IMMUNISATION COALITION

Developments in vaccination during pregnancy

2:50 pm

Prof Peter Richmond

Head of Division, UWA Medical School, Paediatrics, Perth, WA

Maternal Vaccination: current recommendations and emerging vaccines.

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WESFARMERS CENTRE OF VACCINES & INFECTIOUS DISEASES

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Acknowledgement of Country

Declaration of Conflicts of Interest

- Membership of Immunisation committees
  - Australian Technical Advisory Group on Immunisation, 2005-14
  - Chair, WA Vaccine Safety Advisory Committee, 2011 - present
- Scientific Advisory Boards (on behalf of UWA)
  - RSV vaccines, (GSK, Pfizer, Moderna, Sanofi, Clover Biopharmaceuticals)
  - RSV monoclonal antibodies (Astra-Zeneca, Merck, Sanofi)
  - *No personal remuneration*
- Resvinet Board member – RSV advocacy not-for profit organisation
- Vaccine Research
  - Investigator of industry sponsored multi-centre studies for CSL, GSK, Medimmune, Merck, Pfizer, Sanofi, Novartis

Talk Summary

- Lessons from maternal pertussis vaccine implementation
- Case for COVID-19 vaccination in pregnancy
- Maternal Vaccination for RSV
- Implications for use of maternal vaccines in the future

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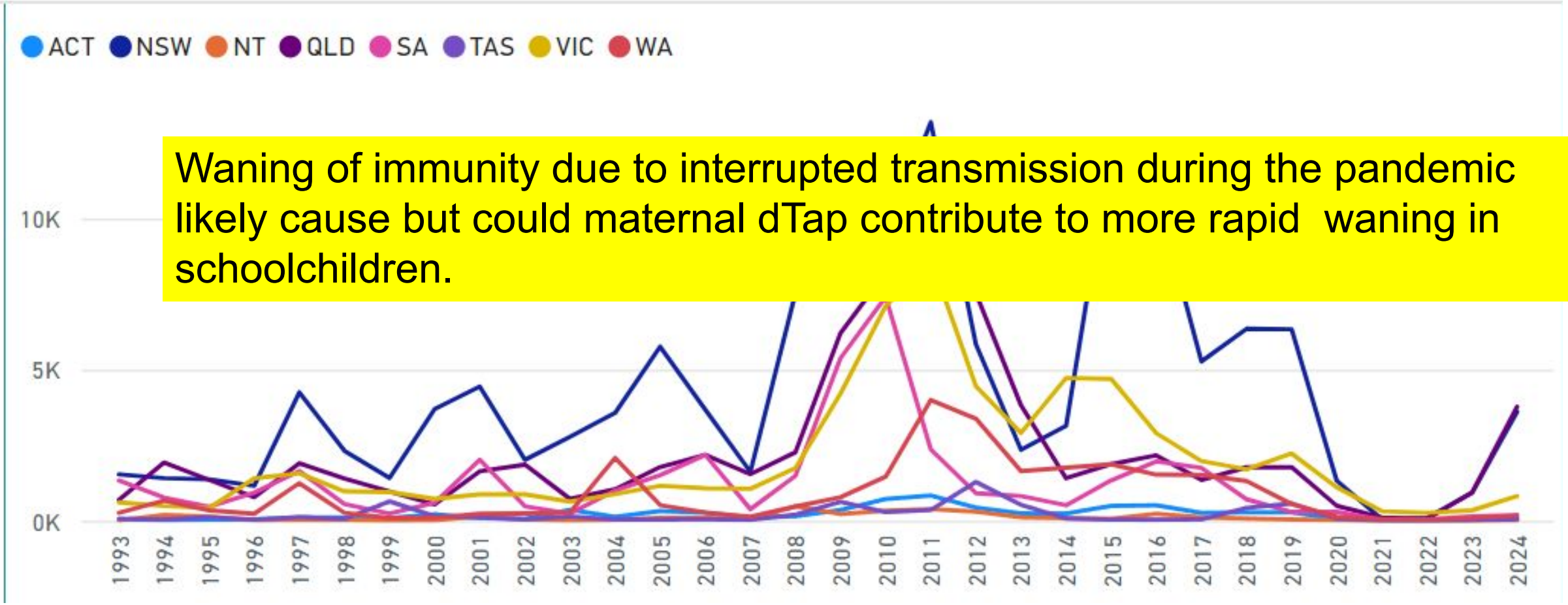
Pertussis notifications in Australia to June 2024



Waning of immunity due to interrupted transmission during the pandemic likely cause but could maternal dTap contribute to more rapid waning in schoolchildren.

- Rapid increase since 2022: 482 to 8640 this year to date (86% in NSW & Qld) in mainly paediatric population: 8.6% cases 0-4 yrs; 17% 5-9 yrs; 39% 10-14 yrs

Time for a pertussis only vaccine for pregnancy?

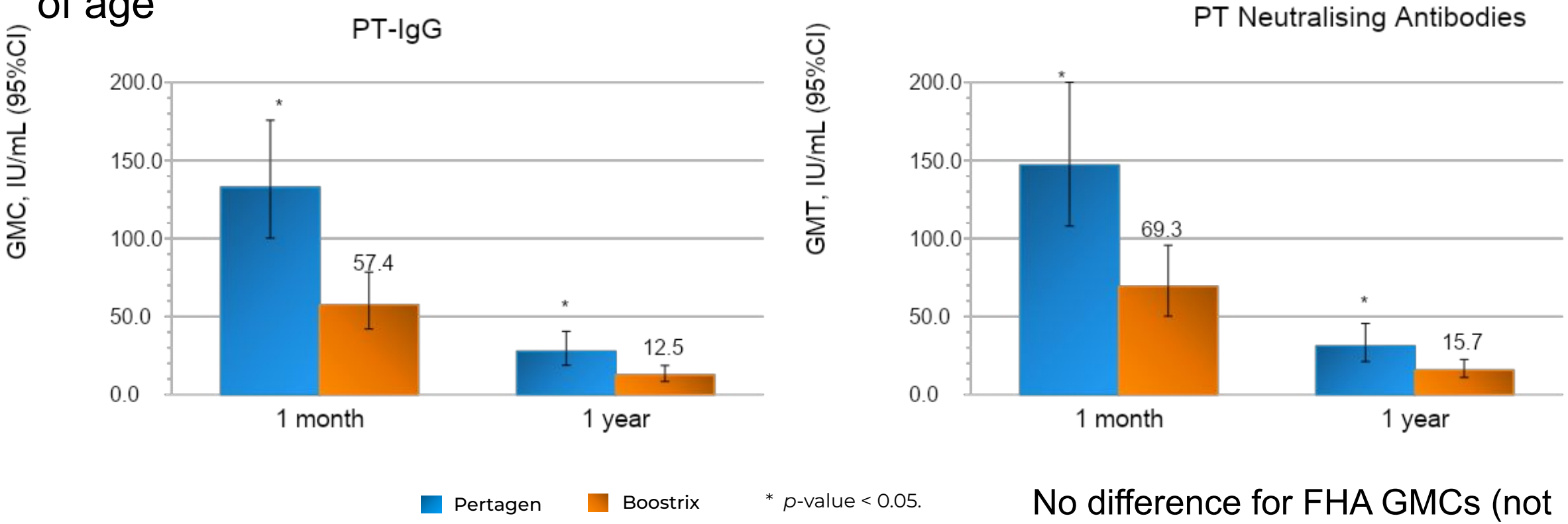
- Acellular pertussis vaccine (dTap; **Boostrix, Adacel**)
  - Chemical methods conformational changes to the antigen[2]
  - Immunogenic in adults but waning PT (and FHA, Pertactin, Fim2/3) after 12 mths

- Monovalent recombinant pertussis vaccine (PT_{gen} and FHA) **Pertagen® (aP_{gen})**
  - Genetically detoxified pertussis toxin (PT_{gen}) broad, durable protection[3]
  - Currently the only pertussis “stand-alone” vaccine available in the world.
  - Licensed for booster use in Thailand and Singapore
  - Free for each pregnancy in Thai health program since 2024[4]

[1] *Edwards KM, Decker MD. Pertussis vaccines. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KM, eds. Plotkin's Vaccines. 2017:726.*
[2] *Advisory Committee on Immunization Practices (ACIP), DHHS, Summary Report, October 24-25, 2018, Atlanta, Georgia.*
[3] *Poolman JT. Expert Rev Vaccines. 2014; 13:10, 1159-62.*

Next generation Pertussis monovalent vaccine for pregnancy

Pertagen® genetically detoxified PT-FHA vaccine in young adults 18 -30 years of age

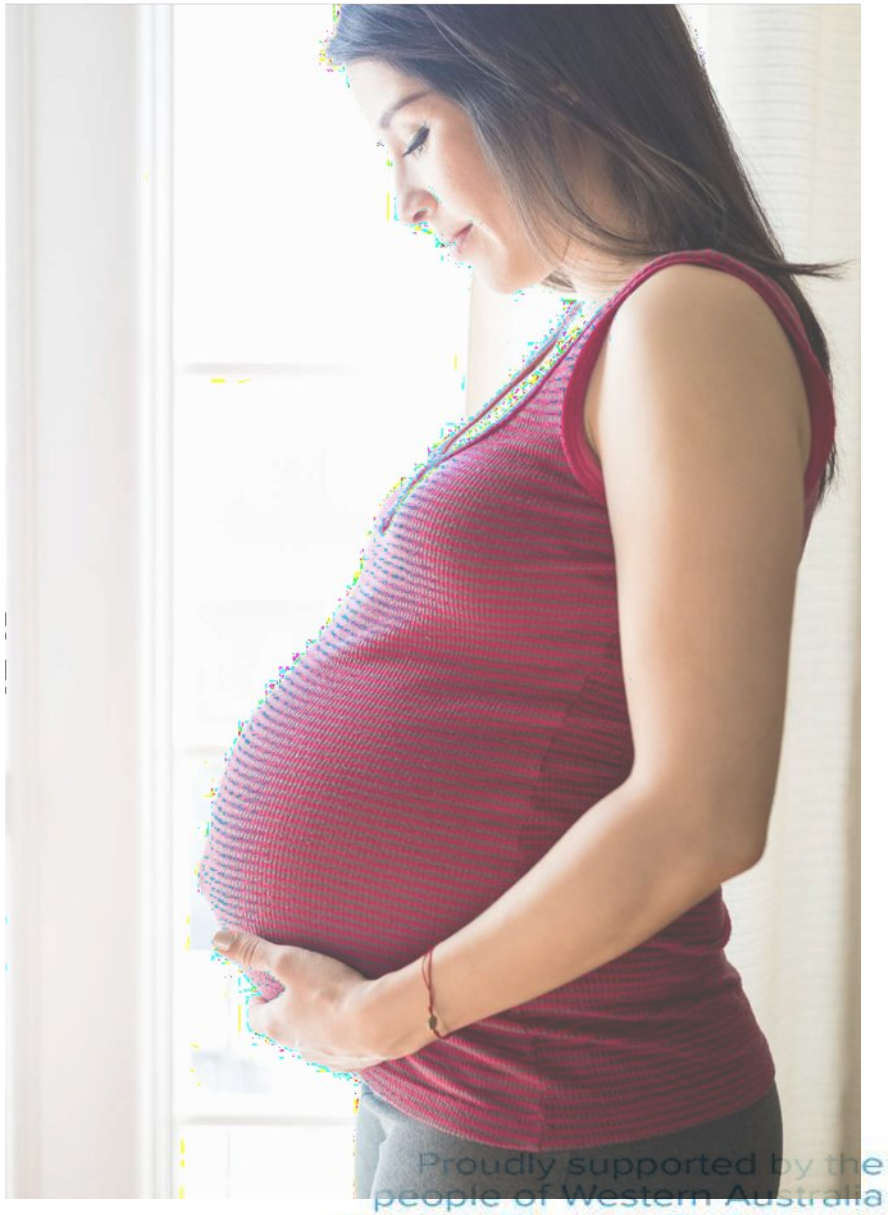


No difference for FHA GMCs (not shown)

- Recently submitted to TGA for registration in adults including in pregnancy

Hutton H et al *Pertagen® is a safe and effective stand-alone Pertussis vaccine CDIC Brisbane, 2024*

Case for Covid-19 Vaccination



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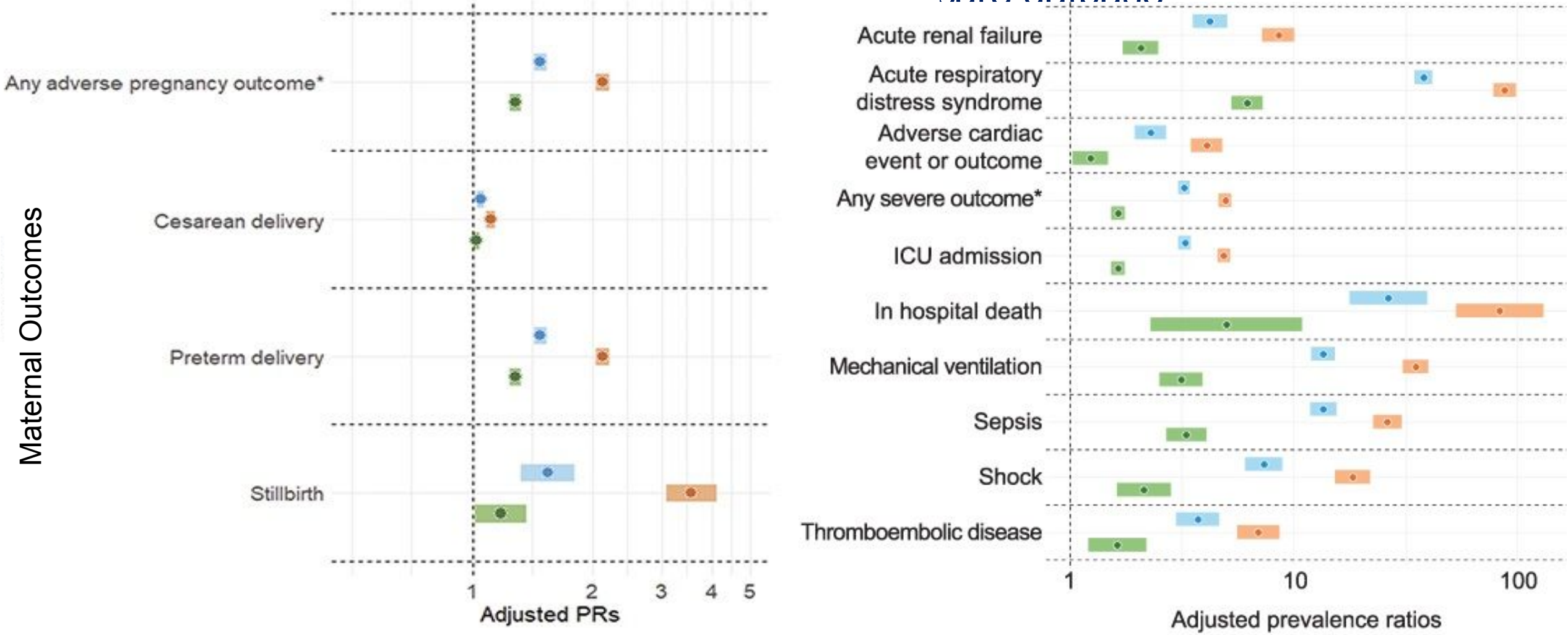
ATAGI Recommendations for Pregnancy

Vaccine	Recommendation	Comments
Influenza	Recommended for all pregnant women at any stage of pregnancy, particularly if in 2nd or 3rd trimester during the influenza season	Protects the mother, and her newborn baby in the first few months after birth.
dTpa (diphtheria-tetanus-acellular pertussis)	Recommended mid 2nd trimester and early 3rd trimester of each pregnancy (ideally at 20–32 weeks)	Reduces the risk of pertussis in pregnant women and their young infants by 90%.
COVID-19	Not routinely recommended in previously vaccinated women but can be considered. Vaccine can be given at any stage of pregnancy.	*Routinely recommended in USA* *Established safety profile and evidence of protection*

Maternal Complications of COVID-19 – still an issue with Omicron

recently published US data from the Premier Healthcare database



2022 Omicron period: 780,000 deliveries; 56,618 COVID-19 cases (1.6%)

Jeffrey et al Obstetrics & Gynecology Jan 2024;

The case for recommending maternal COVID vaccine

PAEDS Paediatric Active Enhanced Disease Surveillance An NCIRS led collaboration

COVID-19 Admissions 2020 – April 2024	
Clinical COVID-19 cases	2078
Aboriginal Torres Strait Islander	6.5%
Medical Co-morbidity	24%
Maternal vaccine	15%
Antibiotic use	19%
Antiviral use	5.3%
Oxygen use alone	4.6%
High flow Nasal prongs	4.2%
Ventilator support	2.7%
ICU Admission	5.2%

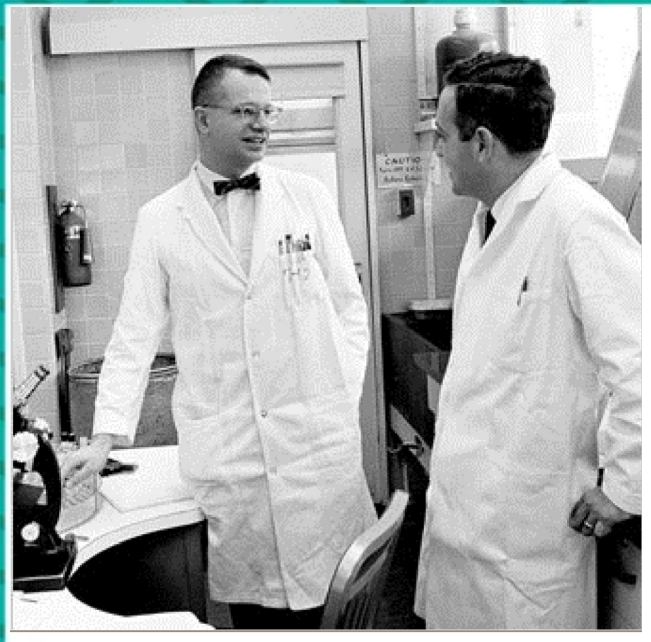
- Burden of diseases in mother and obstetric complications ✔
- Burden of disease in infants <6 months
  - 48% of all paediatric COVID admissions (✔)
  - Incidence vs severity median stay 1.2 days
- Safety of vaccination ✔
- Effectiveness of vaccines
  - Maternal VE 61%
  - Infant VE 56% at mths; 34% at 6 mths

Should we have a more positive ATAGI recommendation for COVID vaccine in pregnancy?

"Not routinely recommended in previously vaccinated women but can be considered"

to

Recommended for those pregnant women who wish to decrease the risk of complications in pregnancy and the risk of infant admission to hospital in the first 3 months of life



The long journey to RSV vaccines

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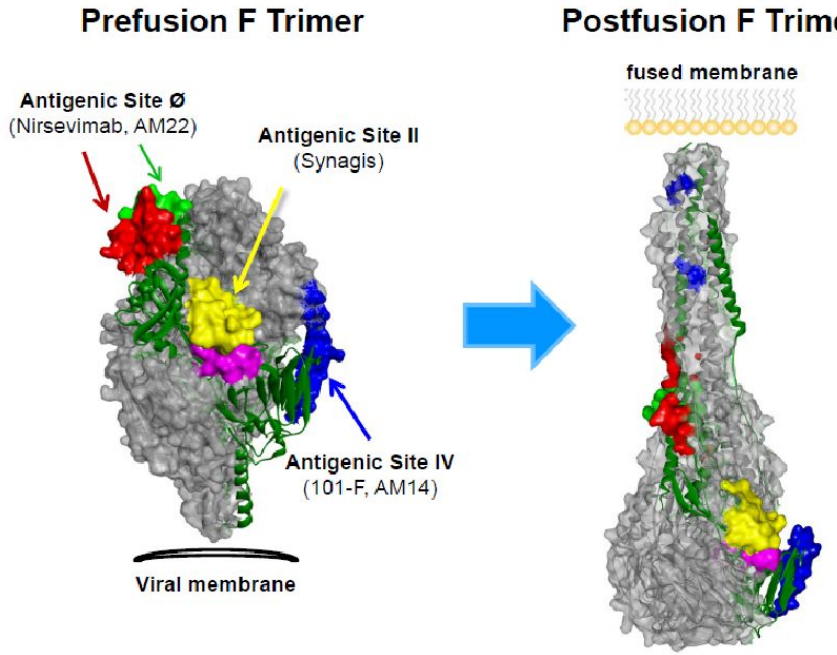
AN EPIDEMIOLOGIC STUDY OF ALTERED CLINICAL REACTIVITY TO RESPIRATORY SYNCYTIAL (RS) VIRUS INFECTION IN CHILDREN PREVIOUSLY VACCINATED WITH AN INACTIVATED RS VIRUS VACCINE

ALBERT Z. KAPIKIAN,[1] REGINALD H. MITCHELL,[2] ROBERT M. CHANOCK,[1] RUTH A. SHVEDOFF[1] AND C. ELEANOR STEWART[1]



Only prefusion F can bind host cells for RSV to infect

Antibodies specific to the prefusion form are most effective at blocking virus infection

McLellan et al Science Nov 2013

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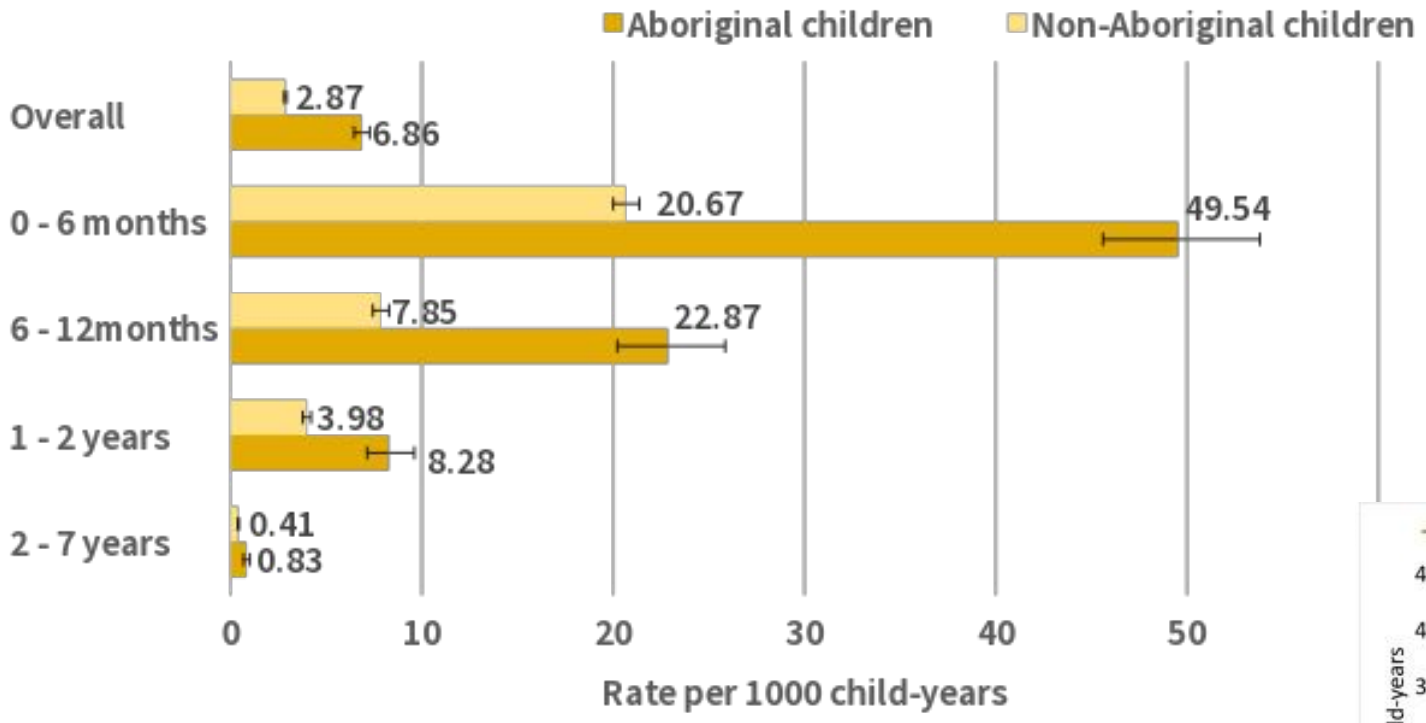
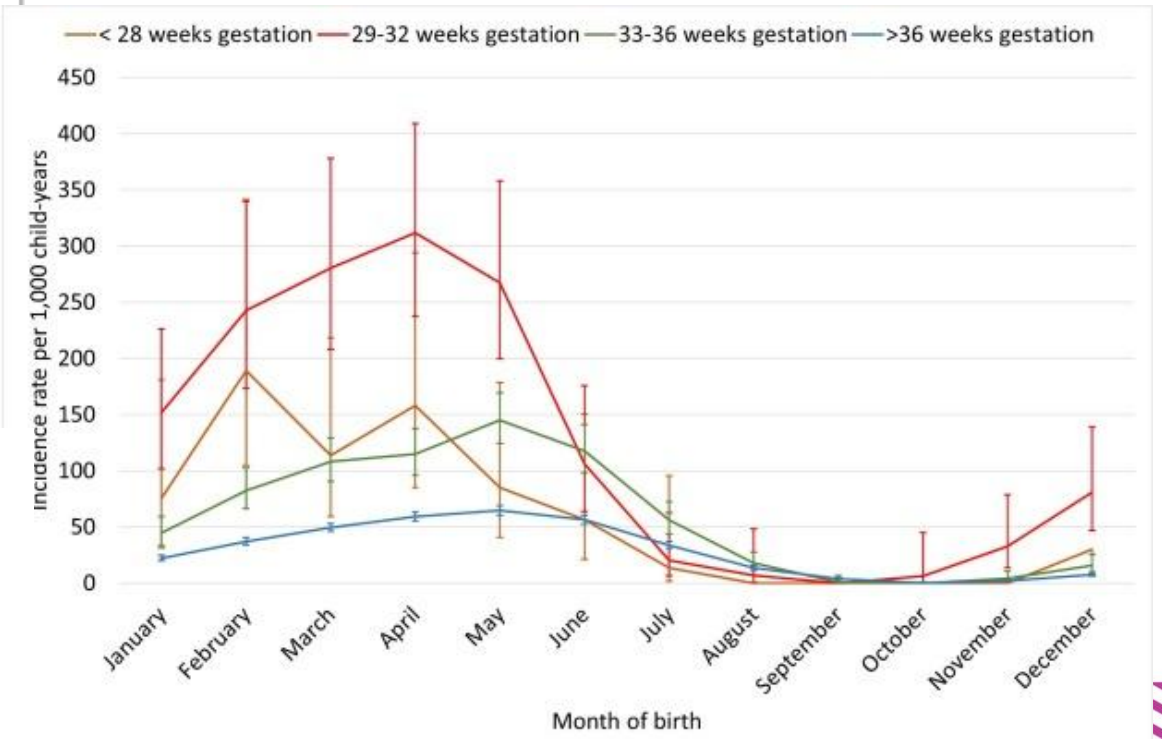
Risk factors for RSV-hospitalization rates (WA)



Sarna, Determining the true incidence of seasonal RSV-confirmed hospitalizations in preterm and term infants in WA. Vaccine 2023; 41:5216-20

Huong Le, unpublished data

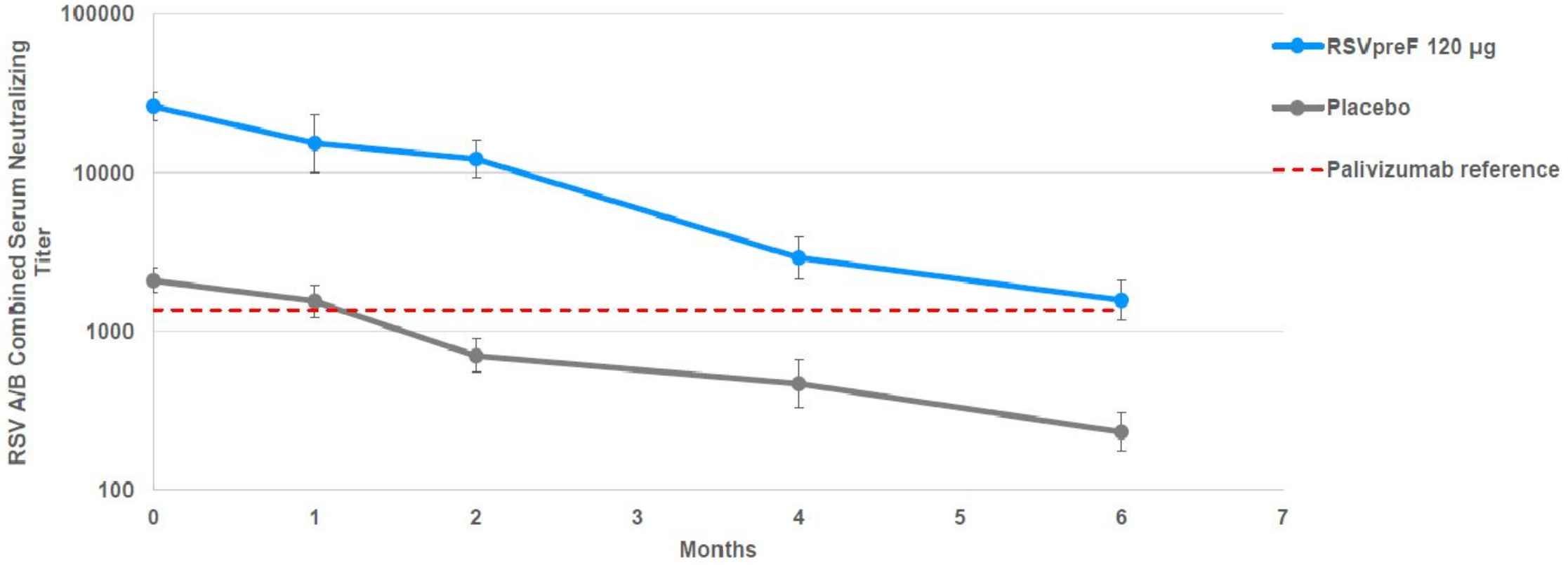
- Highest in infants < 6 mths
- Incidence >2x higher in Aboriginal infants
- Routine data underestimates by ~30%
- Prematurity, chronic medical problems and timing of birth important risk factors
- **83% of RSV hospitalisations however are in otherwise healthy infants**



- Recurrent viral-induced wheeze and asthma more common after infant RSV hospitalisation
  - 11% hospitalised or treated in Emergency Dept. by 5yrs

Maternal RSV vaccination maintains protective antibody levels to 6 months

RSV A/B Combined 50% Geometric Mean Neutralizing Titers by Month in Infants born to Mothers Vaccinated at 24-36 weeks



---Palivizumab reference line = 50% A/B neutralizing titer of a 100ug/mL palivizumab dose, demonstrated to be efficacious in preventing infant RSV-associated ICU admission (Forbes ML, Kumar VR, Yogev R, et al. Hum Vaccin Immunother 2014;10:2789-94.)

Simoes et al NEJM 2022; 386:1615-1626

Efficacy of RSV Vaccine in Pregnancy

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

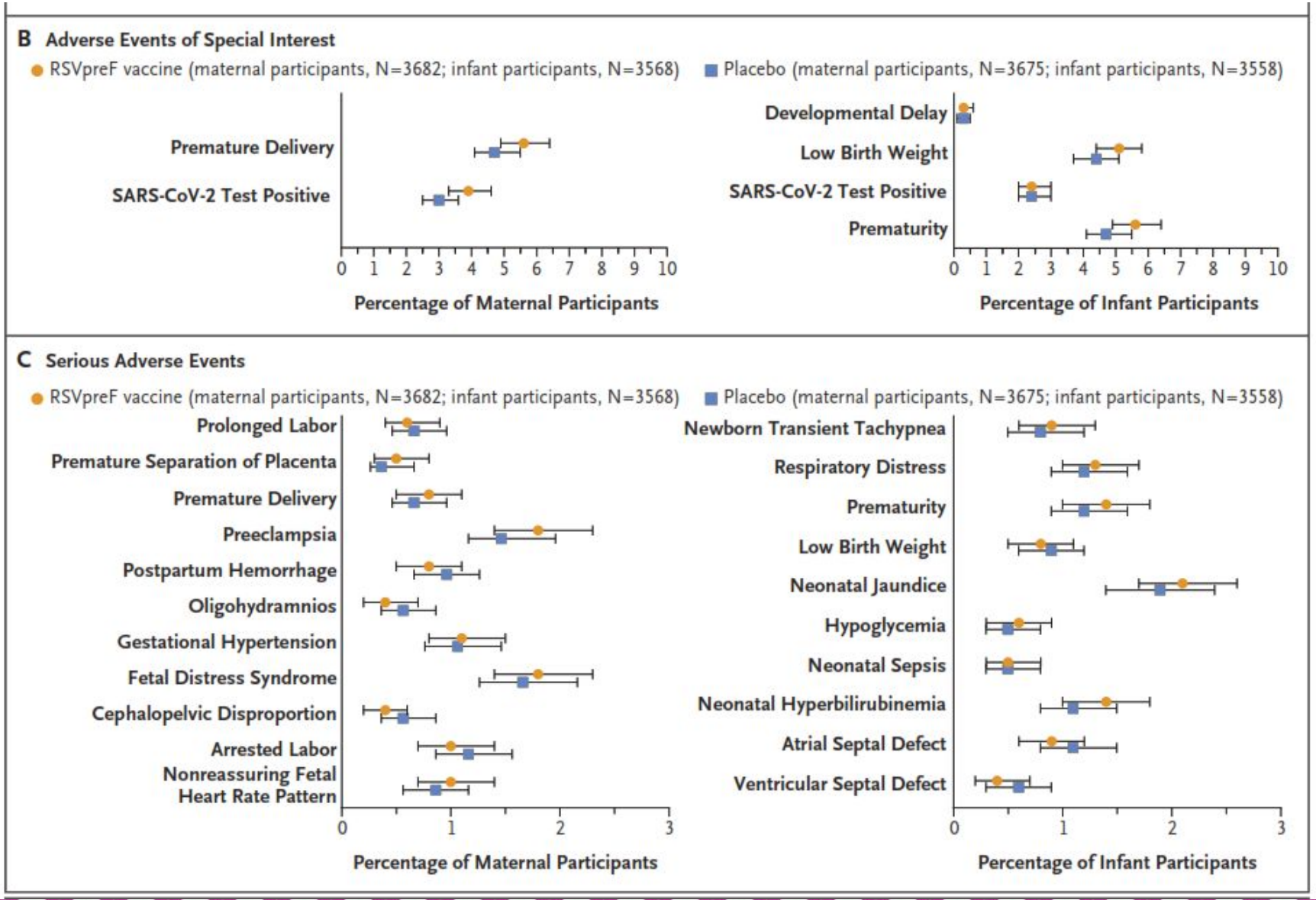
Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

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*

Global study recruited 7,386 healthy pregnant mothers

Safe, well tolerated and minimal reactogenicity

Maternal bivalent RSV vaccine safety



Maternal Bivalent pre-F RSV vaccine efficacy (final)

Outcome	Vaccine Efficacy (95% CI)		
	Over 3 months	Over 6 months	Over 12 months
Any Medically-attended RSV LRTI	**57.6%** (31.1%, 74.6%)	**49.2%** (31.4%, 62.8%)	***40.2%**** *(16.2 – 58.9%)*
Severe Medically-attended RSV LRTI	**82.4%** (57.5%, 93.9%)	**70.0%** (50.6%, 82.5%)	N/A
Hospitalisations with RSV ALRTI	**69.7%** (15.9 – 89.5%)	**55.3%** (23.8 – 74.6%)	**24.2%** (-11.1– 48.6%)
Any Medically-attended RSV RTI	**41.7%** (21.8 – 56.9%)	**37.9%** (25.2 – 48.5%)	N/A

- Vaccine well-tolerated with no safety concerns for vaccinated mothers and their newborns
- Approved by FDA registration in May 2023, EMA in Aug 2023, TGA March 2024
- More than 1 million doses given in the USA with no safety concerns

Munjal RSVVW, Bombay Feb 2024
Kampmann et al. *N Engl J Med* 2023; 388:1451-1464*

Potential Program Points to consider

- Timing of vaccination during pregnancy – variable recommendations

	Europe (EMA)	USA (FDA)	UK (MHRA)	TGA	ATAGI
Gestation (weeks)	24 to 36	32-36	28 - 36	24 -36	?

- Will improve coverage with year-round MV but seasonal may be more cost effective
- Variable RSV seasons in tropical vs temperate regions
- Co-administration with maternal pertussis boosters[1]
  - no impact on RSV, TT, DT, pertussis toxin responses, lower FHA & PRN levels
- Timing of boosters uncertain (at least 2+ years)
- Use in national programs will be influenced by cost-effectiveness
  - Now being considered for introduction in LMICs through GAVI
- Parental acceptance important
  - 79.3% of future Australian reported acceptance of MV[2]

1. *Petersen JT et al J Infect Dis 2022; 225:2077-86*
2. *Holland C. et al Acta Paediatrica 2024; 00:1-9*

Rationale for Maternal RSV vaccine

- Maternal vaccines:
  - Vaccinating pregnant women to protecting young infants through passive transfer of maternal antibodies during the last trimester
  - Mothers more influenced by protection of baby than themselves
  - Accepted strategy for the prevention of infant disease (pertussis, influenza, tetanus, *COVID*)
  - Potential additional protection in upper respiratory tract through breast milk
  - Provides active immunity in mother so also potential protection in future pregnancies
  - Broader repertoire of antibodies against F-protein
  - More amenable for use in LMICs
- Monoclonal antibodies
  - Alternative or complementary to maternal vaccination strategy
  - Important in premature infants as reduced maternal IgG transfer
  - Able to target other groups including older at-risk infants
  - Easier to administer as a seasonal dose
  - Demonstrated high uptake and VE (82%) in Europe, being used in WA, Qld

Maternal Immunsiation Summary

- Maternal immunisation is a safe and effective way to protect young infants using different vaccine platforms
- Interactions between maternal and infant pertussis vaccines need to be considered
- Have we undersold the benefits of COVID vaccines?
- mRNA vaccines may be a solution for congenital CMV infection but will need to raise awareness for parents
- Group B Streptococcus and CMV vaccines also on the horizon
- Will be scheduling these vaccines if successful be an issue?

Acknowledgements

- Telethon Kids Institute
  - Jennifer Kent, Ushma Wadia and Vaccine Trials Group
  - Hannah Moore, Chris Blyth & Infection Epidemiology team
  - Sonia MacAlister, Ruth Thornton and BRIDG team
  - Wesfarmers Centre of Vaccines and Infectious Diseases Community Reference Group
- Australian and Overseas investigators and companies involved in maternal vaccine trials
- Annette Regan ar [illegible]al
- ACIP for public provision of meeting data

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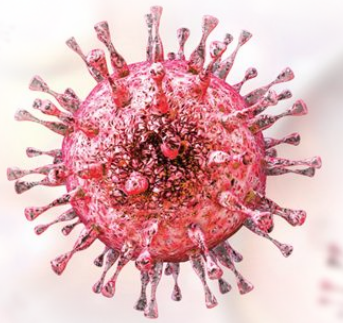
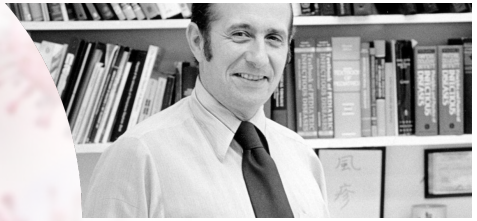
Progress in vaccine development to prevent congenital Cytomegalovirus infection

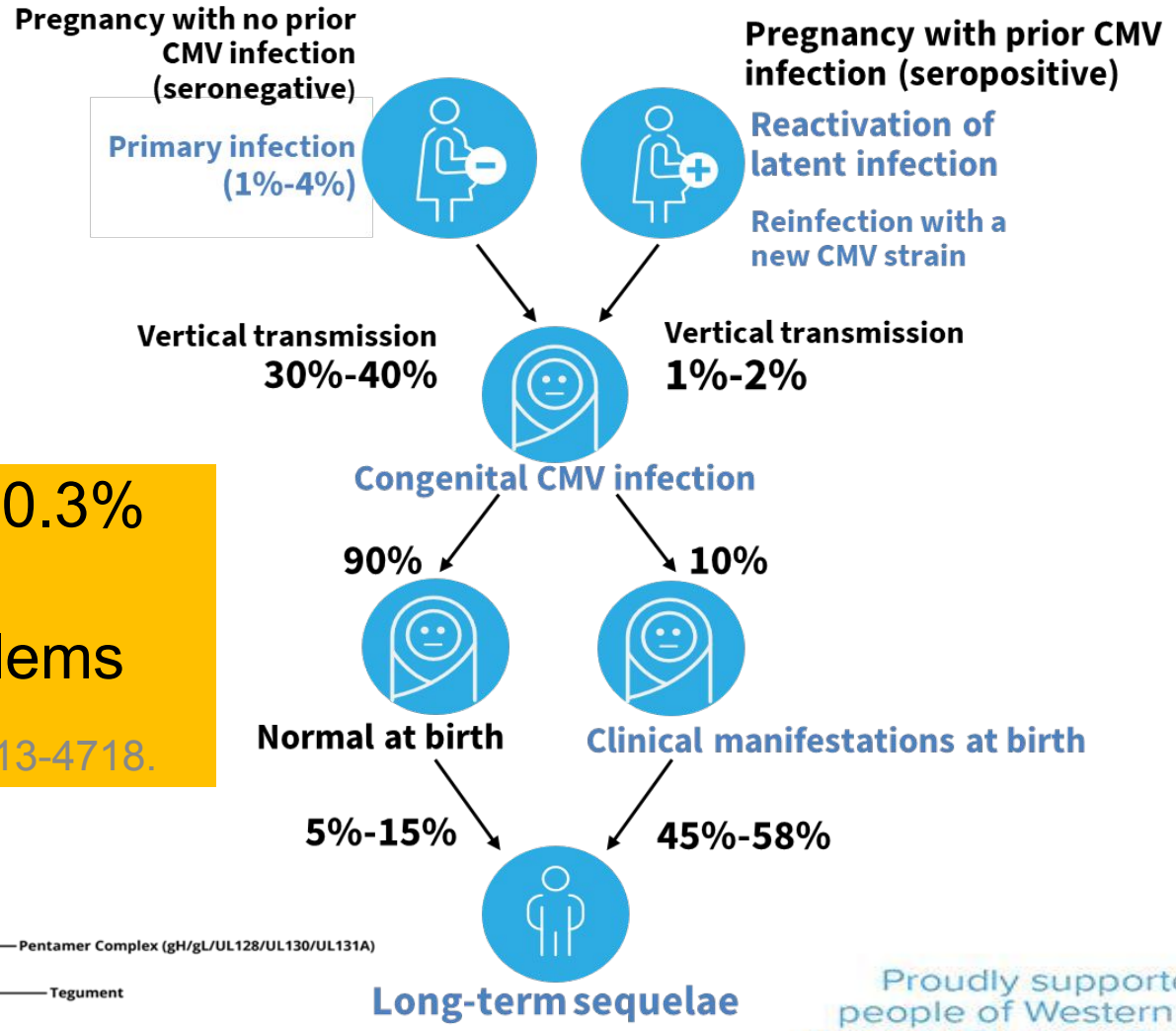




Stanley Plotkin

- cCMV prevalence estimated at 0.3% in Australia and 1 in 5 will have severe, life-altering health problems

Munro SC, et al. J Clin Microbiol. 2005;43(9):4713-4718.



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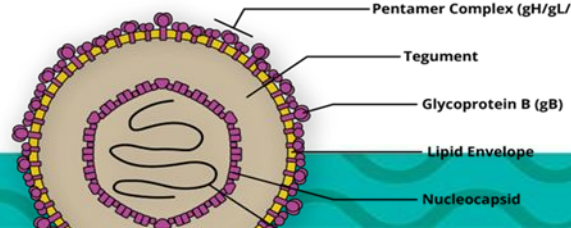

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Moderna's CMV vaccine mRNA-1647 Phase 3 study in women aged 16-40 years

- includes 6 mRNAs (five encode the pentamer, the 6th encodes for the gB antigen; total 100ug mRNA)
- Promising safety and immunogenicity results from Phase 2 study in health adults
- Enrolled over 7000 seronegative and seropositive women
- Receiving 3 vaccine doses of mRNA-1647 under 0-1-6 mth schedule
- Follow-up 2.5 years for CMV illness and pregnancy
- Completed recruitment
- Results expected in 2026
- Potential for adolescent, pre-pregnancy or maternal vaccine