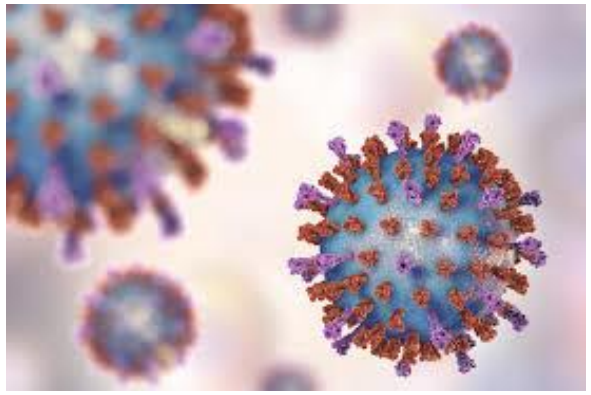


murdoch children's research institute

The Royal Children's Hospital Melbourne

RSV monoclonal antibody (mAb): current state of play

Victorian DH webinar

Monday 9th December 2024

Professor Nigel Crawford

Declarations of interest (DOI)

Director of SAEFVIC based at MCRI, Parkville & Medical Head RCH Immunisation service.

Current Chair of the Australian Technical Advisory Group on Immunisation (ATAGI).

Lead investigator of an ongoing ‘SARI/ RSV surveillance study’, in collaboration with WHO Influenza collaborating centre, funded by the Australian Department of Health.

This presentation presents my own views and not necessarily those of my affiliations.

Nil pharmaceutical industry declarations.

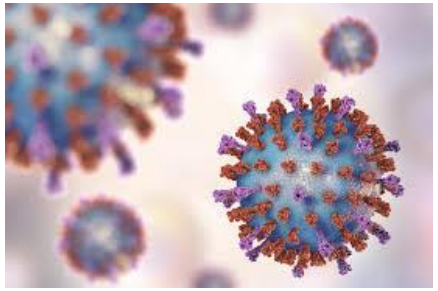
Topics

1. RSV – the virus

2. Product (Niservimab) available in Victoria in 2025

3. Clinical advice

The virus…

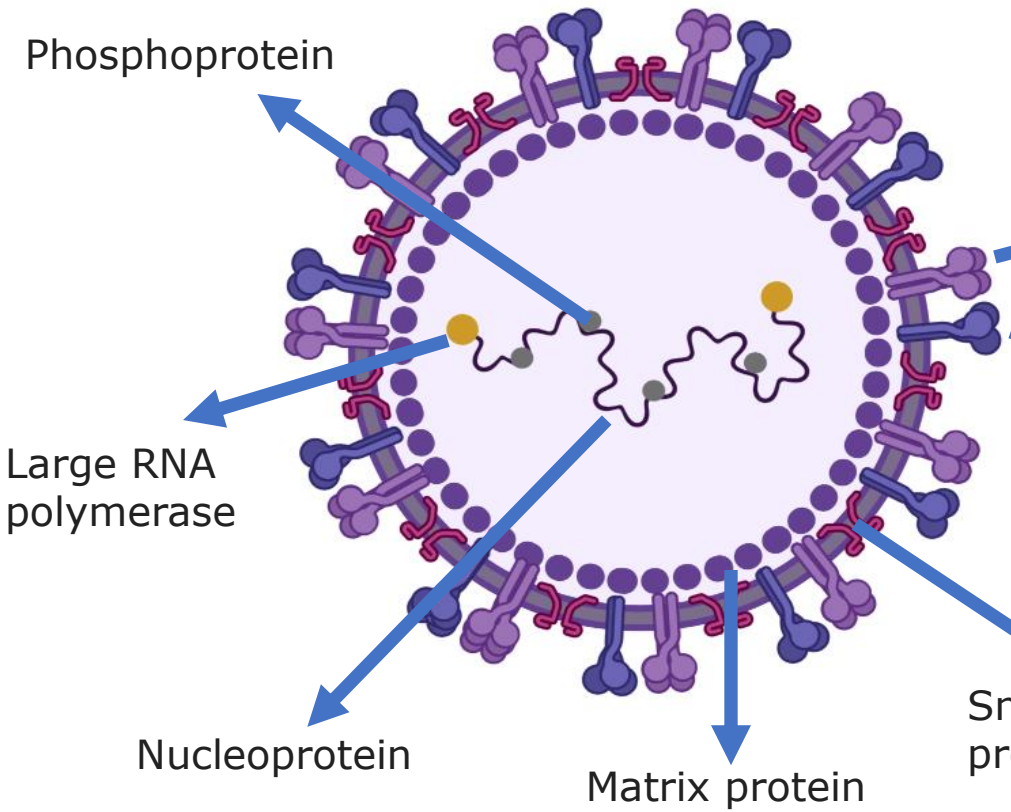


- Respiratory syncytial virus (RSV) is a single-stranded RNA orthopneumovirus that belongs to the Pneumoviridiae family.
- Human RSV exists as 2 antigenic subgroups, **A and B**, which can cocirculate during the same season and exhibit genome-wide sequence divergence.

- Of the 8 structural proteins, 3 are in the surface viral membrane with the two key targets being the attachment (**G**), and the fusion (**F**) glycoproteins,
  - The attachment (G) protein targets the ciliated cells of the airways and mediates adherence of the virus to the host cells.
  - The fusion (F) protein initiates viral penetration by fusing viral and cellular membranes and late in the infection causes infected cells to fuse, inducing the production of the characteristic syncytia.

Mejias et al.Ann Allergy Asthma Immunol 125 (2020) 36-46

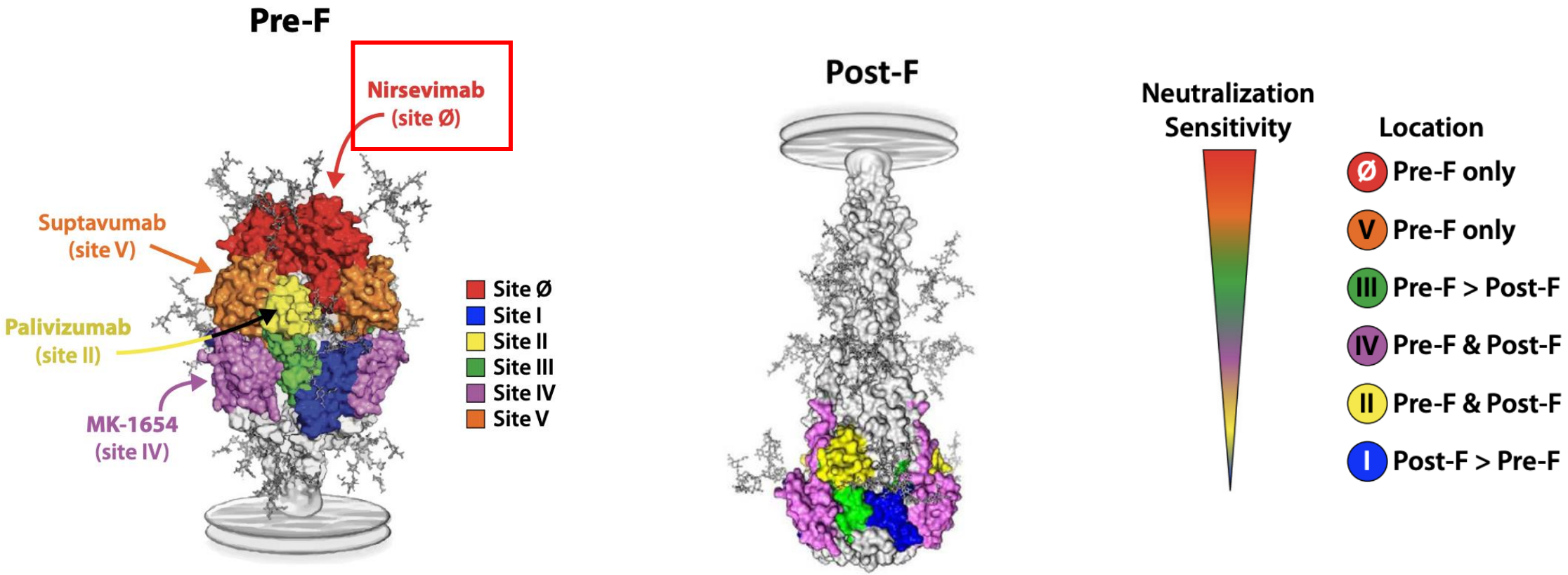
RSV F and G surface glycoproteins are important for both viral infectivity and pathogenesis



Fusion (F) protein:
Merges the viral and cellular membrane to enable the release of viral RNA into the host[1]

Attachment (G) glycoprotein:
Attaches the virus to the epithelial cells of the host[1]

1. Liu H, et al. Influenza Other Respir Viruses 2020;14(4):403-411.



Mejias et al.Ann Allergy Asthma Immunol 125 (2020) 36-46

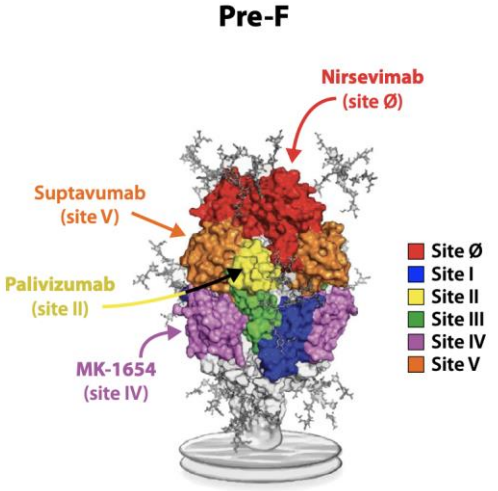
Topics

1. RSV – the virus

2. Product (Niservimab) available in Victoria in 2025

3. Clinical advice

Nirsevimab **(BEYFORTUS)**



- Nirsevimab is a human immunoglobulin G1 kappa (IgG1κ) antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology

- It binds to a highly conserved epitope in antigenic site Ø on the prefusion (F) protein for RSV subtype A and B strains, respectively

- Nirsevimab has an extended half-life of **@ least 5-months**

Niservimab TGA ARTG

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Safety of Nirsevimab for RSV in Infants with Heart or Lung Disease or Prematurity

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

Laura L. Hammitt, M.D., Ron Dagan, M.D., Yuan Yuan, Ph.D., Manuel Baca Cots, M.D., Miroslava Bosheva, M.D., Shabir A. Madhi, Ph.D., William J. Muller, Ph.D., Heather J. Zar, Ph.D., Dennis Brooks, M.D., Amy Grenham, M.Sc., Ulrika Wählby Hamrén, Ph.D., Vaishali S. Mankad, M.D., Pin Ren, Ph.D., Therese Takas, B.Sc., Michael E. Abram, Ph.D., Amanda Leach, M.R.C.P.C.H., M. Pamela Griffin, M.D., and Tonya Villafana, Ph.D., for the MELODY Study Group*

ORIGINAL ARTICLE

Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

This article has been corrected. VIEW THE CORRECTION

Authors: M. Pamela Griffin, M.D., Yuan Yuan, Ph.D., Therese Takas, B.S., Joseph B. Domachowske, M.D., Shabir A. Madhi, M.B., B.Ch., Ph.D., Paolo Manzoni, M.D., Ph.D., Eric A.F. Simões, M.D., +5, for the Nirsevimab Study Group* Author Info & Affiliations

Published July 29, 2020 | N Engl J Med 2020;383:415-425 | DOI: 10.1056/NEJMoa1913556 | VOL. 383 NO. 5

ORIGINAL ARTICLE

Nirsevimab for Prevention of Hospitalizations Due to RSV in Infants

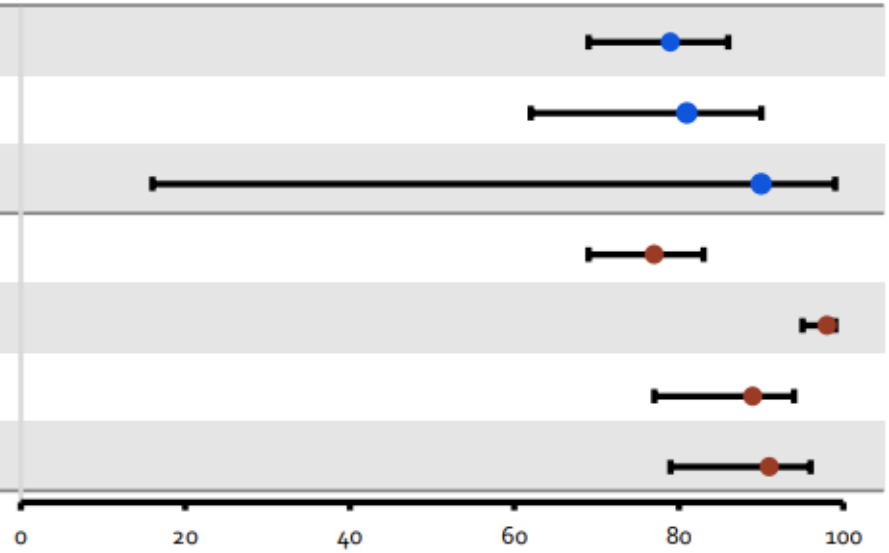
Authors: Simon B. Drysdale, Ph.D., F.R.C.P.C.H., Katrina Cathie, M.D., F.R.C.P.C.H., Florence Flamein, M.D., Ph.D., Markus Knuf, Ph.D., Andrea M. Collins, M.D., Ph.D., Helen C. Hill, Ph.D., Friedrich Kaiser, M.D., +13, for the HARMONIE Study Group* Author Info & Affiliations

Published December 27, 2023 | N Engl J Med 2023;389:2425-2435 | DOI: 10.1056/NEJMoa2309189
VOL. 389 NO. 26

[Nirsevimab for Prevention of Hospitalizations Due to RSV in Infants | New England Journal of Medicine (nejm.org)]

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

Outcome/Analysis	Vaccine efficacy/effectiveness (%)
Clinical trial, RSV-associated LRTI	79 (69-86)
Clinical trial, RSV-associated LTRI with hospitalization	81 (62-90)
Clinical trial, RSV-associated LRTI with ICU admission	90 (16-99)
VISION, RSV-associated emergency department visits	77 (69-83)
VISION, RSV-associated hospitalization	98 (95-99)
NVSN, medically attended RSV-associated ARI episode	89 (77-94)
NVSN, RSV-associated hospitalization	91 (79-96)



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

Nirsevimab impact: ACIP meeting, June 2024

THE LANCET
Infectious Diseases

ARTICLES · Volume 24, Issue 8, P817-828, August 2024 Download Full Issue

Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study

Sonia Ares-Gómez, PhD [a,b,c,†] · Narmeen Mallah, PhD [a,b,d,e,†] · María-Isolina Santiago-Pérez, BS [f,†] · Jacobo Pardo-Seco, PhD [a,b,c,h,†] · Olaia Pérez-Martínez, MD [f] · María-Teresa Otero-Barrós, MD [f] · et al. Show more

- 9408 **(91·7%)** of 10 259 eligible infants in the seasonal + catch-up groups received nirsevimab
  - 348 (97%) of infants in the high-risk group received nirsevimab
- In the combined analysis, 30 (0·3%) of 9408 infants who received nirsevimab and 16 (1·9%) of 851 who did not receive nirsevimab were hospitalised for RSV-related LRTI: **VE 82·0%** (95% CI 65·6–90·2).
- VE **86·9%** (69·1–94·2) against severe RSV-related LRTI requiring oxygen support
  - 69·2% (55·9–78·0) against all-cause LRTI hospitalisations,
  - 66·2% (56·0–73·7) against all-cause hospitalisations

Lancet ID, August 2024

State(s) of play 2024

Government of **Western Australia**
Department of **Health**

About us | Improving health in WA | Health for... | Our performance | Latest news | Reports & publications

Home › Respiratory Syncytial Virus (RSV) immunisation

Respiratory Syncytial Virus (RSV) immunisation

The Queensland Cabinet and Ministerial Directory

net documents | Ministers and Portfolios | Media Statements

Free RSV immunisation program for Queensland infants and young children

NSW Health RSV (respiratory syncytial virus) vulnerable babies program

The information on this page is for healthcare practitioners

If you live in NSW, read more about RSV prevention, symptoms and treatment in the **respiratory syncytial virus (RSV) fact sheet**.

NSW Health RSV (respiratory syncytial virus) vulnerable babies program will be implemented in a phased approach that offers Beyfortus™ (nirsevimab) to the most vulnerable babies from March 2024 to September 2024.

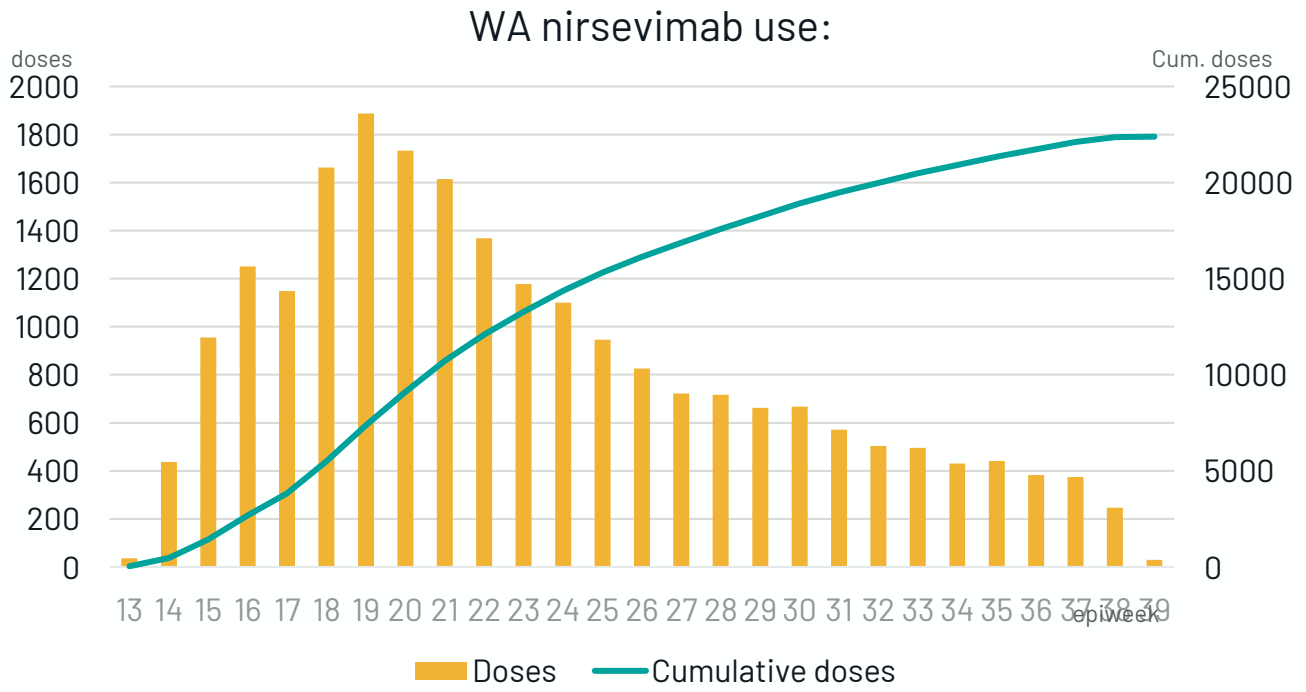
Parents carers can find information on Beyfortus™ (nirsevimab) on the i**nformation for parents and carers webpage**.

WA program

≈ **23,000** children have received Nirsevimab:

- Birth cohort ≈ 80% (AIR) to 85% (STORK) uptake
- Catchup cohort = 66% (AIR)
- Y2 Aboriginal = 30% (AIR)
- Y2 at risk cohort ≈ 30%

Delivered by 1127 providers



Data courtesy of Paul Effler & Chris Blyth (WA Health)

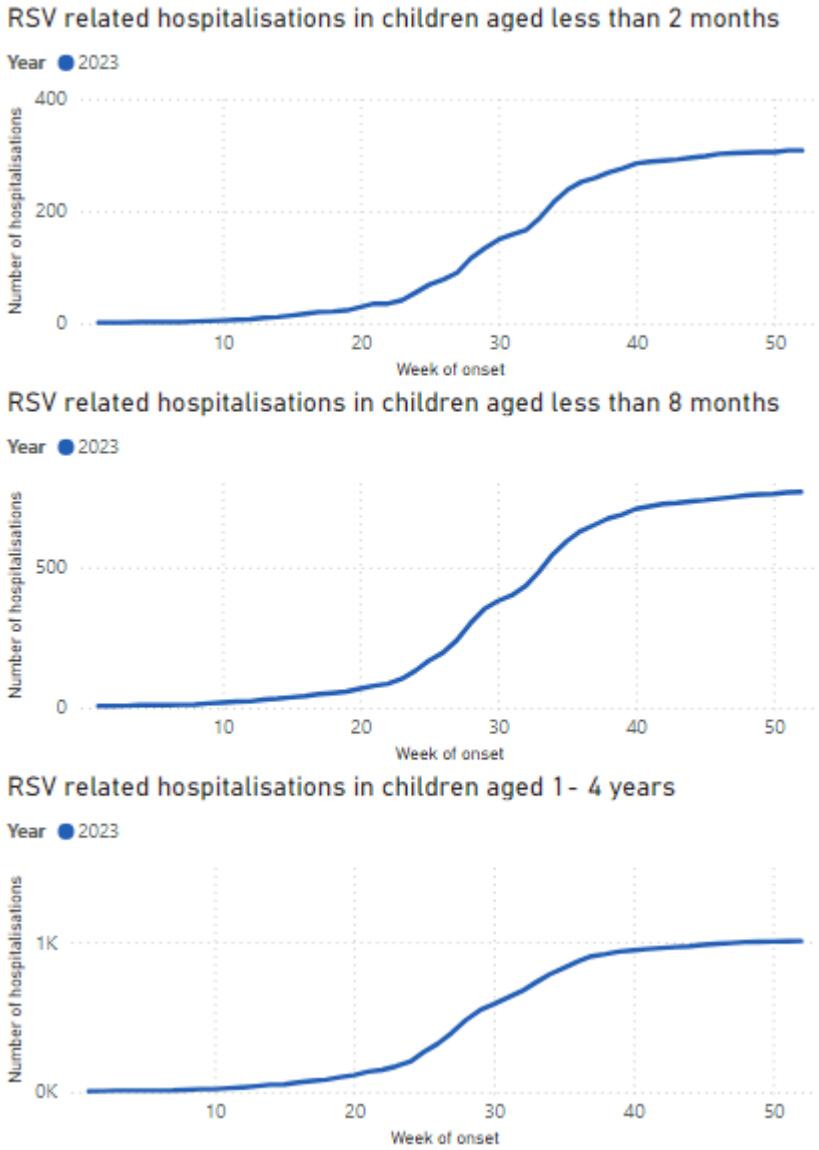
2023

2024

< 2 months

< 8 months

1-4 years



Data courtesy of Paul Effler (WA Health)

2023

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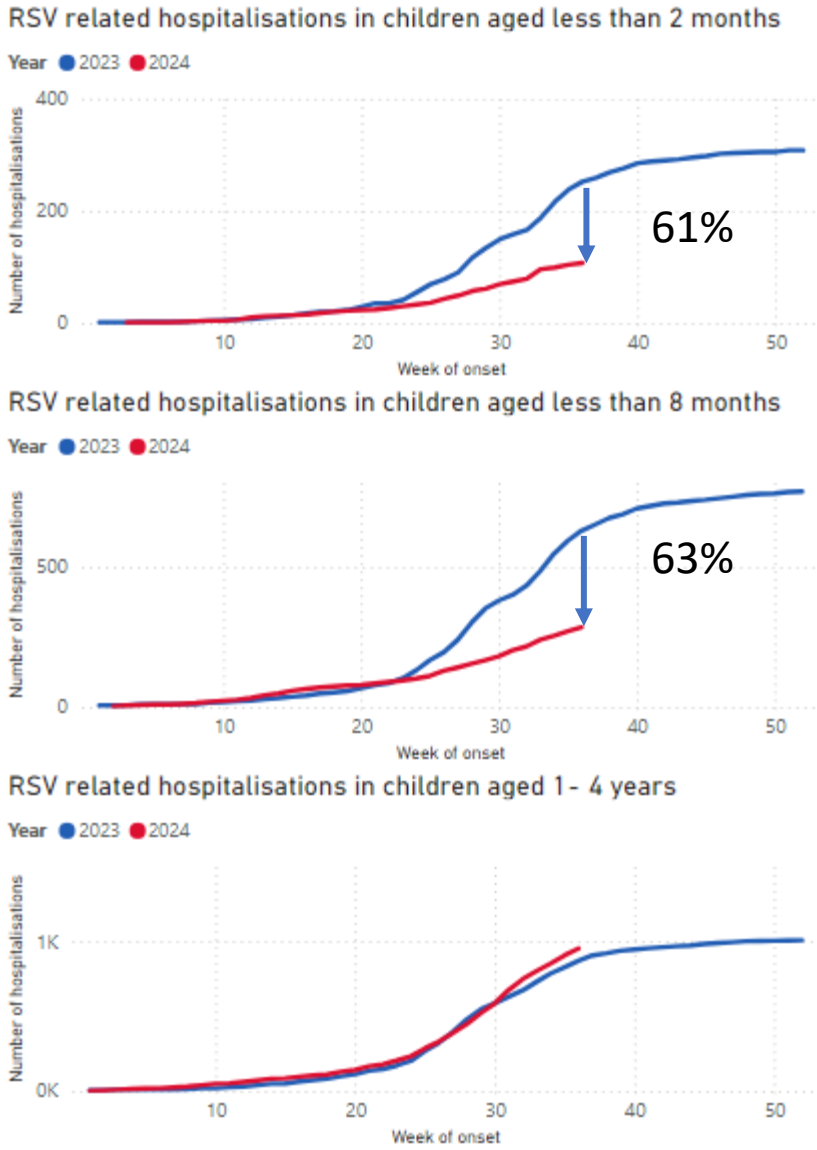


Data courtesy of Paul Effler (WA Health)

Topics

1. RSV – the virus

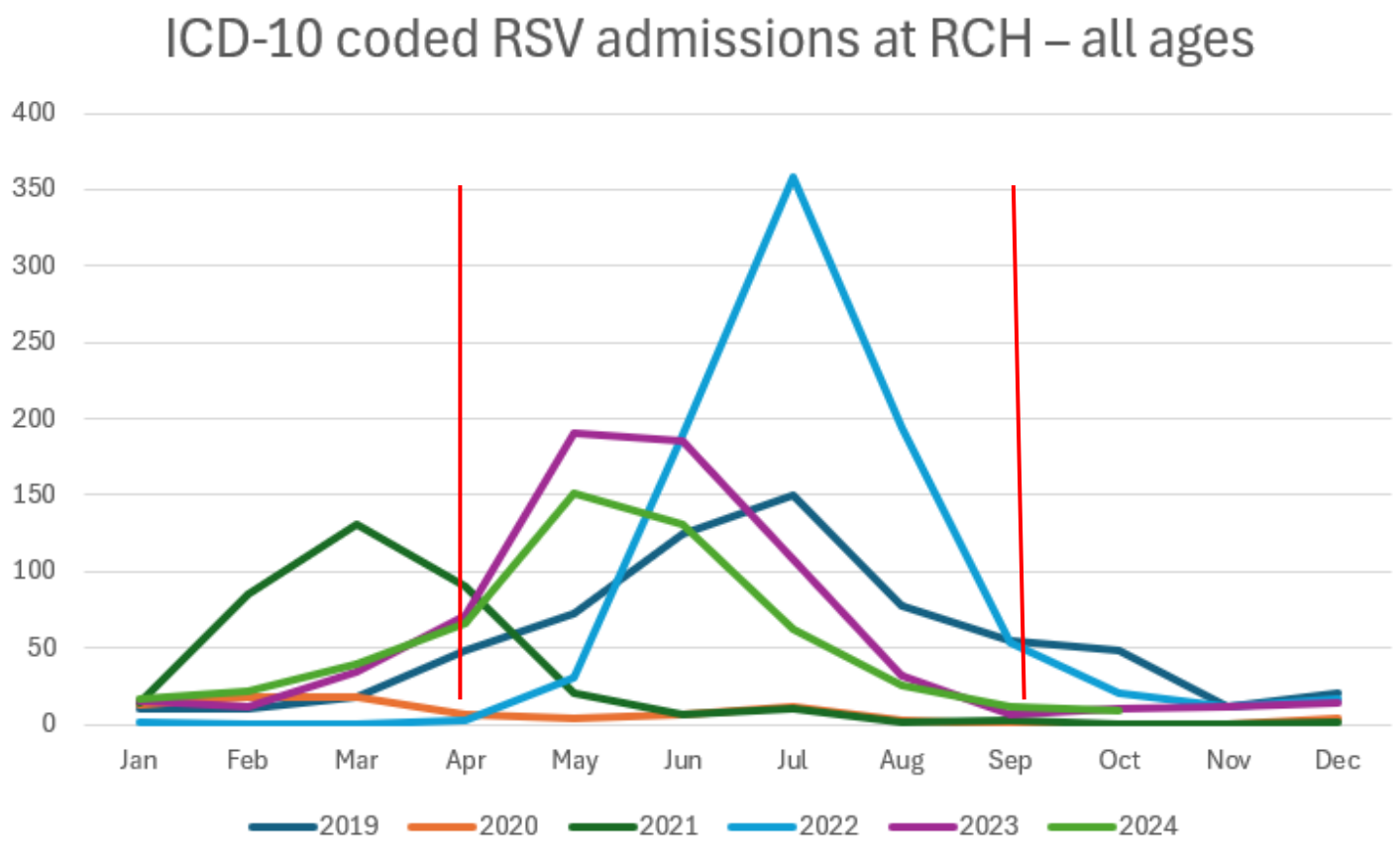
2. Product (Niservimab) available in Victoria in 2025

3. Clinical advice

Clinical presentation to hospital: “bronchiolitis” & pneumonia

- Respiratory illness prodrome
- Peak day 3-4 of illness
- Use of accessory muscles
  - Intercostal recession, tracheal tug
  - Ausculation: wheeze and crackles
  - Infant becomes tiered…
- Supportive treatment
  - Fluids (Nasogastric tube)
  - Oxygen
  - Pressure (high flow, CPAP, intubation)

RSV surveillance @ RCH [2019-24]



- 2021 saw a large out-of-season spike in RSV admissions across Australia as highlighted in green
- Early onset season in 2023 & 2024…
- Back to seasonality pre COVID!

Slide Acknowledgement: Annette Alafaci

Media Release

The Hon Mary-Anne Thomas MP
Leader of the House
Minister for Health
Minister for Health Infrastructure
Minister for Ambulance Services

VICTORIA State Government

Wednesday, 2 October 2024

PROTECTING VICTORIAN NEWBORNS AND INFANTS NEXT WINTER

National RSV Mother & Infant Protection Program (RSV-MIPP)

A nationally consistent immunisation program for mothers and babies will be established in 2025 to protect infants from RSV. The National RSV Mother and Infant Protection Program (RSV-MIPP) will offer immunisation products to pregnant women, and infants.

A single dose of the RSV vaccine, Abrysvo®, will be provided to pregnant women between 28-36 weeks of their pregnancy under the National Immunisation Program (NIP). This vaccine will provide protection against RSV for their infant through the passing of antibodies from the mother to the unborn baby.

The Victorian Department of Health will implement a complimentary infant RSV immunisation program to protect infants most at risk from severe RSV disease. The program will run from April to September 2025.

[Premier press release, Oct 2024]

[Victorian RSV protection program]

Australian Government
Department of Health and Aged Care

Australian Immunisation Handbook

Home | Contents | Diseases | Vaccines | Catch-up vaccination | Resources

Home > Table of contents > Vaccine preventable diseases

Respiratory syncytial virus (RSV)

Information about respiratory syncytial virus (RSV) disease, vaccines and recommendations for vaccination from the Australian Immunisation Handbook.

> This chapter is currently undergoing consultation and seeking National Health and Medical Research Council (NHMRC) approval.

AIH, RSV chapter

Risk factors for severe RSV: AIH

Conditions associated with increased risk of severe RSV disease in infants and young children

- Preterm birth <32 weeks gestational age
- Haemodynamically significant congenital heart disease
- Significant immunosuppression, such as from solid organ transplant, haematopoietic stem cell transplant, or primary immune deficiencies such as severe combined immunodeficiency (SCID)
- Chronic lung disease requiring ongoing oxygen or respiratory support
- Neurological conditions that impair respiratory function
- Cystic fibrosis with severe lung disease or weight for length <10th percentile
- Trisomy 21 or another genetic condition that increases the risk of severe RSV disease

AIH, RSV chapter

Dosing nirsevimab

For infants born during or entering their first RSV season, the recommended dose for nirsevimab is:

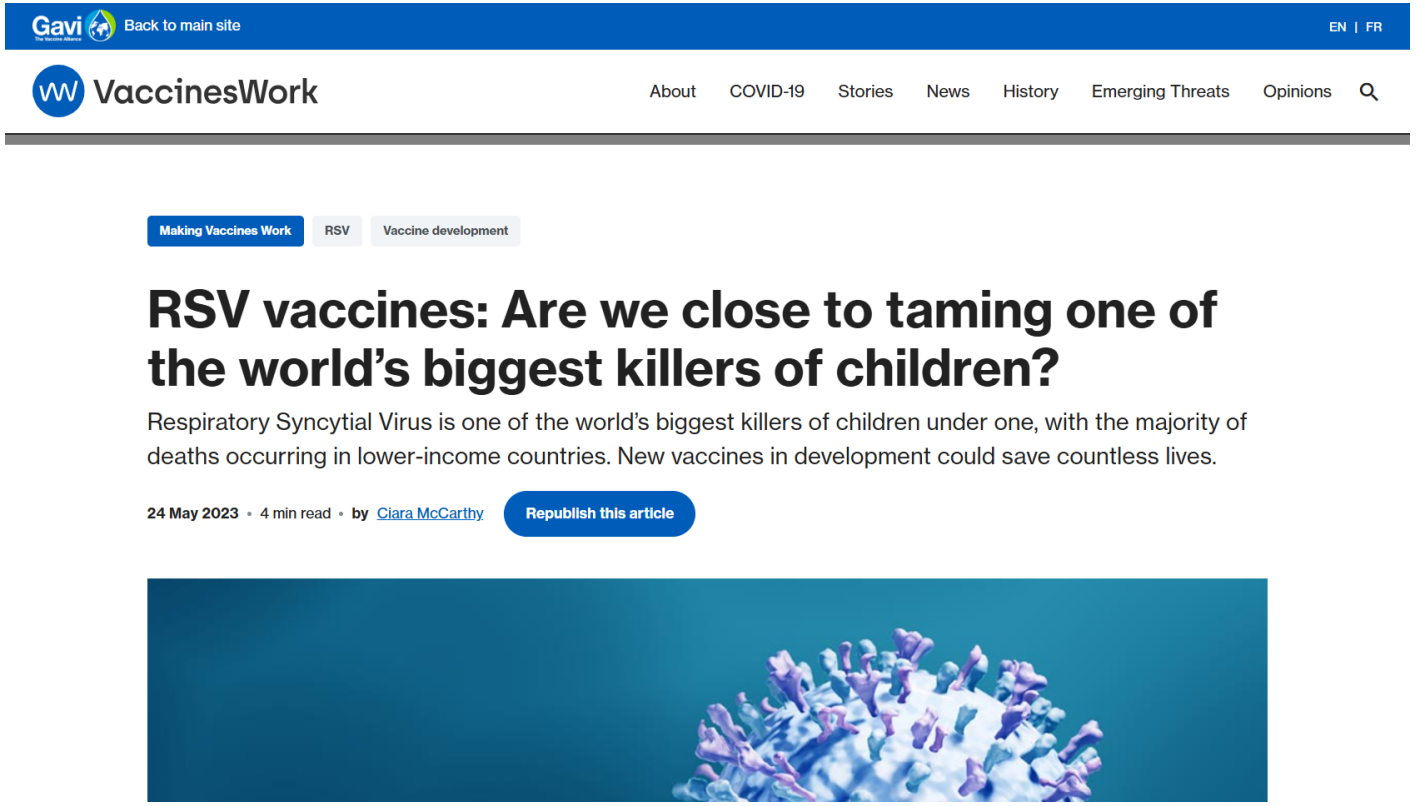
- 50 mg in 0.5 mL if weight is <5 kg (purple plunger rod)
- 100 mg in 1 mL if weight is ≥5 kg (light blue plunger rod)

by intramuscular injection as a single dose.[2,3] Do not divide a 100 mg pre-filled syringe into two 50 mg doses.

For children at an increased risk of severe RSV disease in their second season, the recommended dose for nirsevimab is 200 mg administered as 2 × 100 mg (2 mL total) intramuscular injections in different sites (preferably separate limbs, or else separated by 2.5 cm) at the same visit. This is 4 times more than the dose and volume for a newborn.

ATAGI Nirservimab AIH

Summary



- Great news that Victoria will have access to two 'RSV preventative' products in 2025
  - Maternal vaccine (28+ weeks gestation)
  - Monoclonal antibody (mAb) for infants @ birth + catch-up
    - including into 2nd season for those @ highest risk of severe disease