CDCD Public Health

Immunisation Update Nov 2023

RSV Prevention: now a reality

Professor Peter Richmond
Division of Paediatrics, , University of WA Medical School, Vaccine Trials Group, Telethon Kids Institute
Paediatric Immunologist and General Paediatrician, Perth Childrens Hospital

Acknowledgement of country

I would like to acknowledge the
traditional custodians of the land,
the Noongar Whadjuk people,
and pay my respects to their elders,
past, present and future.

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
- Vaccine Scientific Advisory Boards (on behalf of UWA)
  - GlaxoSmithKline - Pertussis, pneumococcal, RSV vaccines, maternal immunisation, meningococcal & NTHi vaccines
  - Pfizer - Meningococcal, pneumococcal & RSV vaccines
  - Janssen – Bacterial vaccines, RSV vaccine
  - Sanofi – influenza vaccines, RSV mAb
  - Merck – pneumococcal vaccines, RSV mAb
  - Astra-Zeneca – COVID-19, RSV mAb
  - Clover biopharmaceuticals – COVID-19, RSV vaccines
  - Resvinet Board member – RSV advocacy not-for profit organisation
  - *No personal remuneration*
- Vaccine Research
  - Investigator of industry sponsored multi-centre studies for CSL, GSK, Medimmune, Merck, Pfizer, Sanofi, Novartis, Moderna, Clover, Janssen
  - Travel support to present at scientific conferences
    - Sanofi, Pfizer, GSK
  - Research funding for Investigator initiated studies
    - GSK, Merck, Novartis, CSL
  - Views expressed during this presentation are mine only

Talk Summary

- Understanding burden, epidemiology and risk factors for RSV
- Development of new vaccines and monoclonal antibodies for RSV
- Maternal RSV vaccination
- RSV Monoclonal antibodies for infants
- RSV vaccines for older adults

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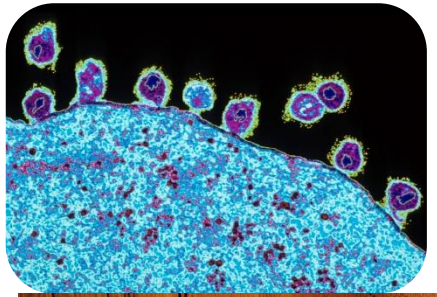
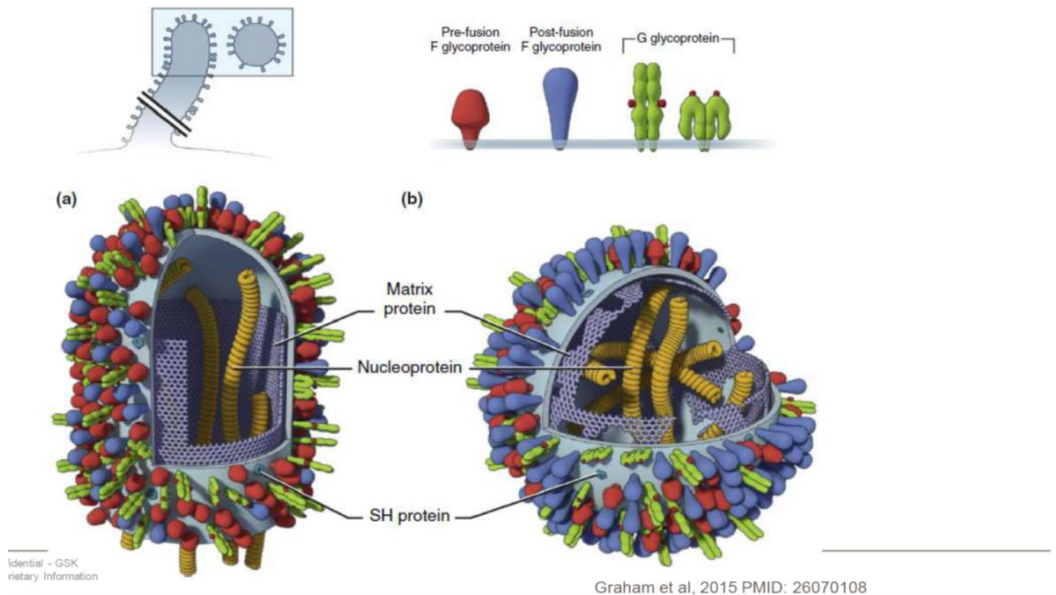
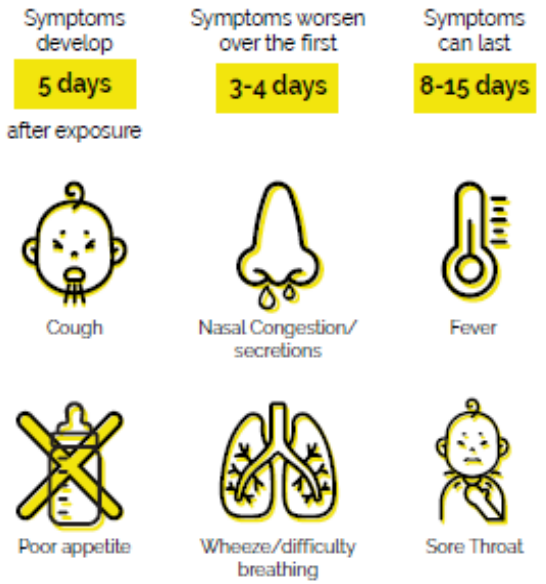
Respiratory Syncytial Virus (RSV)



- a highly transmissible RNA virus through droplets
- infection occurs through upper airway before progressing to lower airways
- Surface proteins critical in infecting cells and the target of neutralising antibodies
- 95% of children infected by 2 years of age
- 1 in 4 will have a lower respiratory tract infection
- Also common cause of otitis media in infants & secondary bacterial infections
- **1 in 10 children will see a doctor due to RSV in the first year of life**



Graham et al, 2015 PMID: 26070108



Acute Consequences of RSV LRTI: Hospitalization

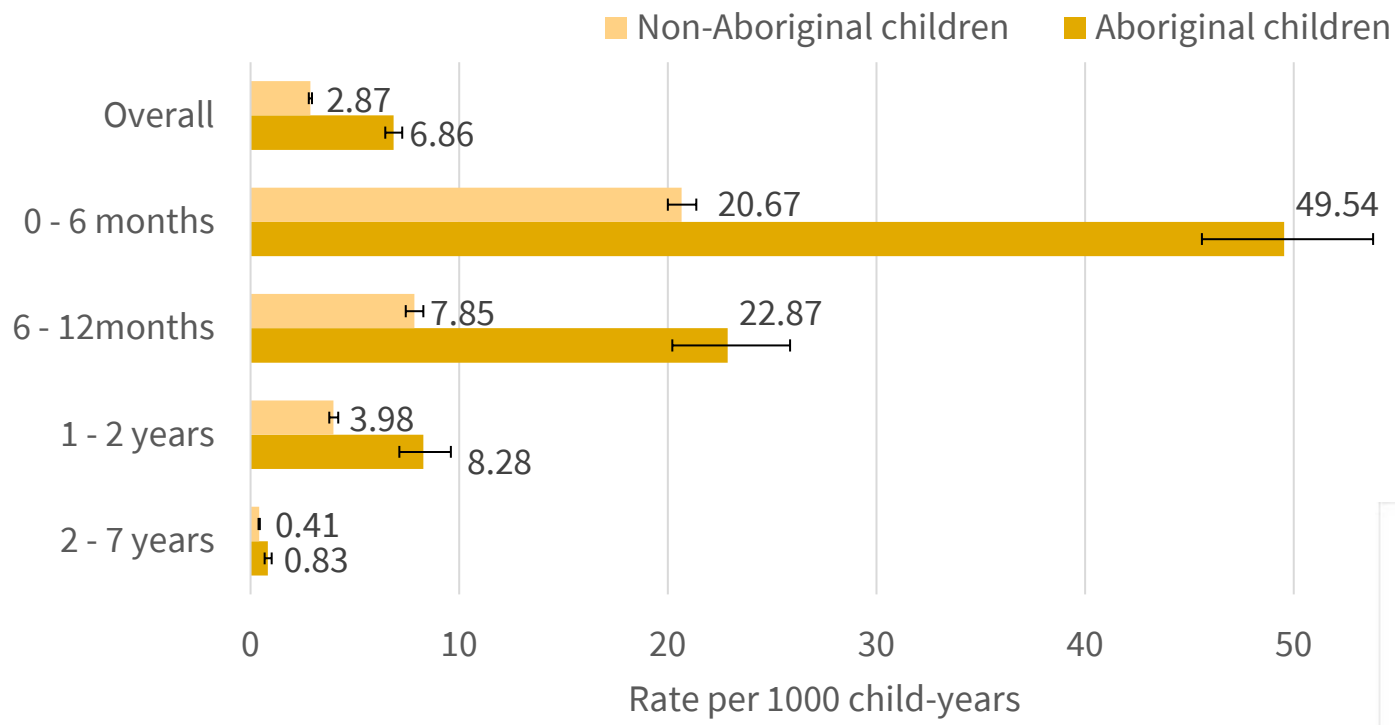
- RSV is a leading cause of paediatric hospitalization
  - ~3.4 million hospitalizations worldwide in children < 5 years old in 2005
  - ~>11,000 hospitalizations in Australia annually in infants < 1 year old
  - Major contributor to winter bed block for paediatric hospitals / wards
  - **One in 50 babies in the first year admitted to hospital**

	General Population Term Children	High-risk Children
Rates of hospitalization	**1%-2.9%**	**5%-10%**
Hospitalization Mean LOS (days)	**3.4**	**5-7**
Require ICU care	**3%-9%**	**10%-50%**
ICU Mean LOS (days)	**3.4**	**4.5-7.2**
Require mechanical ventilation	**1.5%**	**17%-40%**

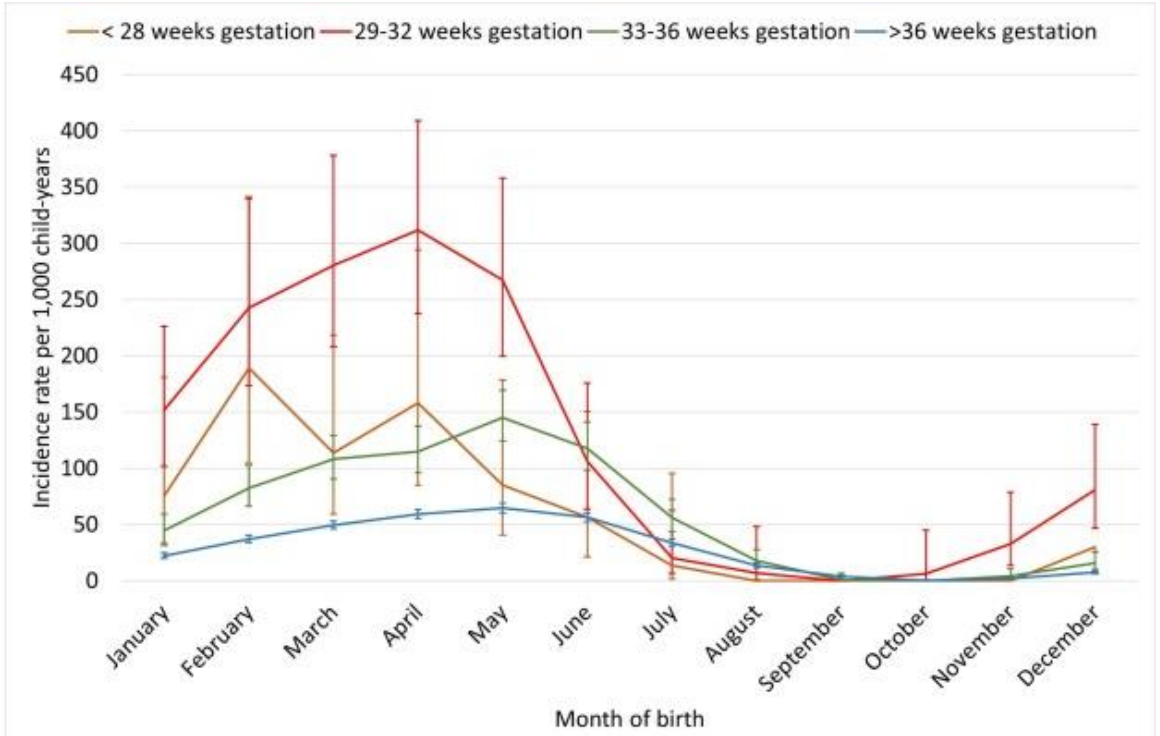
LOS: length of stay

Nair et al. *Lancet* 2010.; Saravanos Med J Aust2019; Boyce et al. *J Pediatr* 2000; Joffe et al. *Pediatrics* 1999; Shay et al. *JAMA* 1999; Griffin et al. *Arch Int Med* 2002; Bockova et al. *Pediatrics* 2002; Horn et al. *J Pediatr* 2003; Moler et al. *Crit Care Med* 1992;

Risk factors for RSV-hospitalization rates (WA)



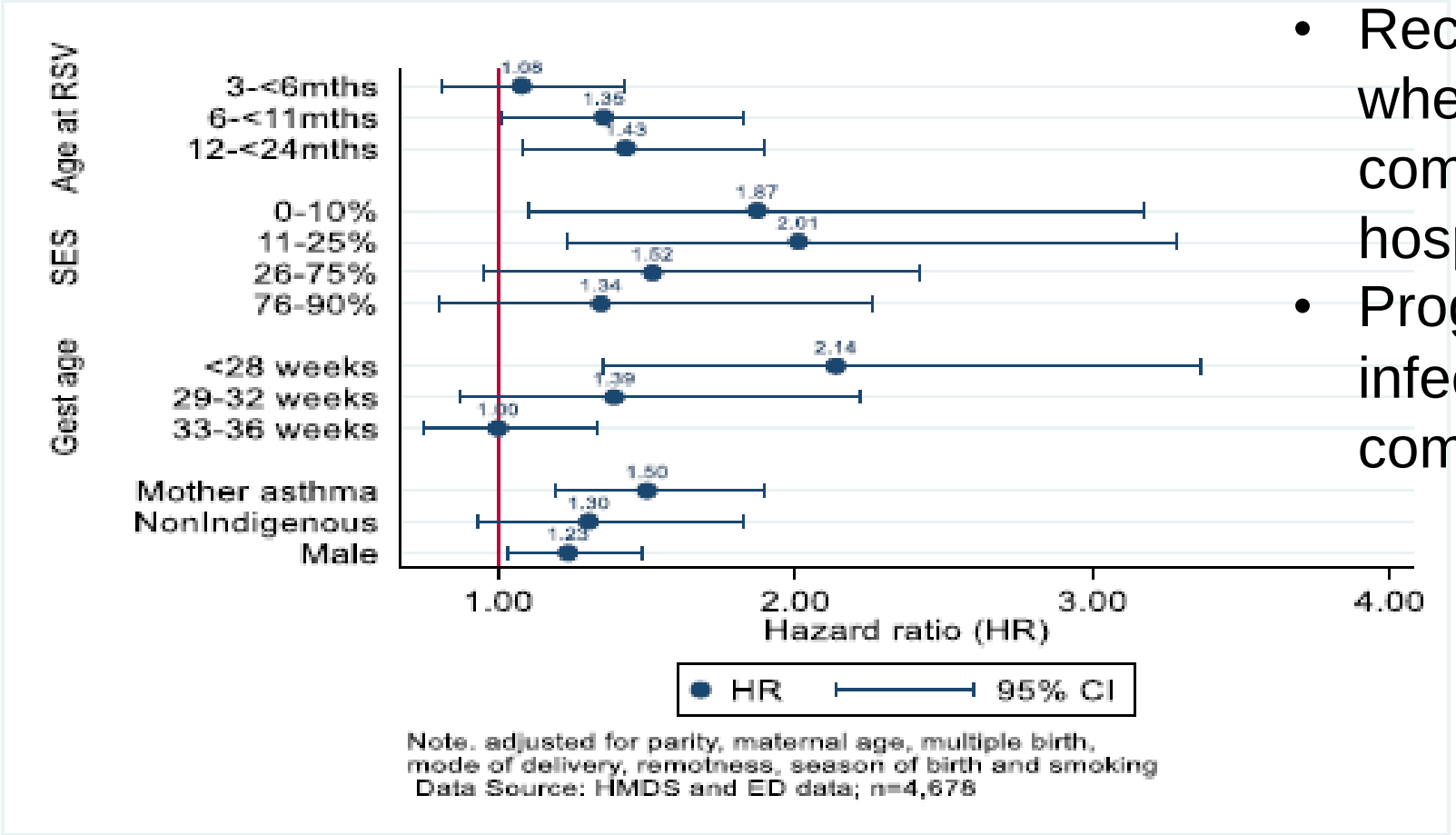
- Highest in infants < 6 mths
- Incidence >2x higher in Aboriginal infants
- Routine data underestimates by ~30%
- Prematurity and timing of birth important risk factors
- **83% of RSV hospitalisations however are in otherwise healthy infants**



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

Long-term consequences of RSV disease

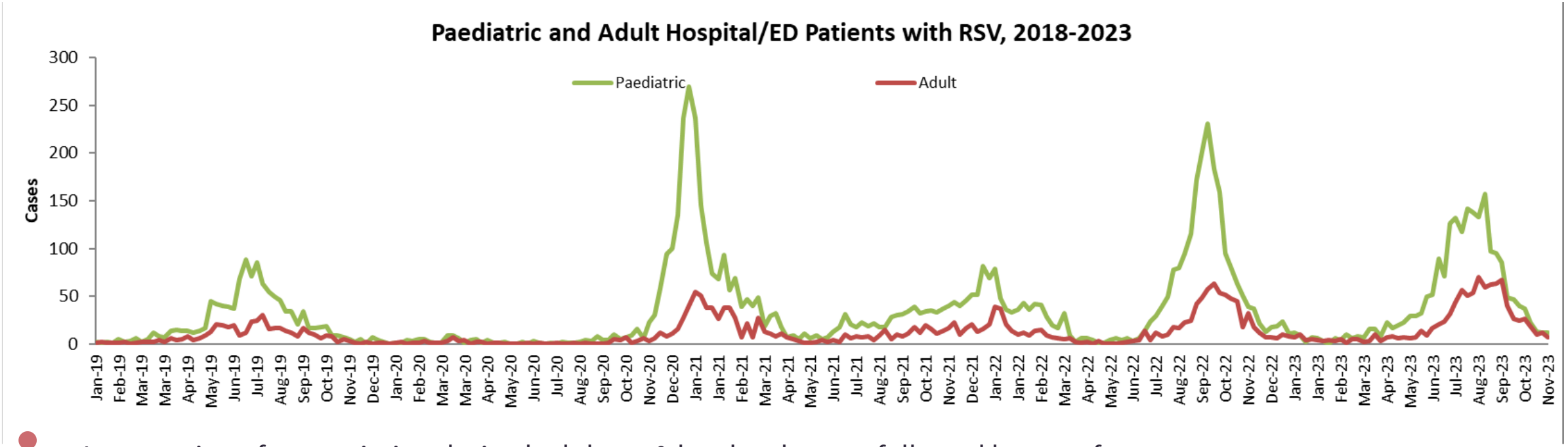


- Recurrent viral-induced wheeze and asthma more common after RSV hospitalisation
- Progression to recurrent chest infect and ear infections also common after RSV illness

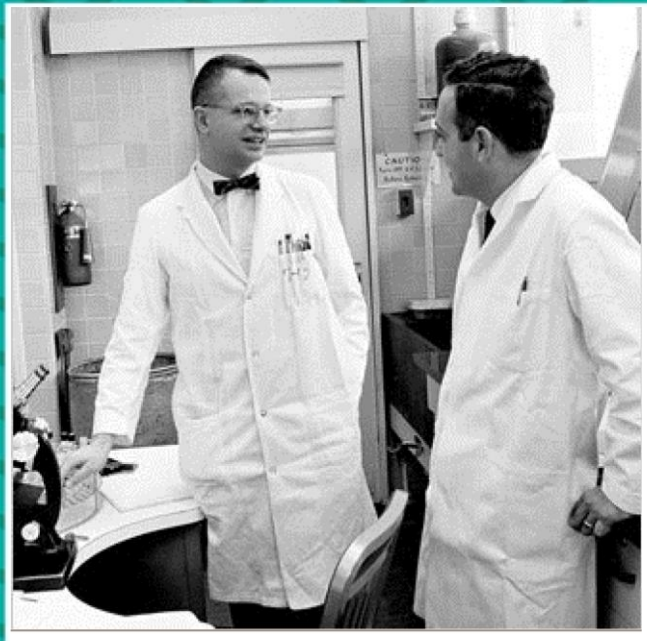
Figure 3. Relative risk of asthma and wheezing after age 2 during the follow-up for children with RSV-confirmed detections before age 2 years, 2000-2012, WA

Gebremedhin RSVVW 2021

RSV Seasonality– Impact of the Pandemic in WA



- Interruption of transmission during lockdown & border closures followed by out of season resurgence
- Increased testing in adults as part of multiplex respiratory PCR use in GP & hospitals
- Using datalinkage with Pathwest data in 2021
  - there were 519 hospital admissions & 270 ED presentations in infants < 12 months;
  - 1/3 of RSV admissions / ED presentations outside metropolitan area; 17.4% in Aboriginal children
- More than 10,000 notifications in WA in 2022 and 2023 (~50% in < 5s)



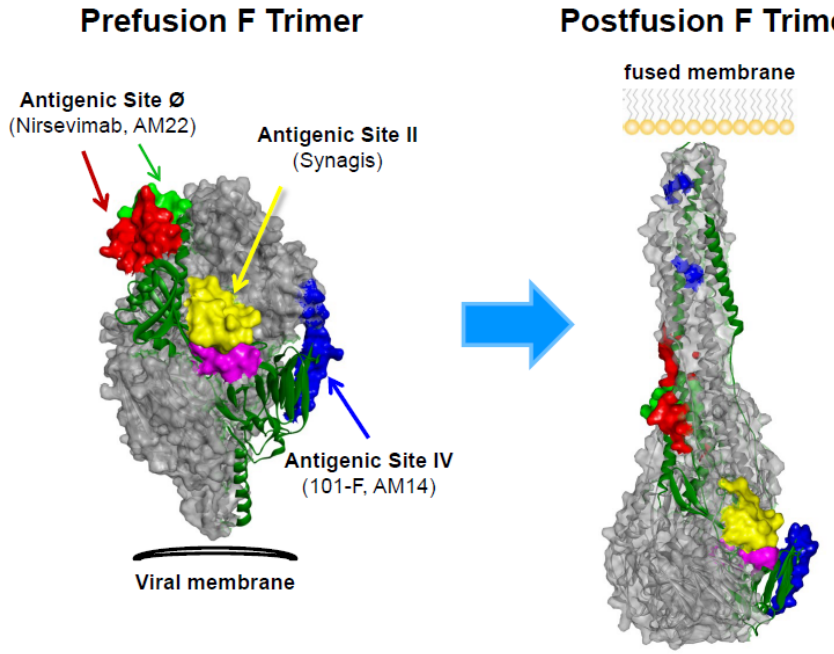
The long journey to RSV prevention

AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 89, No. 4

Printed in U.S.A.

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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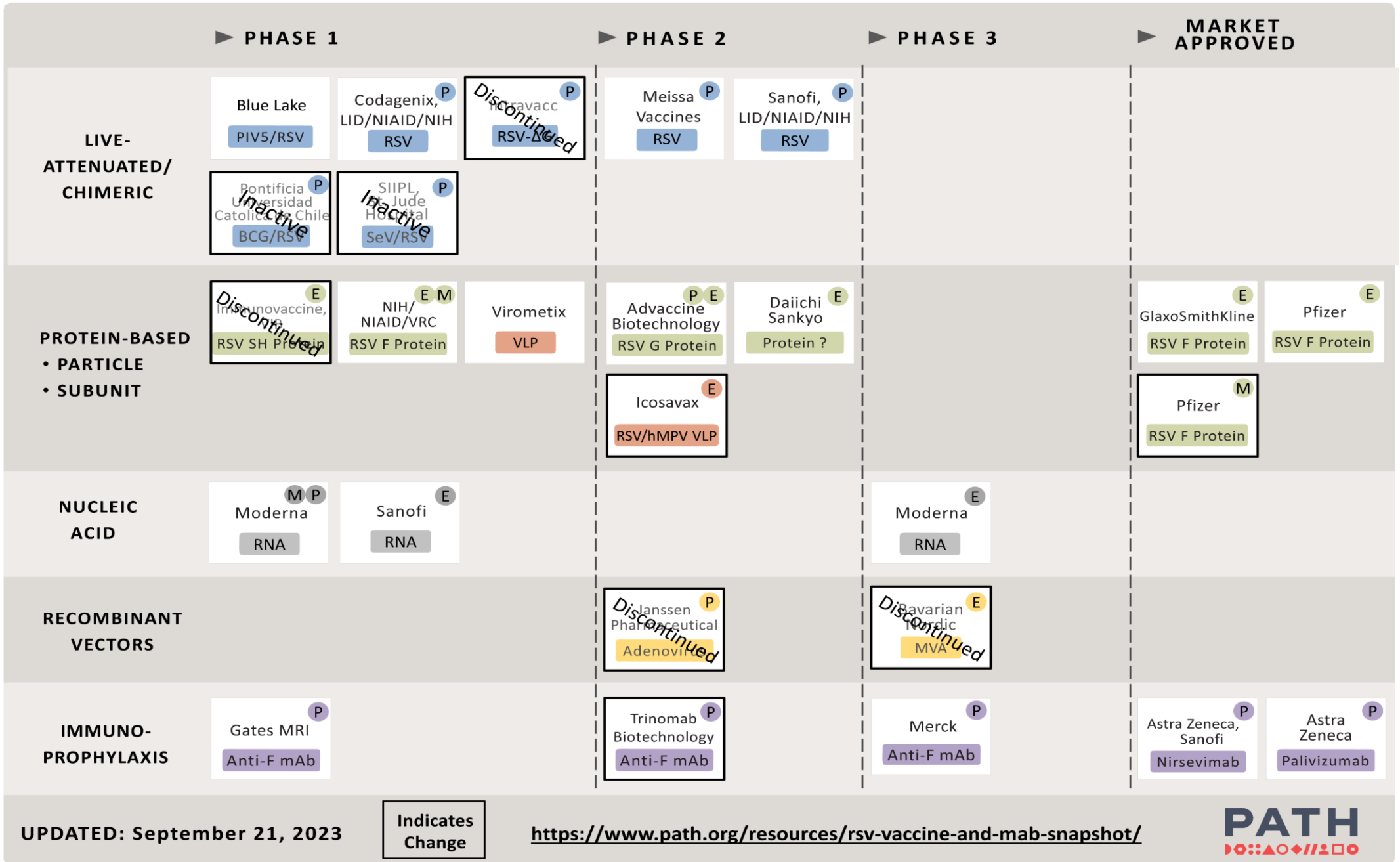
Passive Immunisation for RSV

- protection for infants to young to be vaccinated:
  - Maternal vaccines:
    - vaccinating pregnant women with the goal of protecting the young infant from RSV through passive transfer of maternal antibodies
    - Mothers more influenced by protection of baby than themselves
    - Accepted strategy for the prevention of maternal and infant disease (e.g Influenza, Pertussis)
  - Monoclonal antibodies
    - complements maternal vaccination strategy
    - especially in premature infants as most of IgG transfer occurs in the last trimester of gestation
    - Able to target other groups including older at-risk infants
    - Next generation mAbs designed to provide protection for 5 months after single dose

RSV Vaccine and mAb Snapshot

TARGET INDICATION: P=PEDIATRIC M=MATERNAL E=ELDERLY



UPDATED: September 21, 2023

Indicates Change

https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/

PATH

Addressing RSV in children and adults : what are the approaches?

PATH, 2023. RSV Vaccine and mAb Snapshot. https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/ (accessed Sep 2023)

Maternal Immunisation for RSV prevention: preparing the way

Prepare™

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Respiratory Syncytial Virus Vaccination during Pregnancy and Effects in Infants

S.A. Madhi, F.P. Polack, P.A. Piedra, F.M. Munoz, A.A. Trenholme, E.A.F. Simões, G.K. Swamy, S. Agrawal, K. Ahmed, A. August, A.H. Baqui, A. Calvert, J. Chen, I. Cho, M.F. Cotton, C.L. Cutland, J.A. Englund, A. Fix, B. Gonik, L. Hammitt, P.T. Heath, J.N. de Jesus, C.E. Jones, A. Khalil, D.W. Kimberlin, R. Libster, C.J. Llapur, M. Lucero, G. Pérez Marc, H.S. Marshall, M.S. Masenya, F. Martinón-Torres, J.K. Meece, T.M. Nolan, A. Osman, K.P. Perrett, J.S. Plested, P.C. Richmond, M.D. Snape, J.H. Shakib, V. Shinde, T. Stoney, D.N. Thomas, A.T. Tita, M.W. Varner, M. Vatish, K. Vrbicky, J. Wen, K. Zaman, H.J. Zar, G.M. Glenn, and L.F. Fries, for the Prepare Study Group*

- Provided proof of safety and efficacy of maternal RSV vaccination
  - 39.4% efficacy over 90 days against MA-LRTI
  - Reduced antibiotic prescriptions by 13%
- FDA required repeat Phase 3 study – Novavax has discontinued RSV program

New Maternal RSV Vaccine Efficacy Studies

- GSK pre-F3 protein unadjuvanted vaccine:
  - Recruiting up to 20,000 healthy pregnant mothers
  - Study discontinued due to possible increase in preterm babies in LMICs
    - ? Related to COVID
  - *ClinicalTrials.gov Identifier: NCT04605159*

GRACE
InvestiGational RSV MAternal VaCcinE

- Pfizer bivalent preF protein vaccine

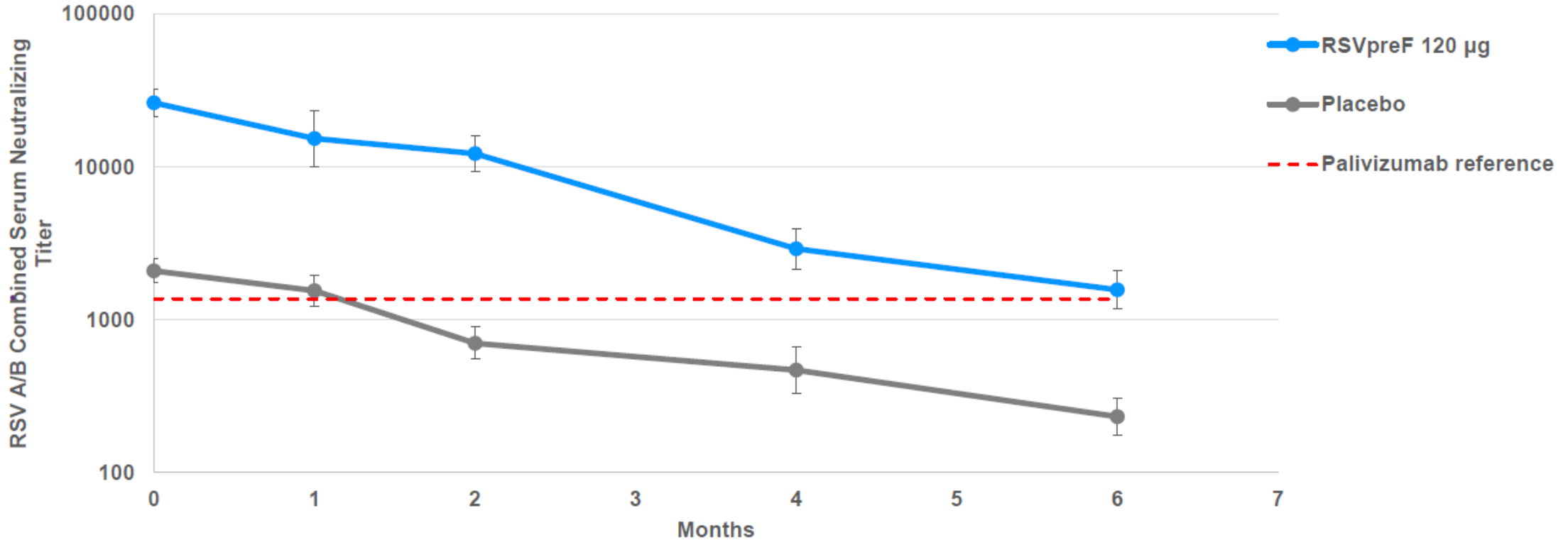
Matisse

  - Recruited 7,300 healthy pregnant mothers
  - randomized 1:1 between ≥24 and ≤36 weeks gestation
  - Efficacy outcome medically attended ALRTI up to 6 months

(*ClinicalTrials.gov Identifier: NCT04424316)*

Maternal RSV vaccination results in protective antibody levels in infants

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.)*

Efficacy of RSV Vaccine in Pregnancy – Matisse

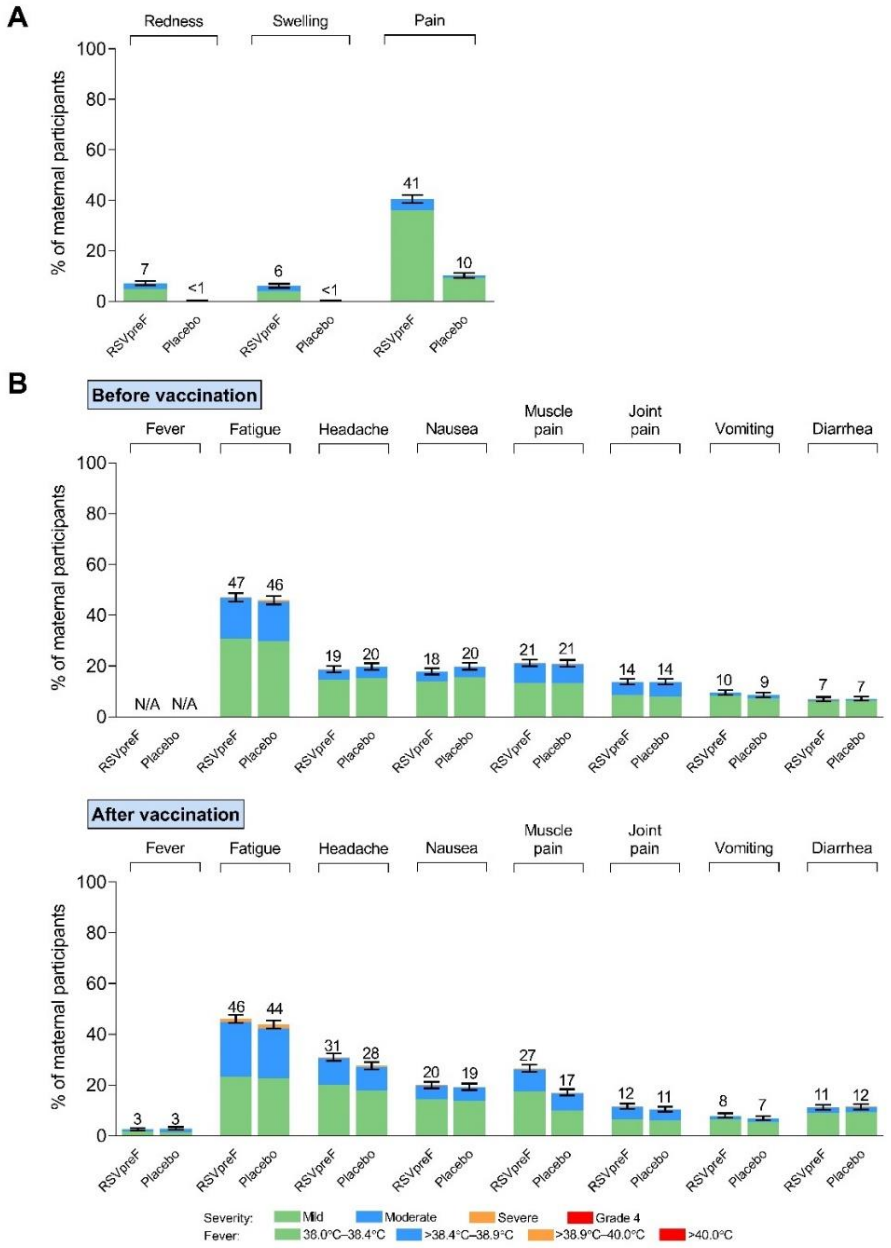
The NEW ENGLAND JOURNAL of MEDICINE

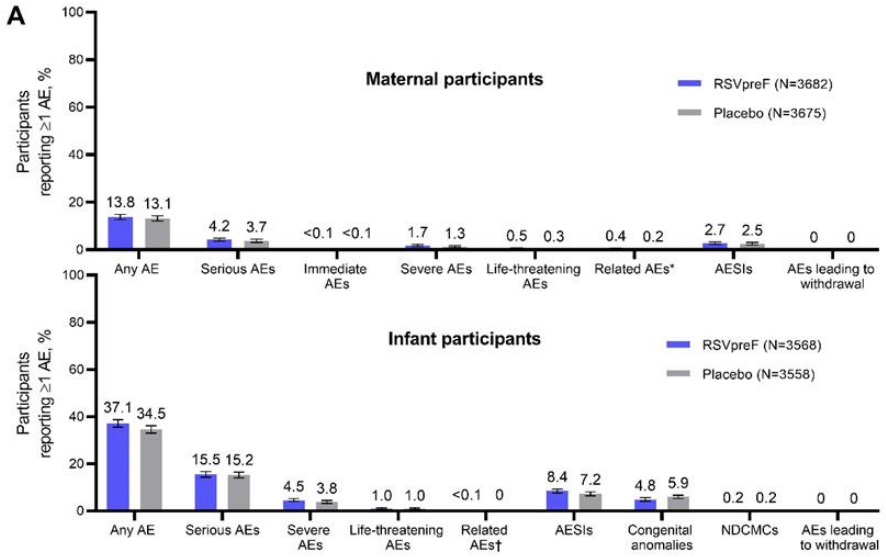
ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

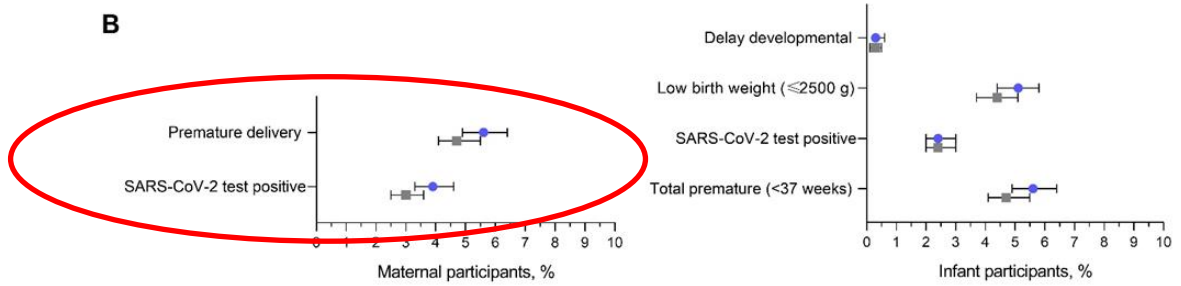
Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

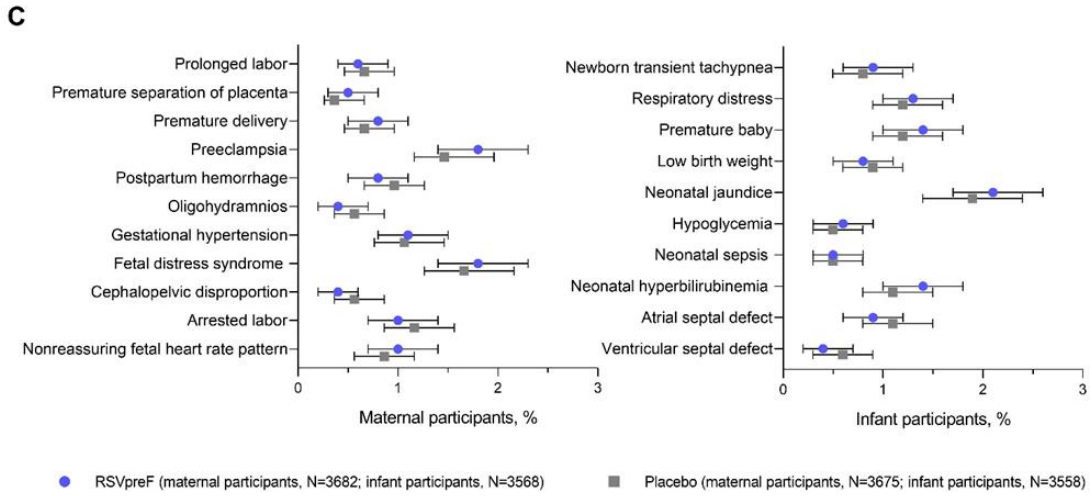
B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam,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

Safety of Maternal bivalent RSV vaccine









Maternal Bivalent pre-F RSV vaccine efficacy

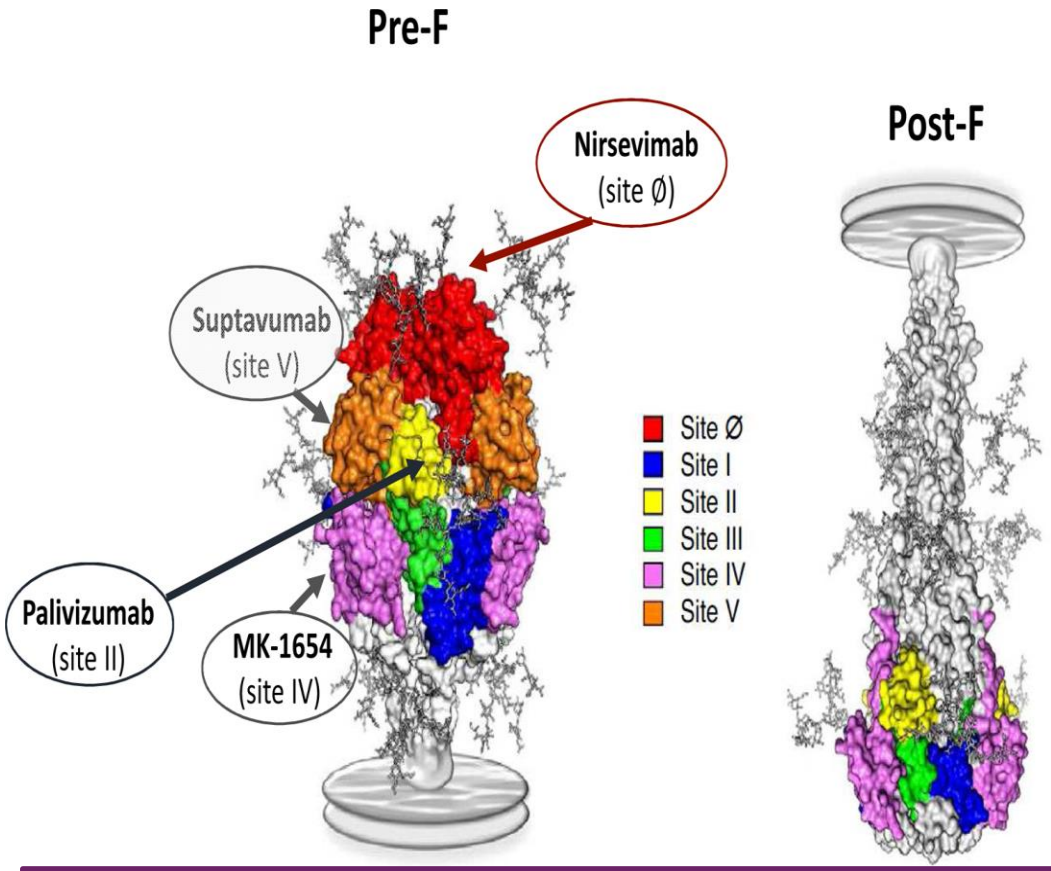
Outcome	Vaccine Efficacy (95% CI)		
	Over 3 months	Over 6 months	Over 12 months
Any Medically-attended RSV LRTI	**57.1%** (14.7%, 79.8%)	**51.3%** (29.4%, 66.8%)	**41.0%** (16.2 – 58.9%)
Severe Medically-attended RSV LRTI	**81.8%** (40.6%, 96.3%)	**69.4%** (44.3%, 84.1%)	N/A
Hospitalisations with RSV ALRTI	**67.7%** (15.9 – 89.5%)	**56.4%** (10.1 – 80.7%)	**33.3%** (-17.6 – 62.9%)
Any Medically-attended RSV RTI	**39.1%** (16.7 – 55.7%)	**37.9%** (24 – 49.5%)	N/A

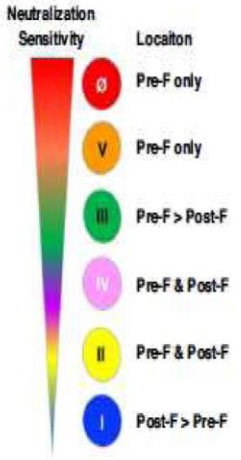
- Vaccine well-tolerated with no safety concerns for vaccinated mothers and their newborns
- Submission for FDA registration in Feb 2023, approved by advisory committee May 2023
- Confirms efficacy of RSV maternal immunisation though duration critical

Maternal RSV immunisation Summary

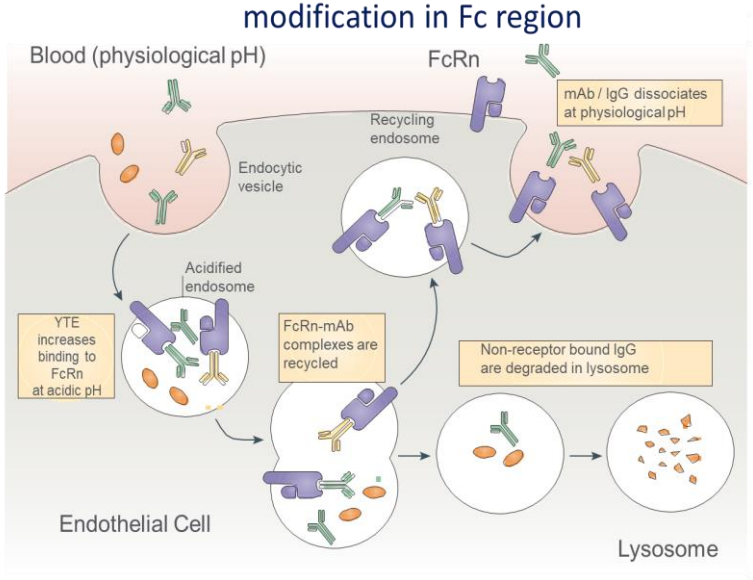
- No safety concerns and well tolerated in pregnant women
- Is immunogenic with passive antibody transfer to the infant and effective against LRTI in the first 180 days
- Appears to prevent both lower and upper respiratory infections
  - ?additional benefit of breast feeding for URTI
- Timing of vaccination during pregnancy and related to season is important
- No evidence of disease enhancement in subsequent year

Next generation RSV monoclonal Antibodies: extended and enhanced protection through passive immunisation





Extending the half-life of humanized Monoclonal antibodies by the YTE modification in Fc region



Enhanced neutralising capacity

Enhanced duration

ORIGINAL ARTICLE FREE PREVIEW

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*

Population & Treatment

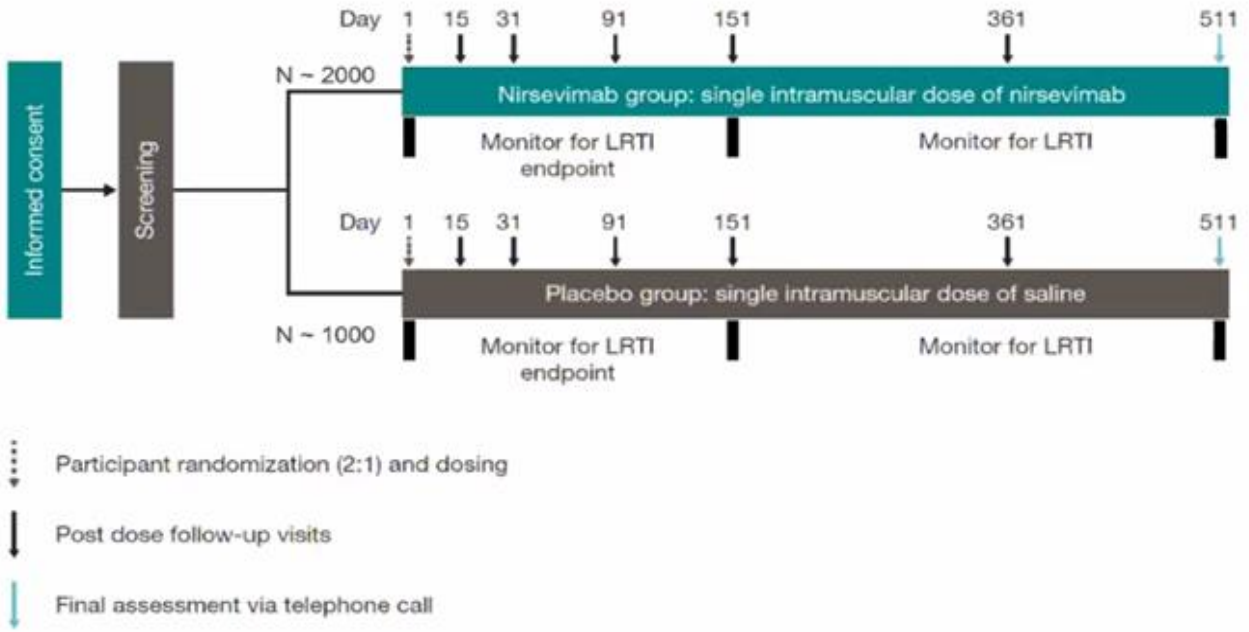
- Infants ≥35 weeks entering their first RSV season
- 2:1 randomisation to a single intramuscular dose of nirsevimab (if <5 kg, 50 mg; if ≥5kg, 100 mg) or placebo

Primary endpoint

- Incidence of medically attended lower respiratory tract infection (MA LRTI) due to RSV over 150 days post-dose

Secondary endpoints

- Incidence of hospitalization due to RSV over 150 days post-dose
- Safety (evaluated through 360 days post-dose)
- Pharmacokinetics
- Anti-drug antibodies



Total 3012 infants enrolled

No safety concerns identified with no differences in related adverse events (1.3%) compared to placebo (1.5%)

Updated data : Muller New England Journal of Medicine 5th April 2023

Nirsevimab efficacy in term and late preterm infants:

Episodes of RSV LRTI up to 150 days

Definition	Placebo (N=1003)		Nirsevimab (N=2009)		Efficacy	
	n	%	n	%	Efficacy	95% CI
MA RSV LRTI	54	5.4	24	1.2	**76.4**	62.3-85.2
MA RSV LRTI with hospitalization	20	2.0	9	0.4	**76.8**	49.4-89.4
MA RSV LRTI (very severe)	17	1.7	7	0.3	**78.6**	48.8-91.0

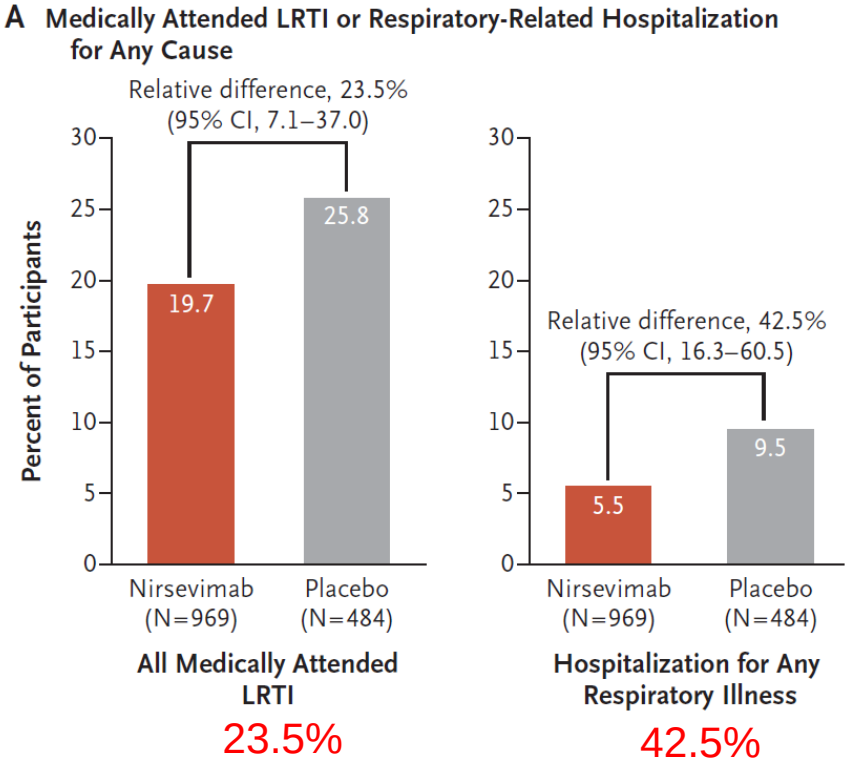
Muller New England Journal of Medicine 5th April 2023

Nirsevimab Efficacy in moderately preterm infants

- 1453 infants between 29 weeks to <35 weeks gestation randomised to 50mg mAb vs placebo (2:1)
- Mean age at enrolments 3.29 mths

Endpoint	Placebo (N=484)	MEDI8897 (N= 969)	Relative risk reduction (95% CI)	P value
Medically attended RSV +ve LRTI	**9.5%** (46)	2.6% (25)	**72.9%** (56-83%)	P < 0.001
RSV LRTI Hospitalisation	**4%** (20)	0.8% (8)	**80%** (55-91%)	P < 0.001

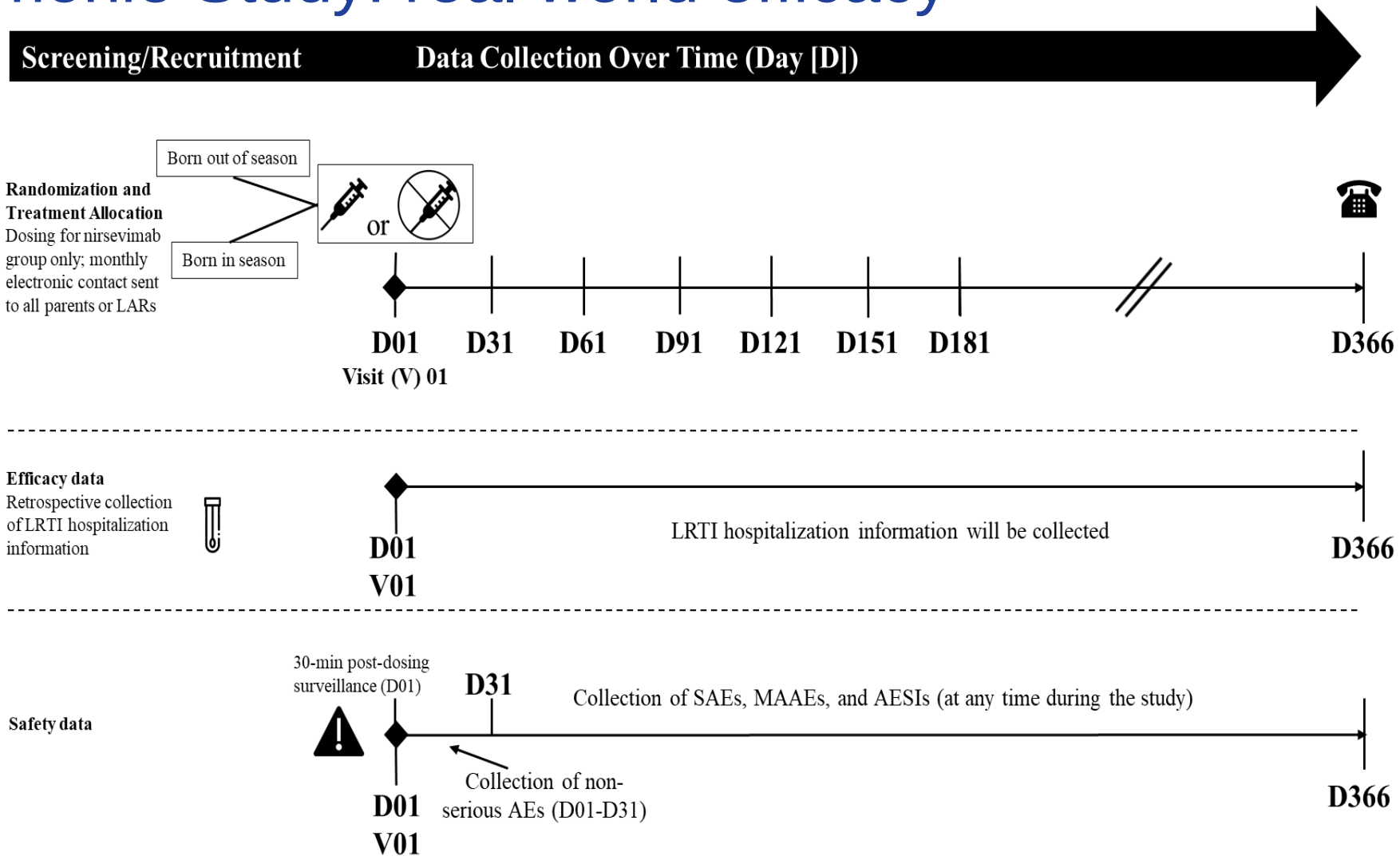
- Similar efficacy for subtypes: RSV A: 5.0% vs 1.1%; RSV B: 4.5% vs 1.4%



Griffin New England Journal of Medicine 2020; 383:415-25; DOI: 10.1056/NEJMoa1913556

Harmonie Study: real world efficacy

- **Open label parallel 2-arm: nirsevimab vs no intervention**
- **8058 healthy infants entering 1st RSV season**
  - **48.6% ≤ 3 mths**
  - **23.7% > 3 to ≤ 6 mths**
  - **27.5% > 6 mths**
  - **13.8% < 37 weeks gestation**
  - **50% born in season**
- **Single on-site visit (randomised 1:1)**
- **Monthly follow-up via e-diary (3 questions)**
- **Enrolment Aug 22-March 23**
  - **Interim Data lock 16 May 23**



Abbreviations: AESI, adverse event of special interest; D, day; LAR, legally acceptable representative; LRTI, lower respiratory tract infection; MAAE, medically attended adverse event; SAE, serious adverse event; V, visit

SB Drysdale, (2023, May 8–12). A Phase 3 randomized open-label study of nirsevimab (versus no intervention) in preventing hospitalizations due to respiratory syncytial virus (RSV) in infants (HARMONIE) [interim, analysis]. ESPID 2023: Lisbon, Portugal.

Efficacy of Nirsevimab on LRTI Hospitalization – Harmonie study 2022-2023 in UK, France & Germany

	Nirsevimab (N=4037)	No Intervention (N=4021)
RSV LRTI Hospitalisation	**N (%)**	**N (%)**
Yes	**11 (0.3%)**	**60 (1.5%)**
No	4026 (99.7%)	3961 (98.5%)
Efficacy	**83.21%** (95% CI 67.8- 92.0)	P <0.0001
All-Cause LRTI Hospitalisation	**N (%)**	**N (%)**
Yes	**45 (1.1%)**	**98 (2.4%)**
No	4026 (99.7%)	3961 (98.5%)
Efficacy	**58.04%** (95% CI 36.7- 71.2)	P <0.0001

The 2-sided 95% CI for the efficacy is calculated by an exact method assuming a binomial distribution of the number of RSV LRTI hospitalizations in the nirsevimab group conditional on the total number in both groups (described by Breslow and Day) accounting for the follow-up time post-dosing/randomization.

SB Drysdale, (2023, May 8–12). A Phase 3 randomized open-label study of nirsevimab (versus no intervention) in preventing hospitalizations due to RSV in infants (HARMONIE) [Oral presentation]. ESPID 2023: Lisbon, Portugal.

Implementation of Nirsevimab in infants :timing of dosing to optimise protection

- Per 1000 children immunised:
  - 93.6 cases MA-LRTI averted (NNT = 10.7)
  - 18.8 cases LRTI hospitalisations averted (NNT = 53.1)

In WA, with 80% coverage: prevent >2200 GP/ED Px & 451 RSV admissions

Protect infants born…	Before the RSV season September to April (up to age 8 months)	During the RSV season May to August
When	Prior to start of the season	Soon after birth before hospital discharge or in first week at GP
Where	At GP, during a routine visit before the start of the RSV season March - April	In hospital or at GP
Implementation	Given with influenza and other NIP vaccines given during routine visits	?Given with Birth Dose of Hepatitis B Vaccine or at specific visit

- Combined programmes with Maternal RSV vaccination?

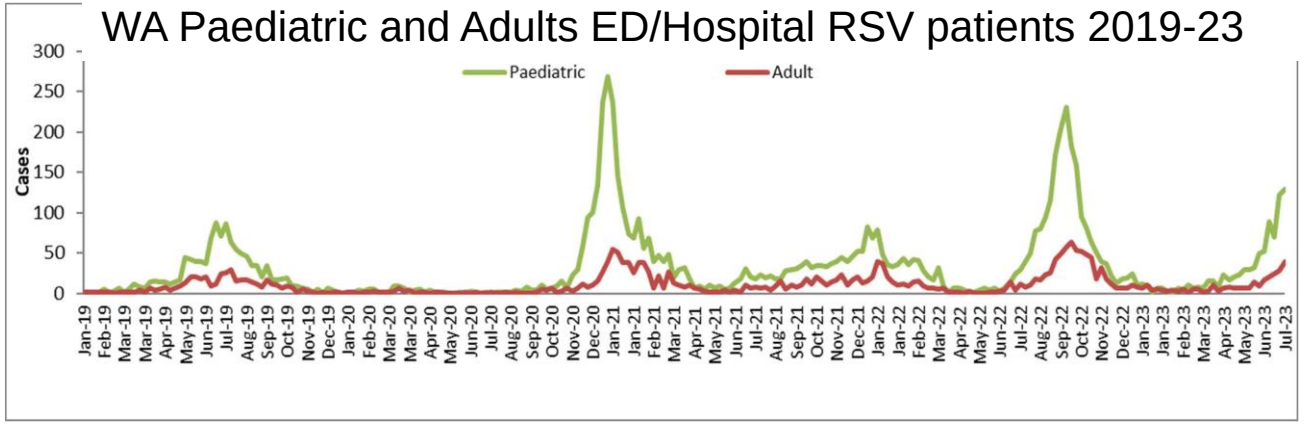
RSV monoclonal antibody summary

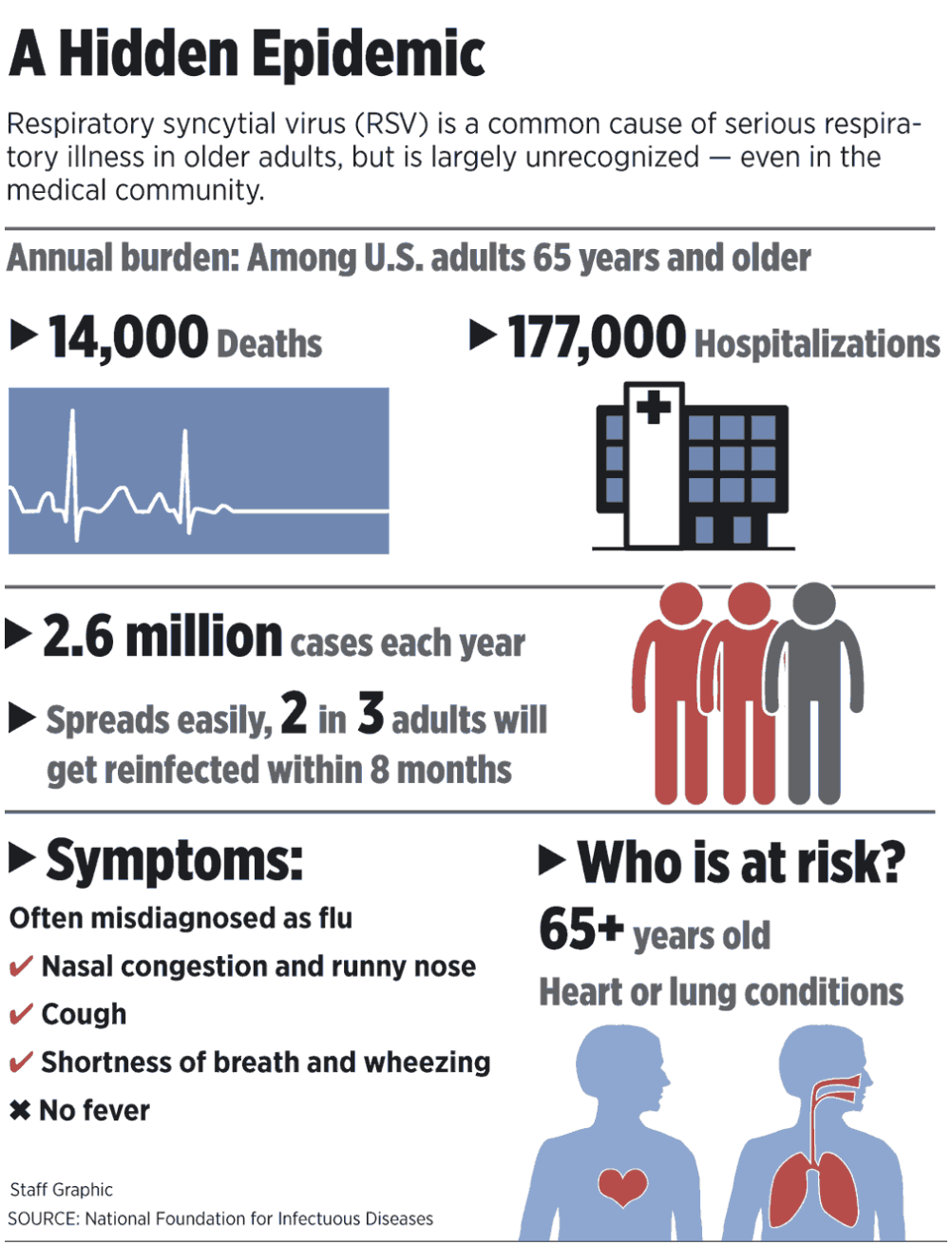
- Nirsevimab was safe and effective in reducing RSV medically attended LRTI and hospitalisations for 5 months in healthy preterm and term infants
- Similar efficacy against both RSV A and B subtypes
- Evidence of impact against overall LRTI and pneumonia hospitalisations
- No safety concerns, well tolerated with no impact of antidrug antibody
- Now registered in Europe & USA and will be registered in Australia shortly
- Universal infant programs with high uptake 
- Ongoing monitoring for effectiveness and variant escape important
- Merck Clesrovimab (MK1654) mAb also now in Phase 2/3 trials
  - Efficacy shown in human RSV challenge model
  - RSV Protect study now at PCH for high-risk infants

RSV vaccines for older adults

Promising results from recent studies

WA Paediatric and Adults ED/Hospital RSV patients 2019-23





RSV burden in older adults

- Frequent, often unrecognized, cause of severe respiratory illnesses
- Relatively little data in older adults due to lack of routine testing
  - 14,435 notifications in 2023 in adults over 65 years*
  - Incidence increases with age
- Burden of severe disease similar to influenza, with variability across seasons
- 94% of adults hospitalised have underlying medical conditions
- High proportion of RSV hospitalisations have severe outcomes, including ICU admission and death
- Long-term health consequences include heart attacks, stroke, COPD exacerbations and reduced lung function

Comparison of RSV Vaccine efficacy in older adults

Increasing severity ↓

AS01E-adjuvanted pre-F protein GlaxoSmithkline (n=24,966)		Bivalent pre-F protein Pfizer (n=34,283)		Moderna[3] mRNA encoding pre-F protein (n=37,500)		Combination hAd26.RSV.preF–RSV preF protein Janssen[4] (n=5782)	
Outcome	Efficacy	Outcome	Efficacy	Outcome	Efficacy	Outcome	Efficacy
RSV Acute RTI	71.7% (CI: 56-82%)	RSV ARTI	62.1% (CI: 37-78%)	RSV ARTI	N/A	RSV ARTI	N/A
RSV Acute LRT disease with ≥2 LRT Sx/signs with 1 LRT sign or 2 LRT signs or 3 LRT Sx	82.6% (CI: 58- 94%)	RSV LRTI with ≥2 Sx/signs	66.7% (CI: 32-99%)	RSV LRTI with ≥2 Sx/signs	83.7% (CI: 66-92%)	RSV LRTI with ≥2 Sx/signs	75% (CI: 50-88%)
		RSV LRTI with ≥3 Sx / signs	85.7% (CI: 37-78%)	RSV LRTI with ≥3 Sx / signs	82.4% (CI: 35-95%)	RSV LRTI with ≥3 Sx / signs	80% (CI: 52-93%),
RSV LRTI with ≥2 LRT signs or PI assessed severe	94.1% (CI: 62-100%)					RSV LRTI with ≥2 Sx or ≥1 LRTI Sx with ≥1 systemic Sx	70% (CI: 44-85%)

Sx – symptoms

1. *Papi et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults N Engl J Med 2023; 388:595-608*
2. *Walsh et al Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults N Engl J Med 2023; 388:1465-1477*
3. *https://investors.modernatx.com/news/news-details/2023/Moderna-Announces-mRNA-1345-an-Investigational RSV vaccine*
4. *Falsey et al. Efficacy and Safety of an Ad26.RSV.preF-RSV preF Protein Vaccine in Older Adults N Engl J Med 2023; 388:609-620*

Paediatric RSV vaccines – recent progress

- Adenoviral vectored RSV vaccines
  - designed to enhance TH1 immune response & reduce likelihood VAED
  - Chimpanzee adenoviral vector vaccine (CHAd155 –RSV; GSK)
  - Human adenoviral vector (Ad26.RSV.preF; Janssen)
  - Both got to Phase 2 trials in infants / toddlers but now discontinued
- Live attenuated RSV vaccines new candidate (Karron NIAD / Sanofi)
  - has deletion of non-essential accessory proteins to yield improved immune responses
  - Currently in Phase1B – 2 trials (*ClinicalTrials.gov Identifiers: NCT03596801; NCT04491877)*
  - Other live attenuated constructs in Phase 1 – 2 trials
- mRNA vaccines (Moderna)
  - RSV & RSV/hMPV vaccines now in early stage trials

Summary

- RSV is a major cause of paediatric and adult respiratory disease and mortality
  - New technologies are delivering effective prevention strategies
- Maternal RSV vaccination
  - Well tolerated and immunogenic with passive antibody transfer
  - Effective against ALRI in the first 6 months
  - No evidence of disease enhancement
- RSV long-acting monoclonal antibodies
  - Safe and highly effective against RSV ALRTI for 5 months
  - Offer increased flexibility in delivery for maximal impact
  - WA could have a universal infant program in 2024
- RSV vaccines in older adults highly effective against mild-moderate disease
- Paediatric RSV vaccines in early phase trials to reduce burden in older children

Acknowledgements

- Telethon Kids Institute
  - Vaccine Trials Group
  - Hannah Moore Minda Sarna, Chris Blyth
- Australian and Overseas investigators involved in trials
- ACIP for public provision of meeting data
- Wesfarmers Centre Community Reference Group
- Funding
  - Telethon-Perth Children's Hospital Research Fund
  - Merck IISP

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WESFARMERS
CENTRE OF VACCINES
& INFECTIOUS DISEASES

How to find out more about RSV?

ReSVINET
RESPIRATORY SYNCYTIAL VIRUS FOUNDATION

8th ReSViNET Conference

February 13 -16, 2024

Mumbai, India मुंबई, भारत

Questions?

TELETHON KIDS INSTITUTE
Discover. Prevent. Cure.

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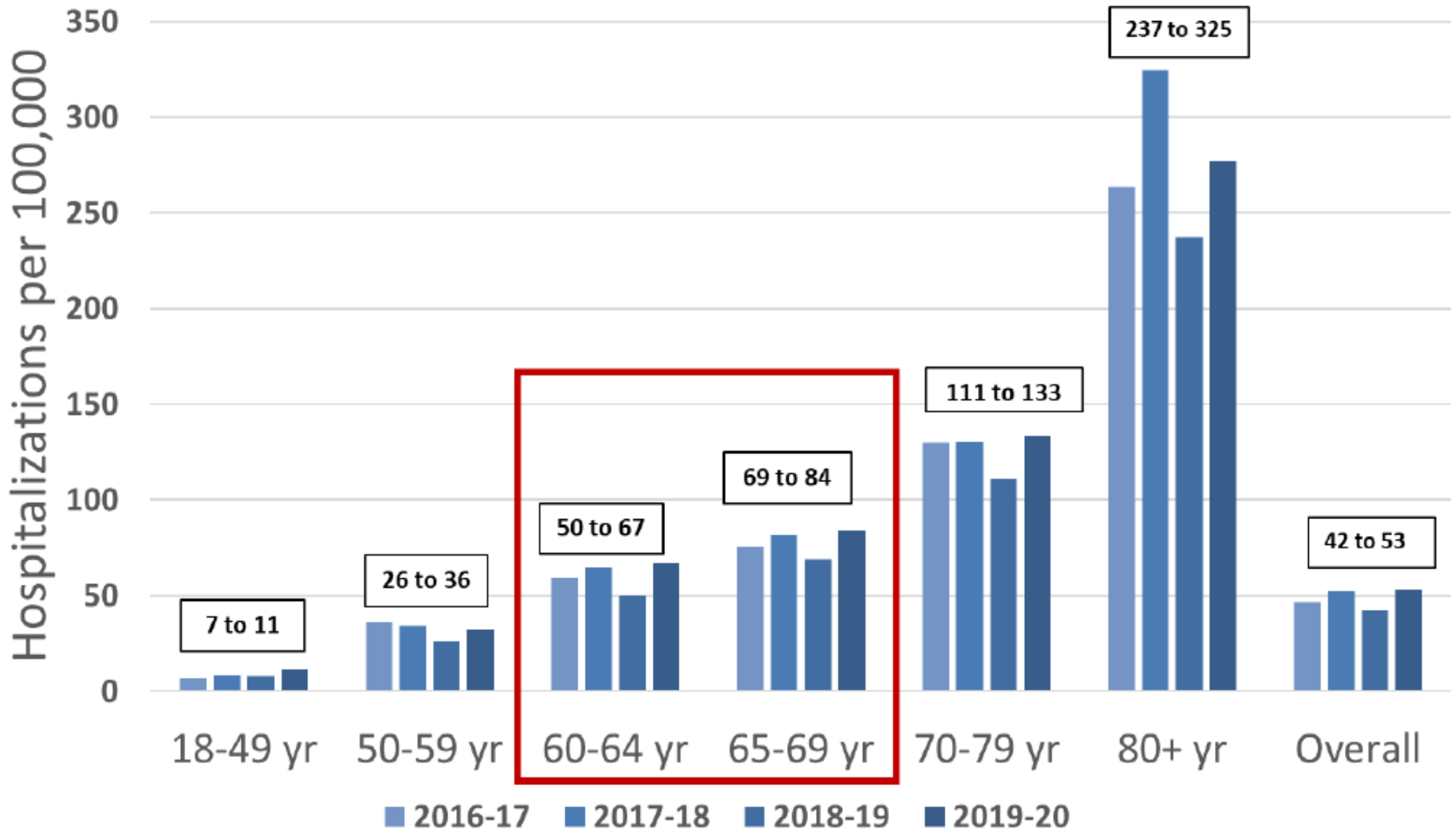
RSV-associated hospitalization rates by adult age group, RSV-NET 2016–2020



RSV-NET: unpublished data. Rates are adjusted for the frequency of RSV testing during recent prior seasons and the sensitivity of RSV diagnostic tests

Which adults are at greatest risk for RSV?

Chronic lung diseases such as COPD and asthma

Chronic cardiovascular diseases such as congestive heart failure and coronary artery disease

Immune compromise

Hematologic disorders

Residents of nursing homes and other long-term care facilities

Neurologic disorders

Endocrine disorders such as diabetes

Kidney and liver disorders

Other underlying conditions or factors that the provider determines might increase the risk of severe respiratory illness

Key Study Definitions

Weekly active surveillance for ARI symptoms
Symptoms trigger nasal swab and possibly a visit

Acute Respiratory Illness (ARI)

1 or more of these symptoms (**new or worsened from baseline**), lasting more than 1 day

- **Nasal discharge**
- **Nasal congestion**
- **Sore throat**
- **Cough**
- **Sputum production**
- **Wheezing**
- **Shortness of breath**

Lower Respiratory Tract Illness (LRTI)

- **Cough**
- **Sputum production**
- **Wheezing**
- **Shortness of breath**
- **Tachypnea**

ARI with ≥ 2 or ≥ 3 lower respiratory tract signs/symptoms (new or worsened)

Severe LRTI (sLRTI)

LRTI criteria plus at least 1 of the following:

- **Hospitalization** due to RSV-LRTI
- New/increased **oxygen supplementation**
- New/increased **mechanical ventilation** (including CPAP)

Positive validated RT-PCR in central laboratory

RSV-ARI

RSV-LRTI

RSV-sLRTI

Lessons from Novavax Prepare RSV efficacy study

Geographic imbalance in efficacy

Primary Endpoint Cases

Day 90 Vac. Efficacy (%) Placebo, Vaccine cases	All	U.S.	S. Africa	ROW*
MS RSV LRTI	39.4 35/1430 41/2765	11.6 6/346 10/652	42.5 22/732 25/1447	54.7 7/352 6/666

U.S. efficacy was low compared to other countries by most measures and appears to be related to timing of immunization, including the negative effects of late gestational age immunization and short intervals to birth, conditions which were more common in U.S. subjects.

- Provides proof of principle of safety of maternal RSV vaccination and efficacy over 90 days
  - Reduced overall antimicrobial prescription by 13%
- Larger proportion of US infants vaccinated several months before start of RSV season
- FDA required repeat Phase 3 study – Novavax has discontinued RSV program

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