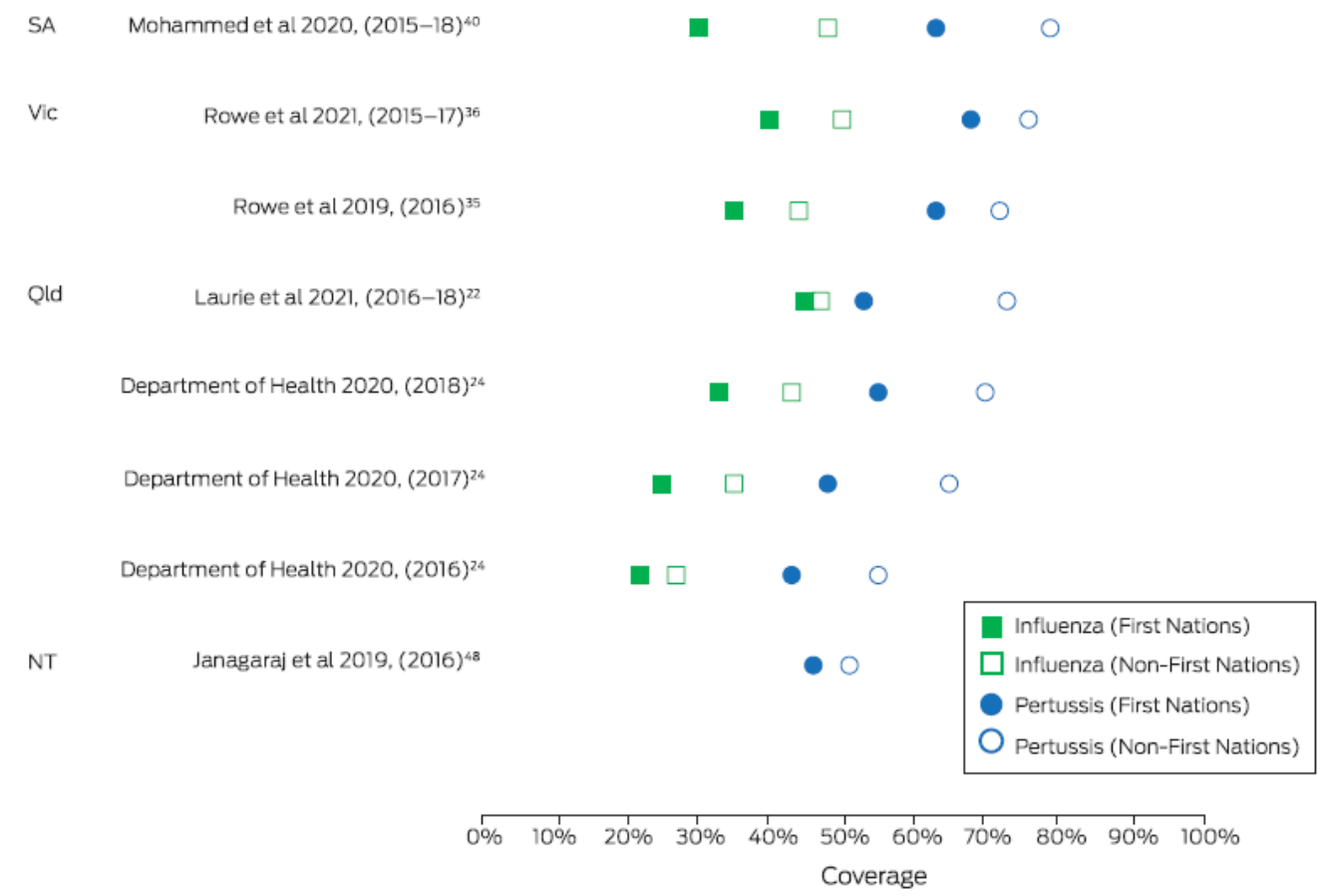
Vaccine coverage and equity



Vaccine coverage and equity

Significant variation in coverage requires attention

6 Studies reporting influenza and pertussis vaccine coverage in pregnancy among First Nations women compared with coverage among non-First Nations women



NT = Northern Territory; Qld = Queensland; SA = South Australia; Vic = Victoria. The study period is denoted in parentheses following the author's name and year of publication. Data on influenza vaccine coverage were not available from the NT study.[48]

Influenza and pertussis vaccine coverage in pregnancy in Australia, 2016–2021

Jocelynne E McRae[1,2], Lisa McHugh[3], Catherine King[1,2], Frank H Beard[1,2], Christopher C Blyth[4,5], Margie H Danchin[6,7], Michelle L Giles[8,9], Hassen Mohammed[10,11], Nicholas Wood[2,12], Kristine Macartney[1,2]

Vaccine coverage and equity

Improving immunisation coverage in pregnant women: a nationwide geospatial retrospective cohort study

UC UNIVERSITY OF CANTERBURY Te Whare Wānanga o Waitaha

UC GEO HEALTH

hrc nz Health Research Council of New Zealand

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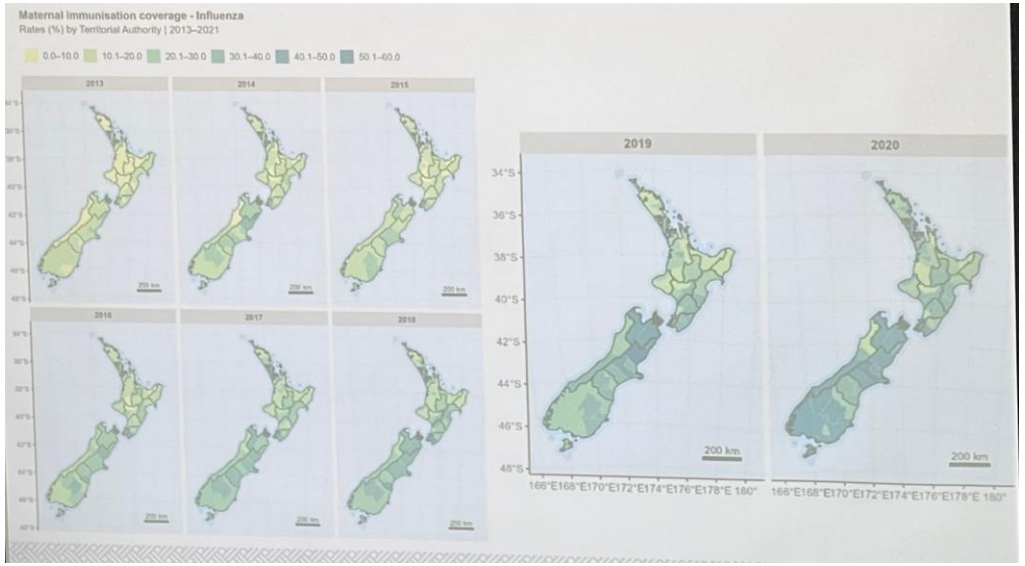
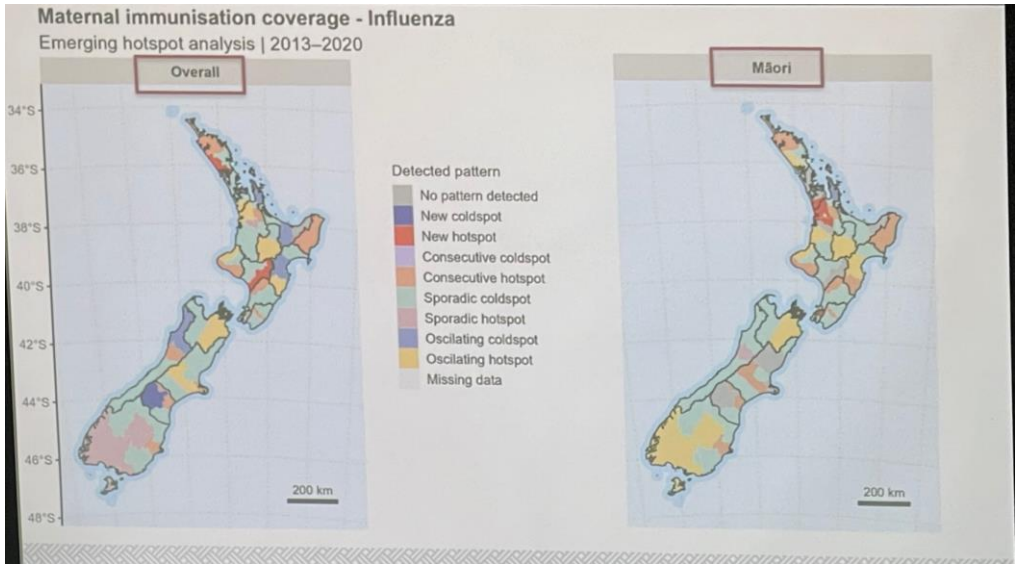
Rationale

UC UNIVERSITY OF CANTERBURY Te Whare Wānanga o Waitaha

- Maternal vaccination remains significantly **below optimal** levels.
- **Geographical disparities** may exist for maternal immunisation coverage but these have not been adequately explored.
- In one of the first examinations of coverage at the national level, compared to NZ European/Other:
  - **Māori and Pacific** women were around half as likely to have received maternal pertussis vaccination (Māori OR=0.55 [95% CI: 0.54, 0.57]; Pacific OR=0.60 [0.58, 0.62]).





Vaccine coverage and equity

UNSW SYDNEY

NCIRS National Centre for Immunisation Research and Surveillance

Maternal uptake and predictors of influenza and pertussis vaccination during pregnancy: a whole of a population-based study

Nusrat Homaira[1,2], Wen-Qian HE[3], Jocelynne McRae[4], Kristine Macartney[3,4], Bette Liu[4,5]

[1]School of Clinical Medicine, Faculty of Medicine, UNSW Sydney, NSW, Australia
[2] Respiratory Department, Sydney Children's Hospital Randwick, NSW, Australia
[3] Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia
[4]National Centre for Immunisation Research and Surveillance (NCIRS), Sydney Children's Hospital's Network, Westmead, NSW, Australia
[5]School of Population Health, UNSW, Sydney, NSW, Australia

Methodology:

Study design and study population:

- Retrospective population-based cohort study using the New South Wales Perinatal Data Collection (NSW PDC).
- The PDC includes records for all births to mothers residing in NSW of babies weighing at least 400gms or of at least 20 weeks' gestation and also includes demographic, pregnancy and birth details.
- Receipt (yes/no) of influenza and pertussis vaccination during pregnancy available from 2016.
- Eligible cohort comprised all pregnant women, who gave birth reported to the PDC between 01 Jan 2016-31 and Dec 2020 (inclusive), in NSW.

	Prevalence ratio for influenza vaccine uptake (95% confidence interval)	Prevalence ratio for pertussis vaccine uptake (95% confidence interval)	Prevalence ratio for influenza and pertussis vaccines uptake (95% confidence interval)
Age in years at delivery			
<20 years	0.89 (0.84-0.94)	0.78 (0.75-0.81)	0.62 (0.58-0.64)
20-24 years	0.89 (0.88-0.91)	0.96 (0.95-0.96)	0.86 (0.85-0.88)
25-29 years	0.94 (0.93-0.95)	0.98 (0.97-0.98)	0.92 (0.91-0.93)
30-34 years	Reference category	Reference category	Reference category
>=35 years	0.99 (0.98-1.00)	1.00 (0.99-1.00)	1.01 (1.00-1.02)
Country of birth			
Born in Australia	Reference category	Reference category	Reference category
Born in other English-speaking country	1.10 (1.08-1.11)	1.02 (1.01-1.03)	1.10 (1.08-1.12)
Born in non-English-speaking country	1.04 (1.03-1.05)	1.03 (1.01-1.02)	1.04 (1.04-1.05)
Index of Relative Socioeconomic Disadvantage			
>75th centile (4, most advantaged)		Reference category	
50-75th Percentile (3)	1.00 (0.99-1.01)	1.00 (1.00-1.01)	1.01(1.00-1.02)
25-50th Percentile (2)	0.96 (0.95-0.97)	0.98 (0.97-0.98)	0.96 (0.95-0.97)
<25th Percentile (1, most disadvantaged)	0.91(0.90-0.92)	1.03 (1.02-1.03)	0.93 (0.92-0.94)
Area of residence			
Major city		Reference category	
Inner regional	1.02 (1.01-1.03)	0.99 (0.98-1.00)	1.01(0.99-1.02)
Outer regional	1.11(1.09-1.13)	0.96 (0.95-0.97)	1.07 (1.05-1.09)
Remote/very remote	1.15 (1.10-1.21)	0.97 (0.94-1.01)	1.14 (1.08-1.20)
Had previous pregnancies lasting >20 weeks gestation			
No		Reference category	
Yes	0.84 (0.84-0.85)	0.92 (0.92-0.93)	0.82 (0.81-0.82)

	Prevalence ratio for influenza vaccine uptake (95% confidence interval)	Prevalence ratio for pertussis vaccine uptake (95% confidence interval)	Prevalence ratio for influenza and pertussis vaccines uptake (95% confidence interval)
Trimester when received the first ANC			
1st	Reference category		
2nd	0.89 (0.88-0.90)	0.83 (0.82-0.83)	0.78 (0.77-0.78)
3rd	0.74 (0.72-0.77)	0.81 (0.80-0.82)	0.67 (0.65-0.69)
Model of care for ANC			
Public hospital	Reference category		
Obstetrician	1.29 (1.28-1.30)	1.05 (1.04-1.05)	1.36 (1.35-1.38)
Midwife	1.05 (1.04-1.06)	1.10 (1.10-1.11)	1.20 (1.19-1.22)
Shared care	1.28 (1.27-1.29)	1.03 (1.03-1.04)	1.32 (1.30-1.33)
Maternal smoking during pregnancy			
No	Reference category		
Yes	0.83 (0.81-0.84)	0.92 (0.91-0.92)	0.82 (0.80-0.83)
Maternal BMI >=25 at 1st ANC			
No	Reference category		
Yes	0.98 (0.97-0.98)	0.98 (0.98-0.99)	0.97 (0.96-0.98)
Chronic maternal hypertension			
No	Reference category		
Yes	0.98 (0.94-1.01)	0.93 (0.90-0.95)	0.96 (0.92-1.00)

Vaccine coverage and equity

UNSW SYDNEY

NCIRS National Centre for Immunisation Research and Surveillance

Maternal uptake and predictors of

	Prevalence ratio for influenza vaccine uptake (95% confidence interval)	Prevalence ratio for pertussis vaccine uptake (95% confidence interval)	Prevalence ratio for influenza and pertussis vaccines uptake (95% confidence interval)
Age in years at delivery			
<20 years	0.89 (0.84-0.94)	0.78 (0.75-0.81)	0.62 (0.58-0.64)
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25-29 years	0.94 (0.93-0.95)	0.98 (0.97-0.98)	0.92 (0.91-0.93)
30-34 years	Reference category	Reference category	Reference category
>=35 years	0.99 (0.98-1.00)	1.00 (0.99-1.00)	1.01 (1.00-1.02)

Proportion of women receiving pertussis vaccine (66.06%) higher compared to influenza vaccine (42.47%) and can be related to maternal risk perception

Prevalence of influenza vaccination 8% lower for women in the most disadvantaged SES category compared to those in highest category.

Also, prevalence of influenza vaccination 17% lower in women who had previous pregnancies

Childhood vaccine uptake (timeliness) affected by many of the same characteristics could be due to some consistent barriers for both maternal and infant vaccination

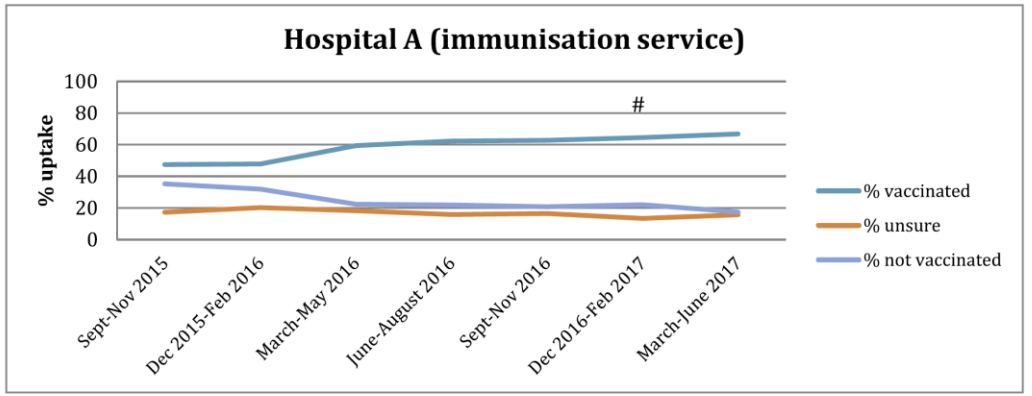
- Receipt (yes/no) of influenza and pertussis vaccination during pregnancy available from 2016.
- Eligible cohort comprised all pregnant women, who gave birth reported to the PDC between 01 Jan 2016-31 and Dec 2020 (inclusive), in NSW.

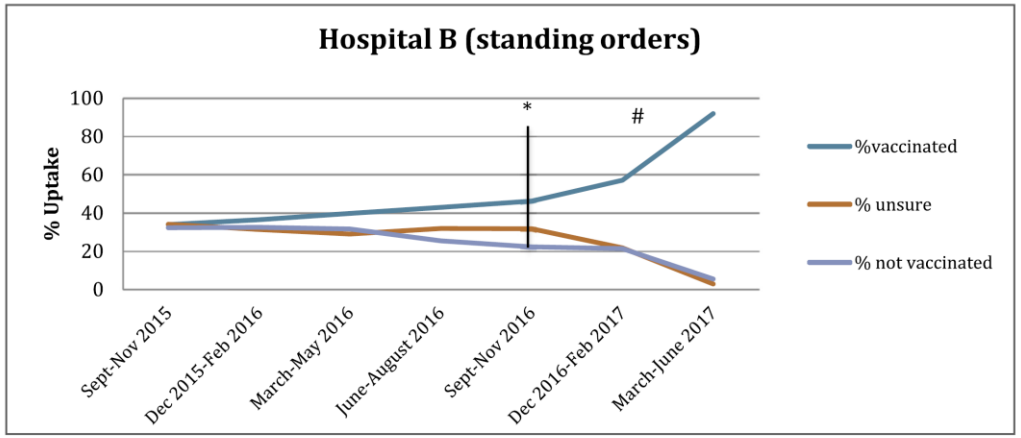
Maternal smoking during pregnancy			
No	Reference category		
Yes	0.83 (0.81-0.84)	0.92 (0.91-0.92)	0.82 (0.80-0.83)
Maternal BMI >=25 at 1st ANC			
No	Reference category		
Yes	0.98 (0.97-0.98)	0.98 (0.98-0.99)	0.97 (0.96-0.98)
Chronic maternal hypertension			
No	Reference category		
Yes	0.98 (0.94-1.01)	0.93 (0.90-0.95)	0.96 (0.92-1.00)

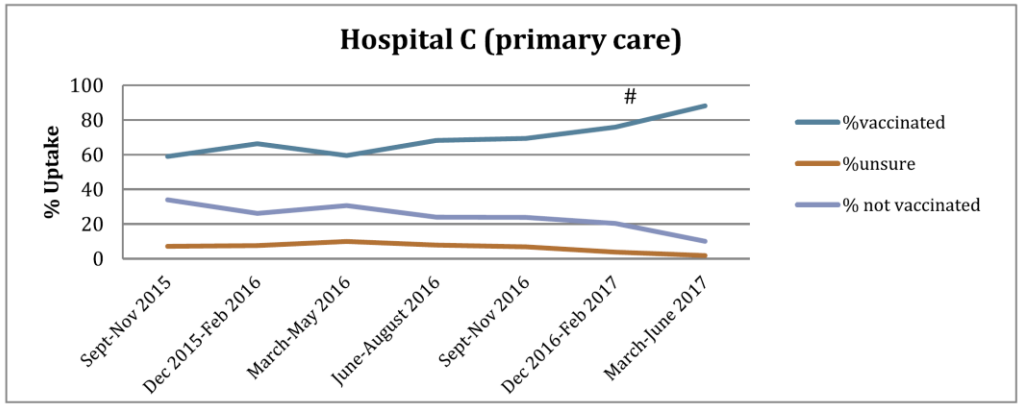
What more can be done?

Three models of care:

- Nurse-led immunisation service
- Standing order for midwife admin
- General practice model







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Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Strategies to implement maternal vaccination: A comparison between standing orders for midwife delivery, a hospital based maternal immunisation service and primary care

Sushena Krishnaswamy [a,b,*], Euan M Wallace [a,c], Jim Buttery [d,e], Michelle L Giles [a,b]

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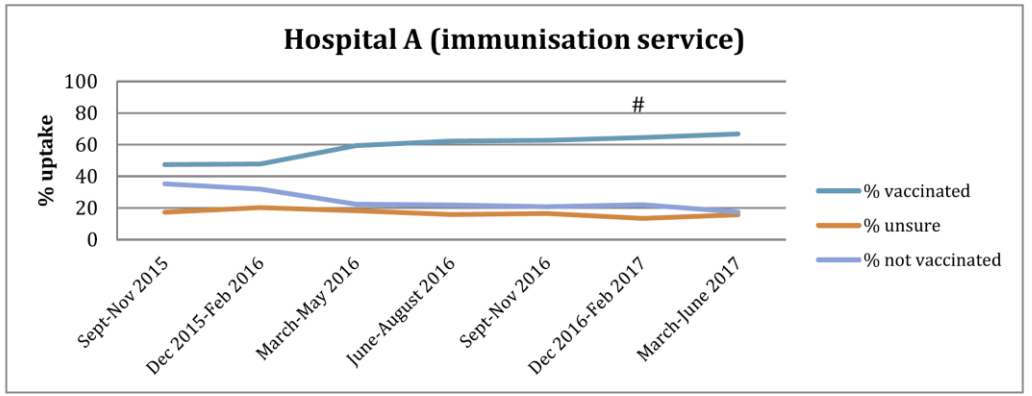
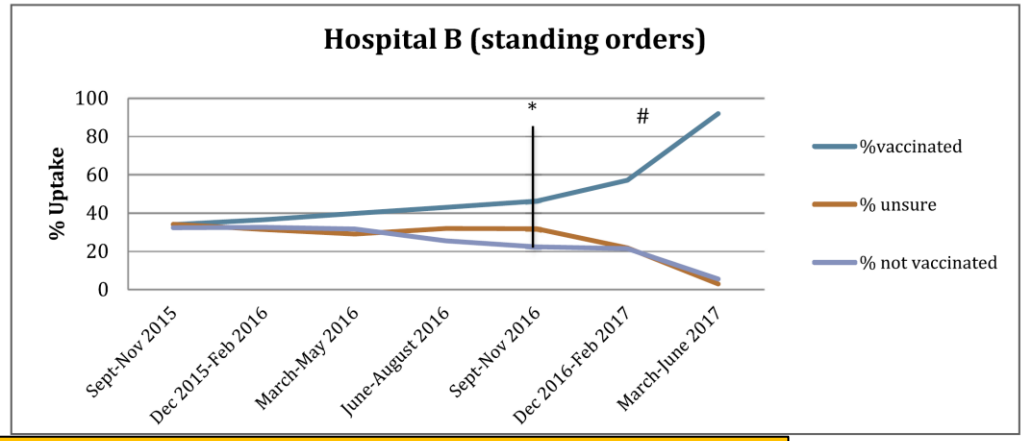
[b] Monash Infectious Diseases, Monash Health, Melbourne, Australia
[c] Safer Care Victoria, Victorian Department of Health and Human Services, Melbourne, Australia
[d] Infection and Immunity, Monash Children's Hospital, Melbourne, Australia
[e] Monash Centre for Health Research and Implementation, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

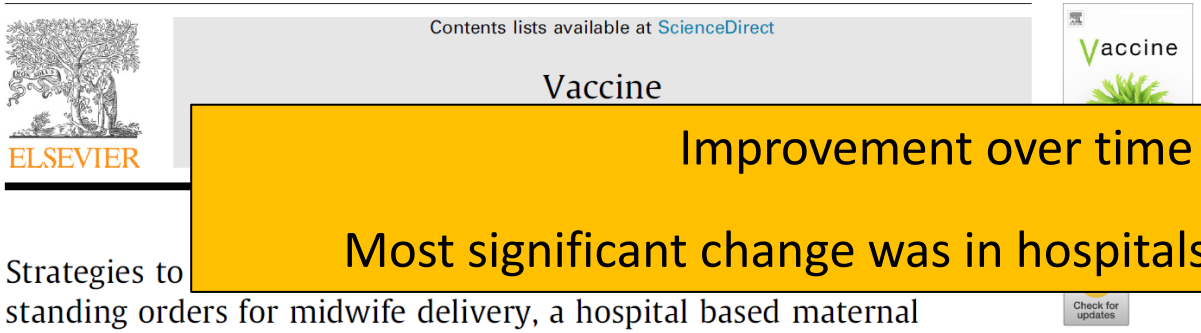
What more can be done?

Three models of care:

- Nurse-led immunisation service
- Standing order for midwife admin
- General practice model







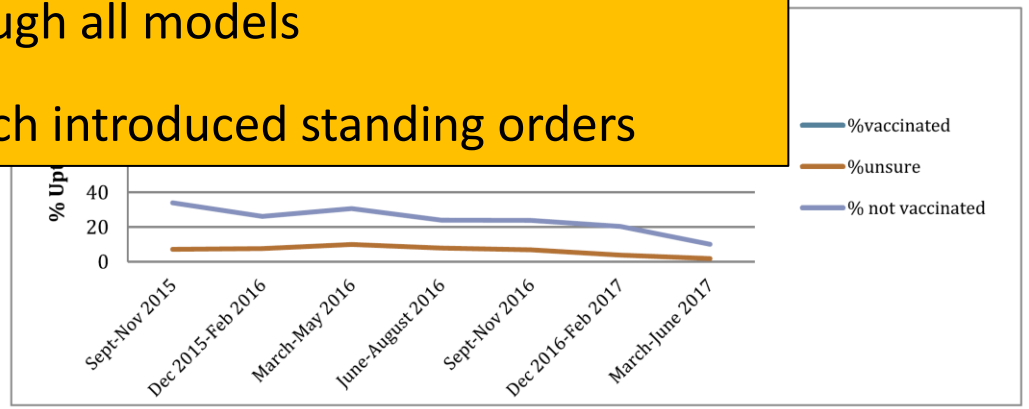
Strategies to … standing orders for midwife delivery, a hospital based maternal immunisation service and primary care

Sushena Krishnaswamy [a,b,*], Euan M Wallace [a,c], Jim Buttery [d,e], Michelle L Giles [a,b]

[a] The Ritchie Centre, Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia
[b] Monash Infectious Diseases, Monash Health, Melbourne, Australia
[c] Safer Care Victoria, Victorian Department of Health and Human Services, Melbourne, Australia
[d] Infection and Immunity, Monash Children's Hospital, Melbourne, Australia
[e] Monash Centre for Health Research and Implementation, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

Improvement over time through all models

Most significant change was in hospitals which introduced standing orders



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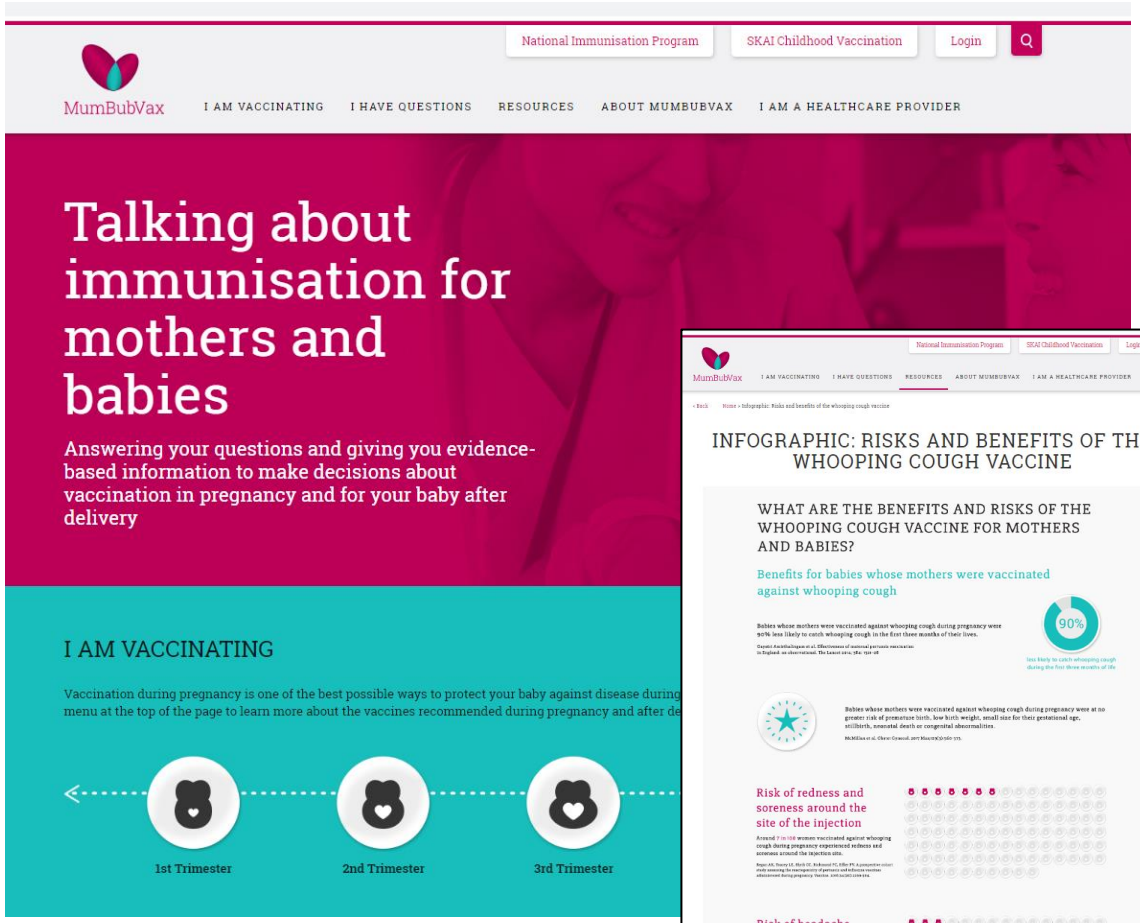
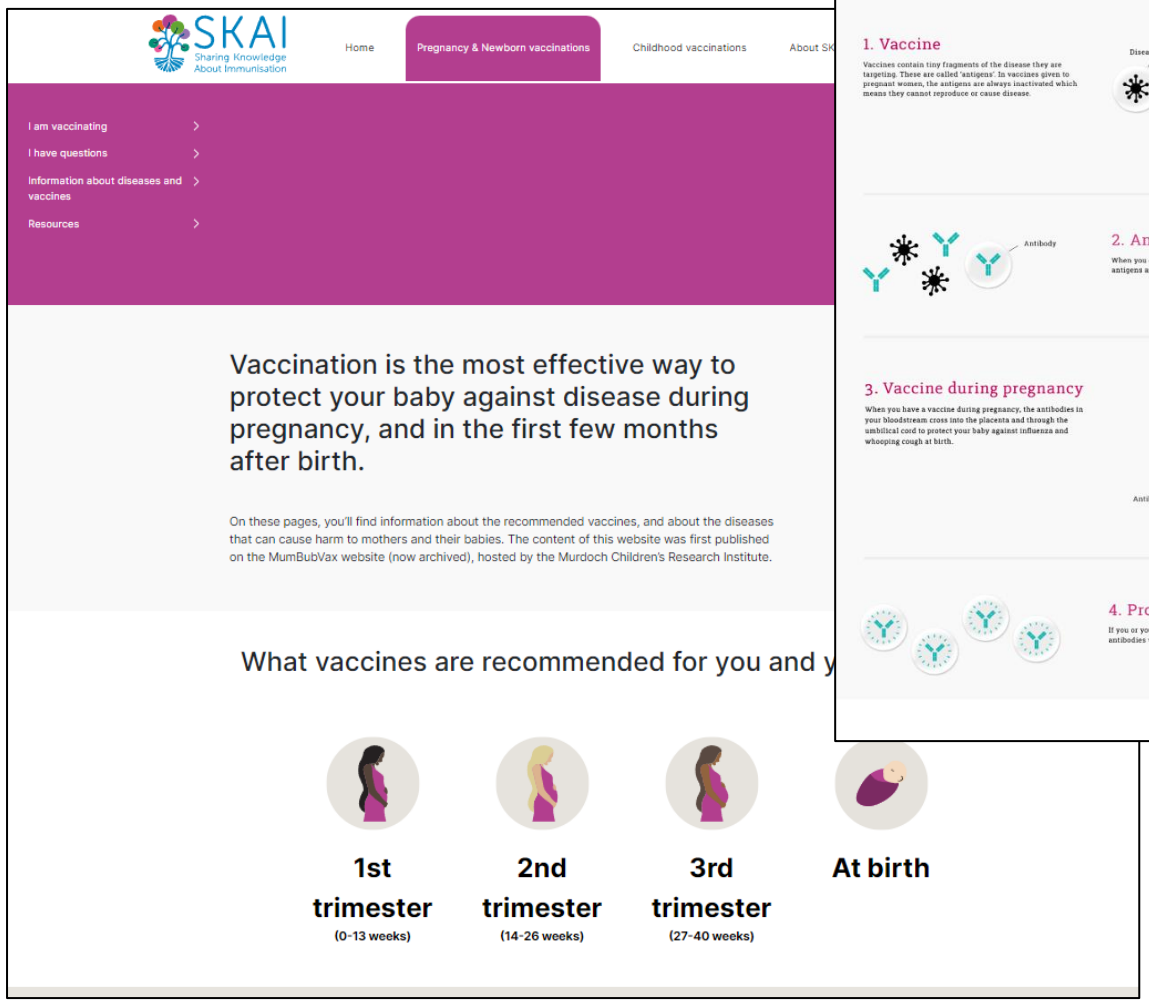
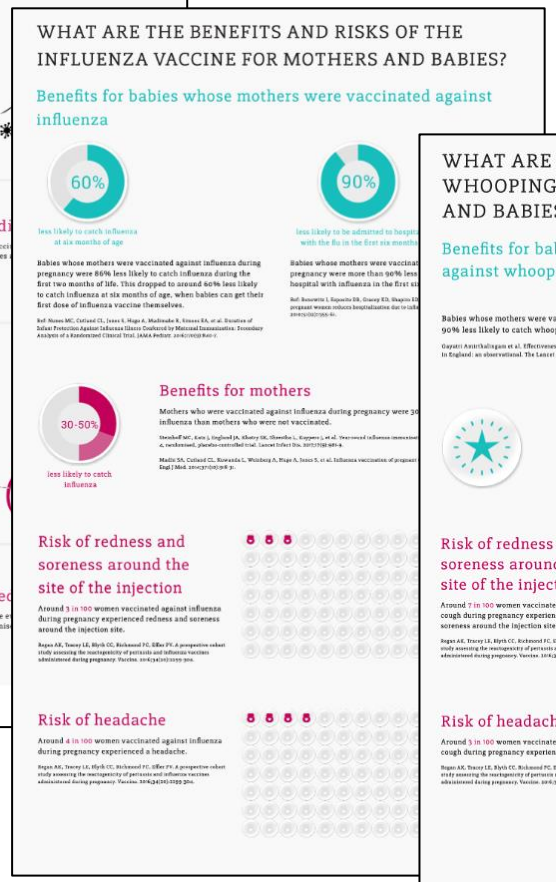


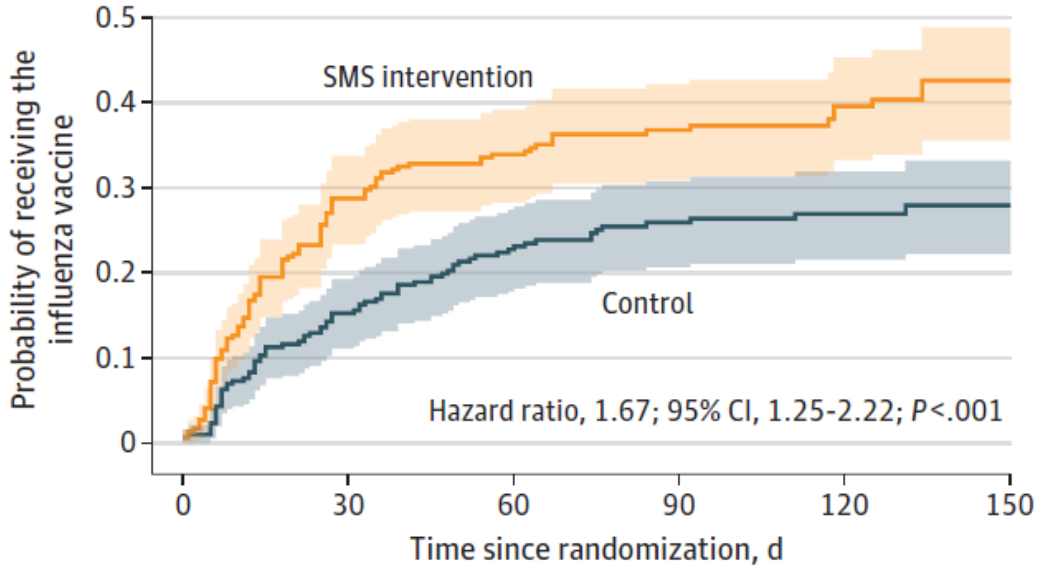
What more can be done?





What more can be done?

Exploring nudges with a waiver



No. at risk						
Control	302	256	216	163	101	54
SMS intervention	293	209	184	127	79	33

SMS indicates short message service.

JAMA Pediatrics | Original Investigation

Short Message Service Reminder Nudge for Parents and Influenza Vaccination Uptake in Children and Adolescents With Special Risk Medical Conditions

The Flutext-4U Randomized Clinical Trial

Jane Tuckerman, PhD; Kelly Harper, BHSc; Thomas R. Sullivan, PhD; Alana R. Cuthbert, PhD; Jennifer Fereday, PhD; Jennifer Couper, MD; Nicholas Smith, PhD; Andrew Tai, PhD; Andrew Kelly, MBBS; Richard Couper, MBChB; Mark Friswell, MBChB; Louise Flood, MBBS; Christopher C. Blyth, PhD; Margie Danchin, PhD; Helen S. Marshall, MD

What more can be done?

Implementing nudges to improve COVID-19 vaccine uptake among pregnant women

Prabha Andraweera, Bing Wang, Margie Danchin, Christopher Blyth, Ivo Vlaev, Jason Ong Jodie Dodd, Jennifer Couper, Thomas Sullivan, Jonathan Karnon, Cusack, Dylan Mordaunt, Dimi Sima Carlson, Jane Tuckerman, Nicholas Herewane, Joanne Koch, Lauren Th Helen Marshall on behalf of the EPI

This study is funded by a NHMRC Partnership grant APP201

Partners: Department of Health, SA Government; Departmer Health, Victorian Government; Department of Health, WA Government; Women's and Children's Health Network; Soutl Adelaide Local Health Network; Northern Adelaide Local Hea Network; Women's and Children's Hospital Foundation; Department of Trade and Investment, SA Government

BACKGROUND: COVID-19 infection during pregnancy has serious adverse consequences for women and their infants. Despite these adverse outcomes and existing evidence on safety of COVID-19 vaccines in pregnancy, vaccine uptake amongst pregnant women is sub-optimal. "Nudges" are subtle behavioural interventions that are designed to encourage positive health behaviours in a range of contexts.

AIM: To assess the effectiveness of a multi-component behavioural nudge intervention on improving COVID-19 vaccine uptake among pregnant women.

METHODS:

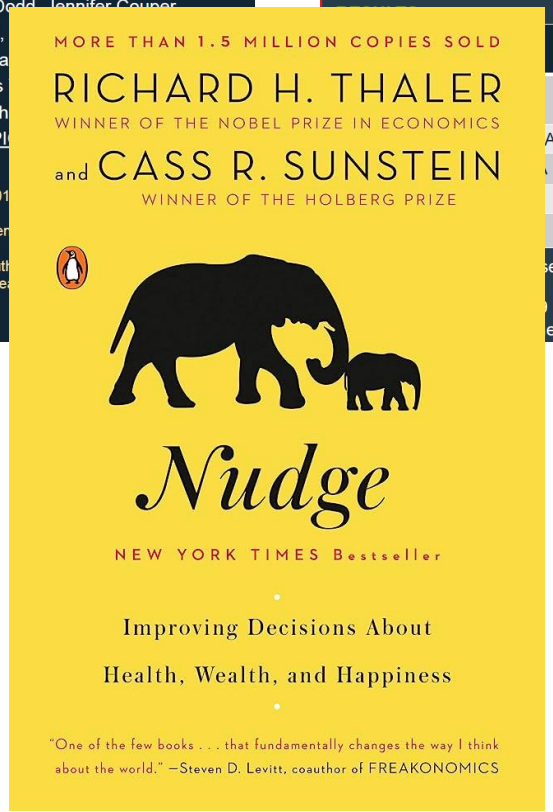
- Twenty participants with diverse skills (pregnant women, obstetricians, midwives, hospital administrative personnel, behavioural scientists, psychologists and graphic designers) from SA, WA and Victoria participated in a nudgeathon to develop the nudge. A 'nudge' comprising three SMS text message reminders with links to vaccine safety information and videos of health professionals and consumers providing advice was developed. Messages sent 1 month apart. First 2 messages – agreement/opt out options.
- A randomised controlled trial of pregnant women at four tertiary hospitals in SA and Victoria. Pregnant women (n = 1086) who have received ≤2 doses of a COVID-19 vaccine (confirmed by the AIR) were randomised (1:1) to standard care or intervention groups.
- Primary outcome – receiving at least 1 dose of a COVID-19 vaccine from randomisation until delivery (confirmed by AIR).

	Screened	Fully vaccinated n (%)	Randomised*	Intervention group	Agreed to get vaccinated n (%)	Opted out n (%)
	1292	814 (63%)	478	238	11 (4.6%)	35 (14.7%)
A	502	330 (65.7%)	172	86	02 (2.3%)	14 (16.3%)
	555	270 (48.6%)	285	142	02 (1.4%)	17 (11.9%)
	464	313 (67.5%)	151	77	07 (9.1%)	06 (7.8%)
	2813	**1727 (61.4%)**	**1086**	**543**	**22 (4.1%)**	**72 (13.1%)**

se: 56 (5.2%), 2 doses: 754 (69.4%)

booster vaccine uptake among pregnant women is sub optimal. The nudge appears to influence e booster vaccine.

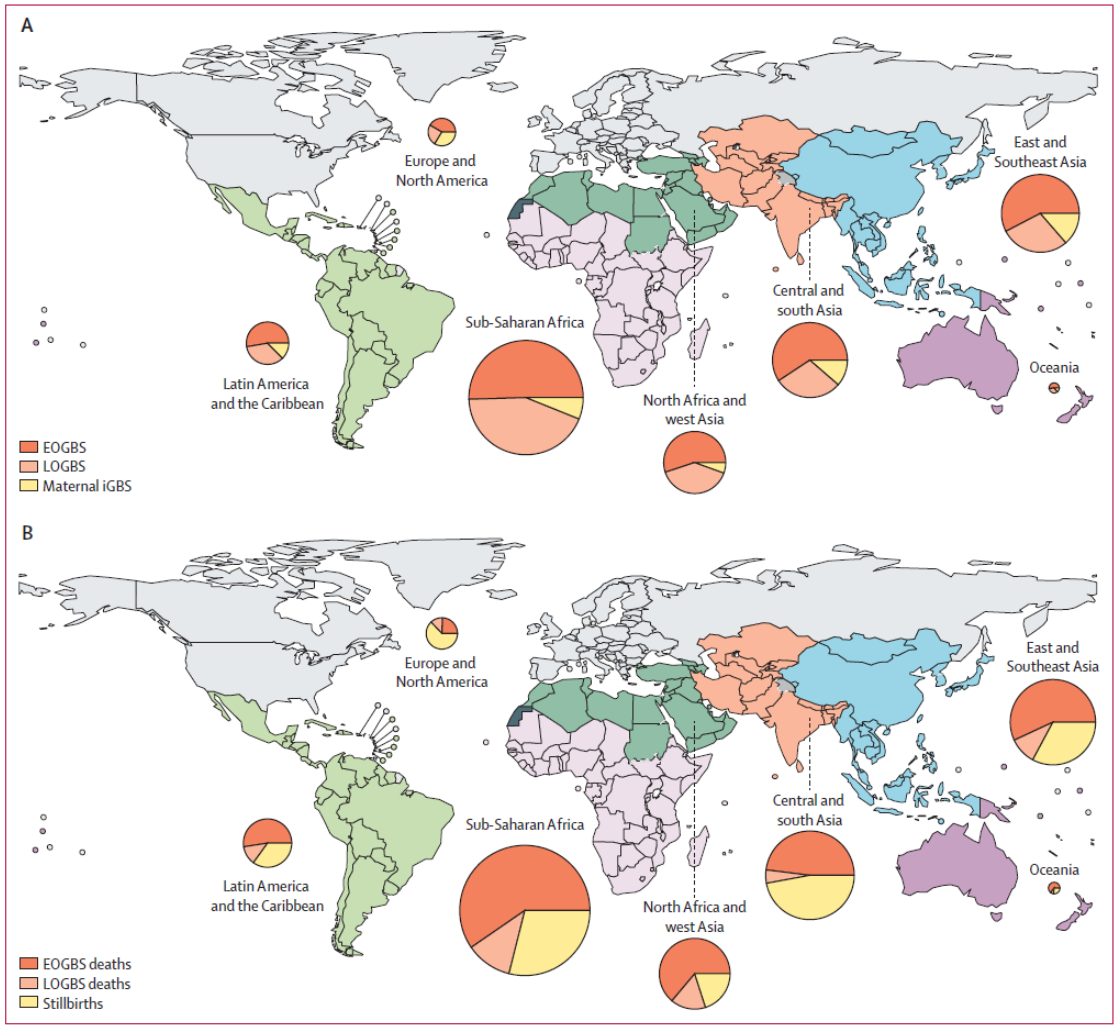
THE UNIVERSITY of ADELAIDE

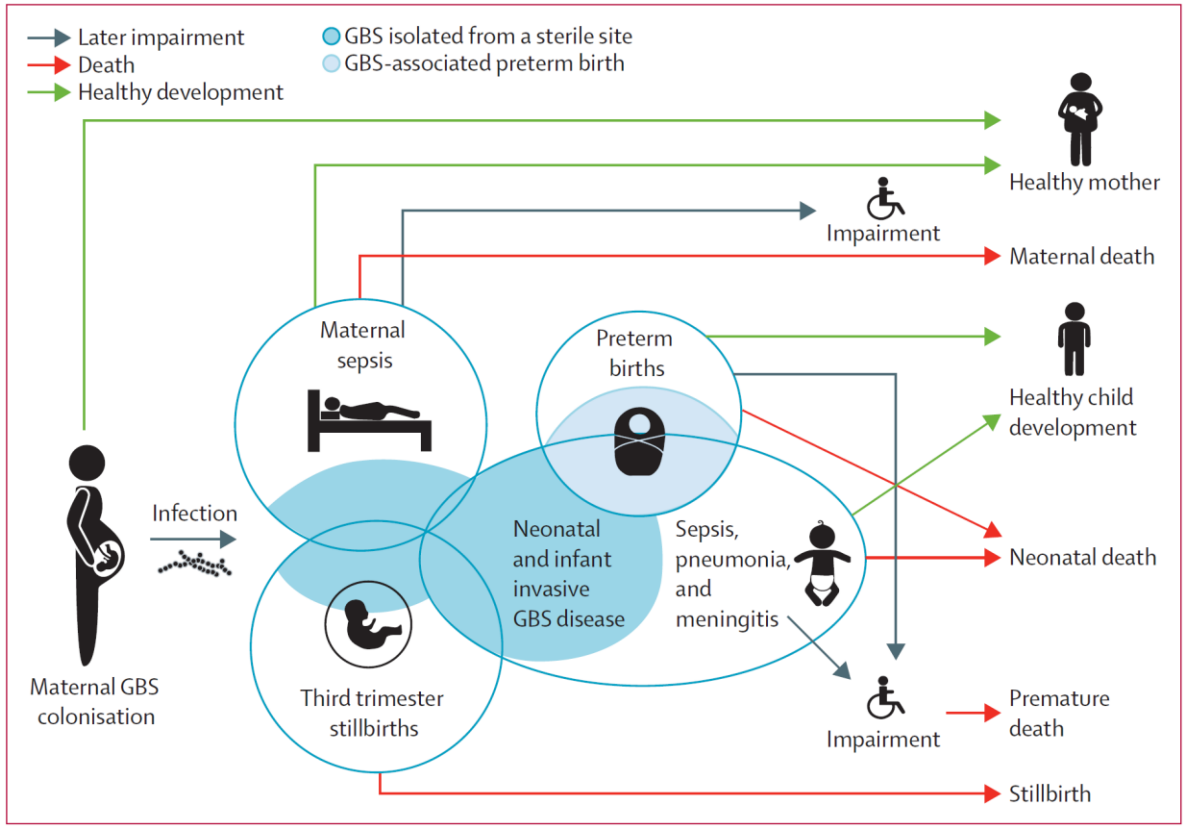


Summary

What's old? With some new bits	Influenza and pertussis
What's not so old?	COVID-19
What's new?	RSV
What are the challenges?	Vaccine coverage and equity
What does the future hold?	Group B streptococcus, CMV

GBS





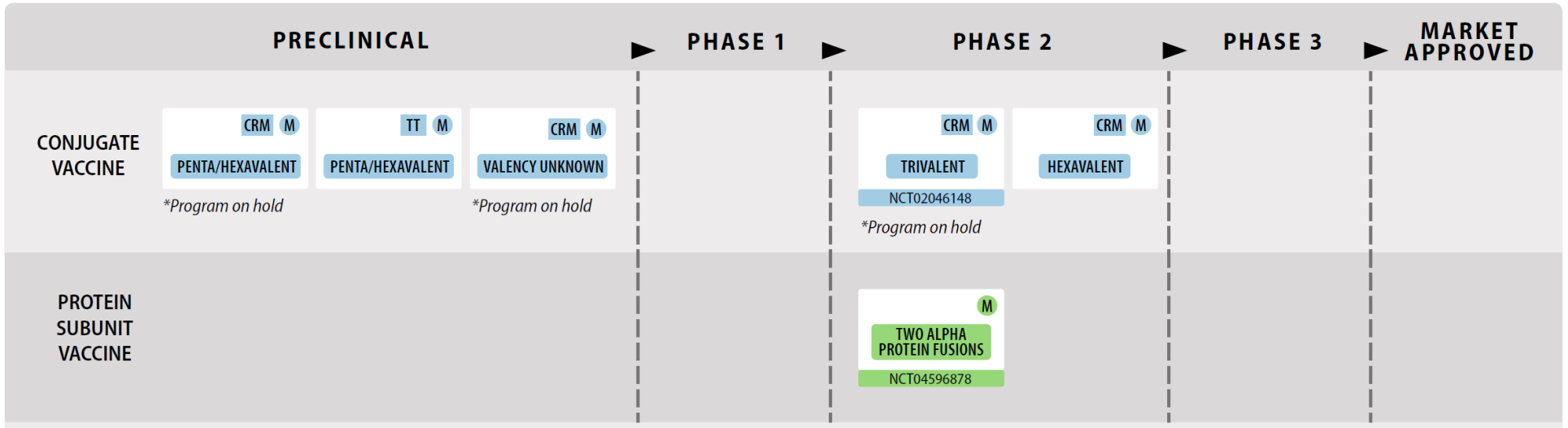
	Stillbirths	EOGBS	LOGBS	Infant deaths after iGBS (both EOGBS and LOGBS)
Sub-Saharan Africa	20 300 (9000–40 500)	90 800 (43 000–186 600)	78 100 (30 000–218 700)	50 600 (23 800–108 400)
North Africa and west Asia	2300 (1000–5800)	29 000 (13 800–58 700)	20 800 (8400–52 800)	9600 (4300–20 800)
Central and south Asia	14 700 (3600–51 500)	47 300 (24 300–89 900)	23 600 (6100–68 600)	16 700 (8200–33 500)
East and southeast Asia	4600 (1100–16 200)	45 700 (21 600–92 900)	22 600 (5700–68 200)	9700 (4200–22 600)
Latin America and the Caribbean	1800 (300–11 700)	12 800 (6700–24 400)	8400 (2700–29 200)	3600 (1600–8200)
Oceania	100 (20–600)	700 (300–1500)	400 (100–2600)	300 (100–900)
Europe and North America	700 (200–1800)	4300 (2000–7600)	2500 (1000–5300)	400 (200–800)
Global	46 200 (20 300–111 300)	231 800 (114 100–455 000)	162 200 (70 200–394 400)	91 900 (44 800–187 800)

Data shown as posterior medians (95% posterior intervals) of GBS-related stillbirths, EOGBS cases, LOGBS cases, and infant deaths during iGBS in 2020 by region. The last two digits in each number were rounded down, except for numbers less than 100, as done in previous estimates. EOGBS=early-onset iGBS. GBS=group B streptococcus. iGBS=invasive GBS. LOGBS=late-onset iGBS.

Table 2: **Sustainable Development Goal region estimates of acute and long-term outcomes**

Goncalves BP et al, Lancet 2022

GBS



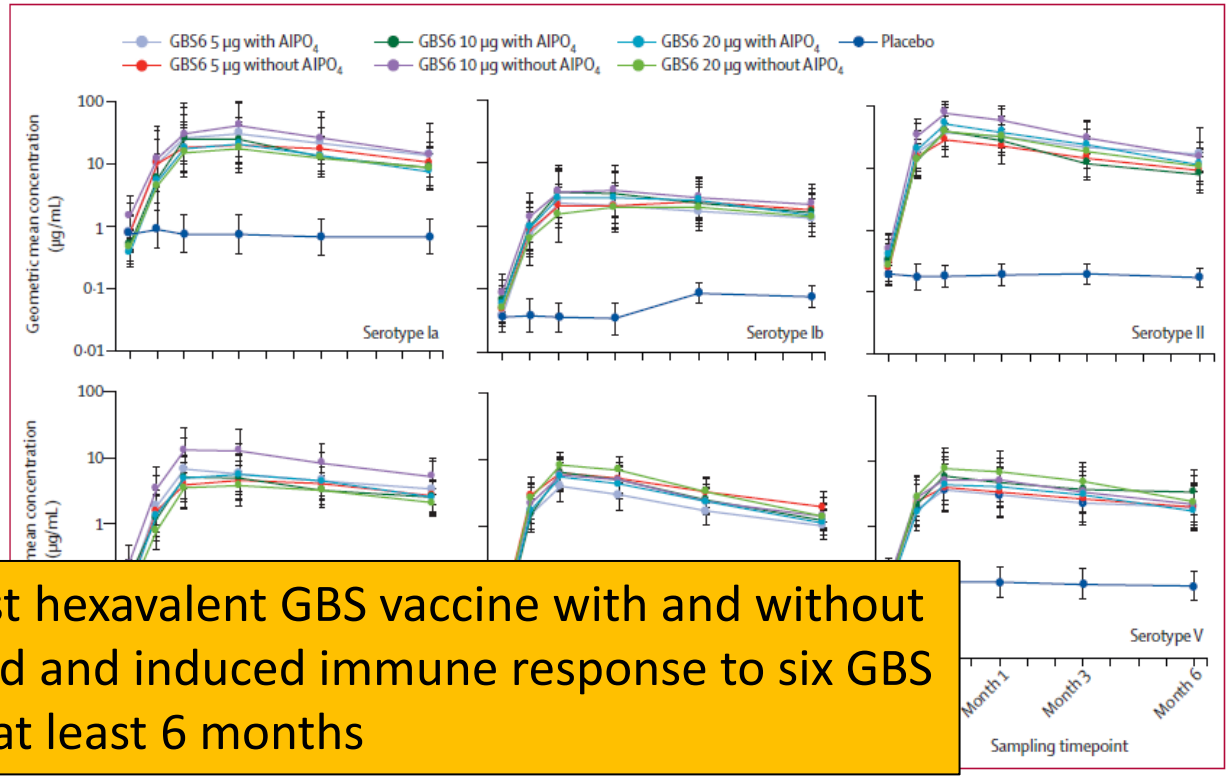
Safety and immunogenicity of a novel hexavalent group B streptococcus conjugate vaccine in healthy, non-pregnant adults: a phase 1/2, randomised, placebo-controlled, observer-blinded, dose-escalation trial

Judith Absalon, Nathan Segall, Stan L Block, Kimberly J Center, Ingrid L Scully, Peter C Giardina, James Peterson, Wendy J Watson, William C Gruber, Kathrin U Jansen, Yahong Peng, Samantha Munson, Danka Pavliakova, Daniel A Scott, Annaliesa S Anderson

Lancet Infect Dis 2021; 21: 263–74
Published Online September 3, 2020

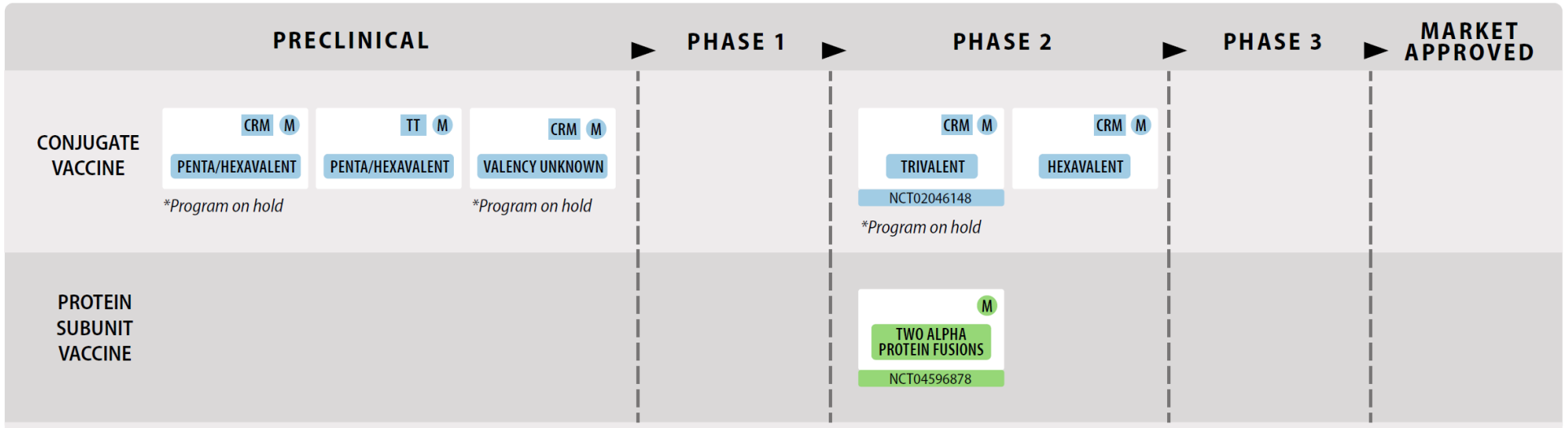
Summary

Background Group B streptococcus (GBS) is a major cause of invasive disease in young infants. Infants born to women with sufficient pre-existing anti-GBS capsular IgG antibodies are at reduced risk of GBS disease, making maternal immunisation a potential strategy for prevention. We aimed to assess the safety and immunogenicity of a novel hexavalent (serotyp



Three doses (5ug, 10ug and 20ug) of the first hexavalent GBS vaccine with and without aluminum phosphate was safe, well tolerated and induced immune response to six GBS serotypes lasting at least 6 months

GBS



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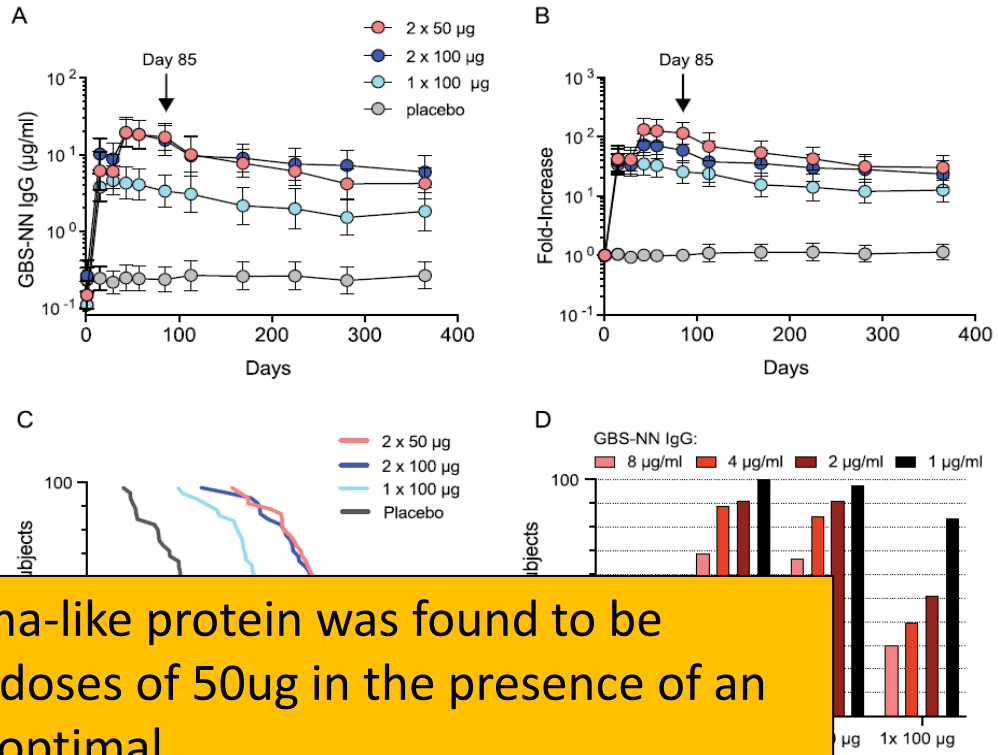
Safety and immunogenicity of a prototype recombinant alpha-like protein subunit vaccine (GBS-NN) against Group B Streptococcus in a randomised placebo-controlled double-blind phase 1 trial in healthy adult women

Per Fischer [a], Andrzej
Bengt Johansson-Lind

[a] Minervax A/S, Ole Maaløes Vej 3, D
[b] Immunology Section, Department
[c] BioKinetic Europe Ltd, 14 Great Vic



GBS-NN targeting the 6 members of the Alpha-like protein was found to be well tolerated and highly immunogenic with two doses of 50ug in the presence of an adjuvant considered optimal

GBS

Limited local serotype data to inform GBS vaccine considerations

135 sterile isolates – PathWest laboratory

Isolate Characteristic		Total (n=135)	Period 1, 2004-2008 (n=44)	Period 2, 2009-2015 (n=43)	Period 3, 2016-2020 (n=48)	p-value
Clonal Complex	1	30 (22.2%)	9 (20.5%)	11 (25.6%)	10 (20.8%)	0.813
	12	13 (9.6%)	7 (15.9%)	4 (9.3%)	2 (4.2%)	0.162
	17	34 (25.2%)	6 (13.6%)	9 (20.9%)	19 (39.6%)	0.012*
	19	18 (13.3%)	7 (15.9%)	7 (16.3%)	4 (8.3%)	0.446
	23	35 (25.9%)	12 (27.3%)	10 (23.3%)	13 (27.1%)	0.889
	Singleton	5 (3.7%)	3 (6.8%)	2 (4.7%)	0	N/A
Capsular Polysaccharide Genotype	Ia	36 (26.7%)	13 (29.6%)	11 (25.6%)	12 (25%)	0.869
	Ib	11 (8.2%)	6 (13.6%)	3 (7.0%)	2 (4.2%)	0.239
	II	8 (5.9%)	3 (6.8%)	2 (4.7%)	3 (6.3%)	0.906
	III	49 (36.3%)	10 (22.7%)	16 (37.2%)	23 (47.9%)	0.042*
	IV	4 (3.0%)	0	1 (2.3%)	3 (6.3%)	N/A
	V	21 (15.6%)	10 (22.7%)	9 (20.9%)	2 (4.2%)	0.026*
	VI-IX	6 (4.4%)	2 (4.6%)	1 (2.3%)	3 (6.3%)	0.662
Candidate vaccine coverage	Pfizer hexavalent	129 (95.6%)	42 (95.5%)	42 (97.7%)	45 (93.8%)	0.662

Isolate Characteristic		Total (n=135)	Period 1 2004-2008 (n=44)	Period 2 2009-2015 (n=43)	Period 3 2016-2020 (n=48)	p-value
Surface protein genes	ALPCN (BCA)	26 (19.3%)	12 (27.3%)	7 (16.3%)	7 (14.6%)	0.254
	ALP1 (EPS)	32 (23.7%)	10 (22.7%)	10 (23.3%)	12 (25%)	0.964
	ALP2/3N	23 (17.0%)	10 (22.7%)	8 (18.6%)	5 (10.4%)	0.275
	RIB	53 (39.3%)	12 (27.3%)	18 (41.9%)	23 (47.9%)	0.118
Candidate vaccine coverage	Minervax NN	134 (99.3%)	44 (100%)	43 (100%)	47 (97.9%)	N/A

Hilpipre G, Furfaro L, Porter M, Blyth CC, Yeoh DK et al. Submitted for publication

CMV

112. Interim Results From a Phase 2, Randomized, Observer-Blind, Placebo-Controlled, Dose-Finding Trial of an mRNA-Based Cytomegalovirus Vaccine in Healthy Adults

Lori Panther, MD, MPH[1]; Carlos Fierro, MD[2]; Daniel Brune, MD[3]; Richard Leggett, DO[4]; James Peterson, MD[5]; Paul Pickrell, MD[6]; Jiang Lin, PhD[1]; Kai Wu, PhD[1]; Heather Lee, BS[1]; Roxane Hasselbeck, BA[1]; Andrew Natenshon, MA[1]; Jacqueline Miller, MD[1]; [1]Moderna, Inc., Cambridge, Massachusetts; [2]Johnson County Clin-Trials, Lenexa, Kansas; [3]Optimal Research, Peoria, Illinois; [4]Crossroads Clinical Research, Victoria, Texas; [5]Foothill Family Clinic, Salt Lake City, Utah; [6]Tekton Research, Austin, Texas

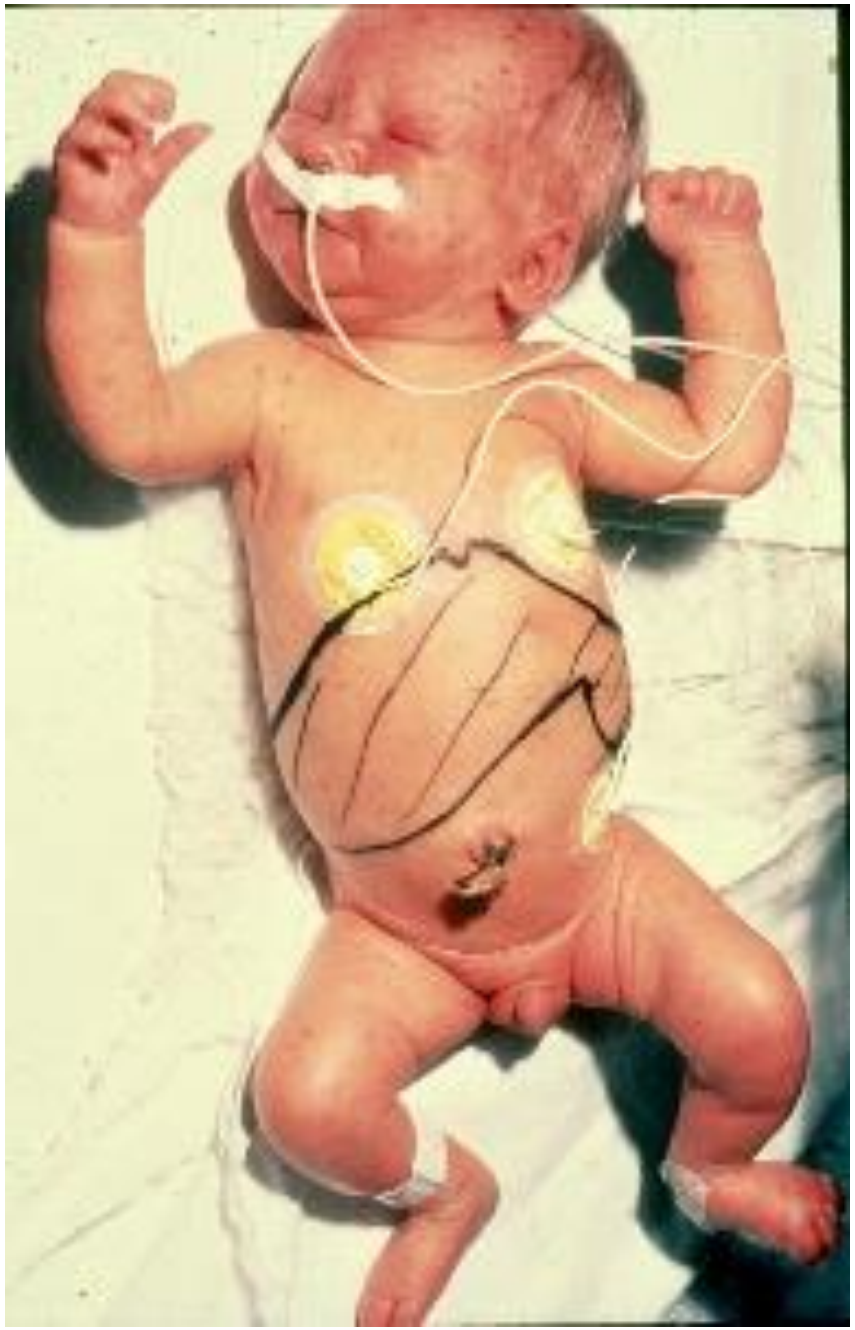
Session: 34. Adult Vaccines
Thursday, October 20, 2022: 12:15 PM

Background. Cytomegalovirus (CMV) is the most common congenital viral infection and can cause severe long-term health consequences, including hearing loss and neurodevelopmental delay. A safe and effective method for prevention of CMV infection is an unmet need and public health priority. An mRNA-based vaccine against CMV, mRNA-1647, is in development and consists of 6 mRNA sequences encoding 2 CMV antigens (glycoprotein B and the pentameric glycoprotein complex) in a lipid nanoparticle formulation.

Methods. In this Phase 2, randomized, placebo-controlled, observer-blind, dose-finding trial, safety and immunogenicity of mRNA-1647 was evaluated in healthy adults aged 18 to 40 years (NCT04232280). In Part 1, CMV-seronegative and CMV-seropositive men and women were randomized 3:1 to receive mRNA-1647 (doses of 50, 100, or 150 μg) or placebo at Months 0, 2, and 6. The 100-μg dose was chosen for Part 2. In Part 2, CMV-seronegative and CMV-seropositive women were randomized 3:1 to receive mRNA-1647 100 μg or placebo at Months 0, 2, and 6. Safety endpoints were solicited local and systemic adverse reactions, unsolicited adverse events (AEs), and medically attended AEs through 7 days, 28 days, and 6 months after vaccination, respectively, and serious AEs throughout the study. Humoral immunogenicity endpoints were antigen-specific binding antibody titers and neutralizing antibody titers against epithelial cell infection and against fibroblast infection.

Results. In Parts 1 and 2, 252 and 63 participants were randomized, respectively. Interim analysis (IA) of Part 1 through 1 month after Dose 3 indicated that mRNA-1647 100 μg was generally well-tolerated, induced robust antibody responses in CMV-seronegative participants, and boosted antibody titers in CMV-seropositive participants. An additional IA of Part 1 through end of study and Part 2 through 1 month after Dose 3 showed no notable differences in the safety profile compared with the previous IA (Part 1, 1 month after Dose 3); immunogenicity data for this additional IA is being generated.

Conclusion. Available data from this Phase 2 trial suggest that mRNA-1647 100 μg was immunogenic in CMV-seronegative and CMV-seropositive participants and was generally well-tolerated. The mRNA-1647 candidate vaccine is being evaluated in a Phase 3 trial.



CMV

What is CMV?

Cytomegalovirus, shortened to CMV, is a leading cause of birth defects around the world. CMV is a common viral infection that usually goes unnoticed or only causes mild symptoms in most people. But if a woman becomes infected with CMV while she is pregnant, she can pass the infection to her unborn baby. This can cause her child to suffer long-term disability due to birth defects, including hearing loss, or even death in very severe cases. Currently, there is no approved vaccine against CMV.

CMV is the #1 infection that causes birth defects in the U.S. and one of the most common infectious causes of birth defects globally.

How Participation Works