



IMMUNISATION
COALITION

Respiratory Syncytial Virus (RSV) Disease & Prevention

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Introduction to RSV

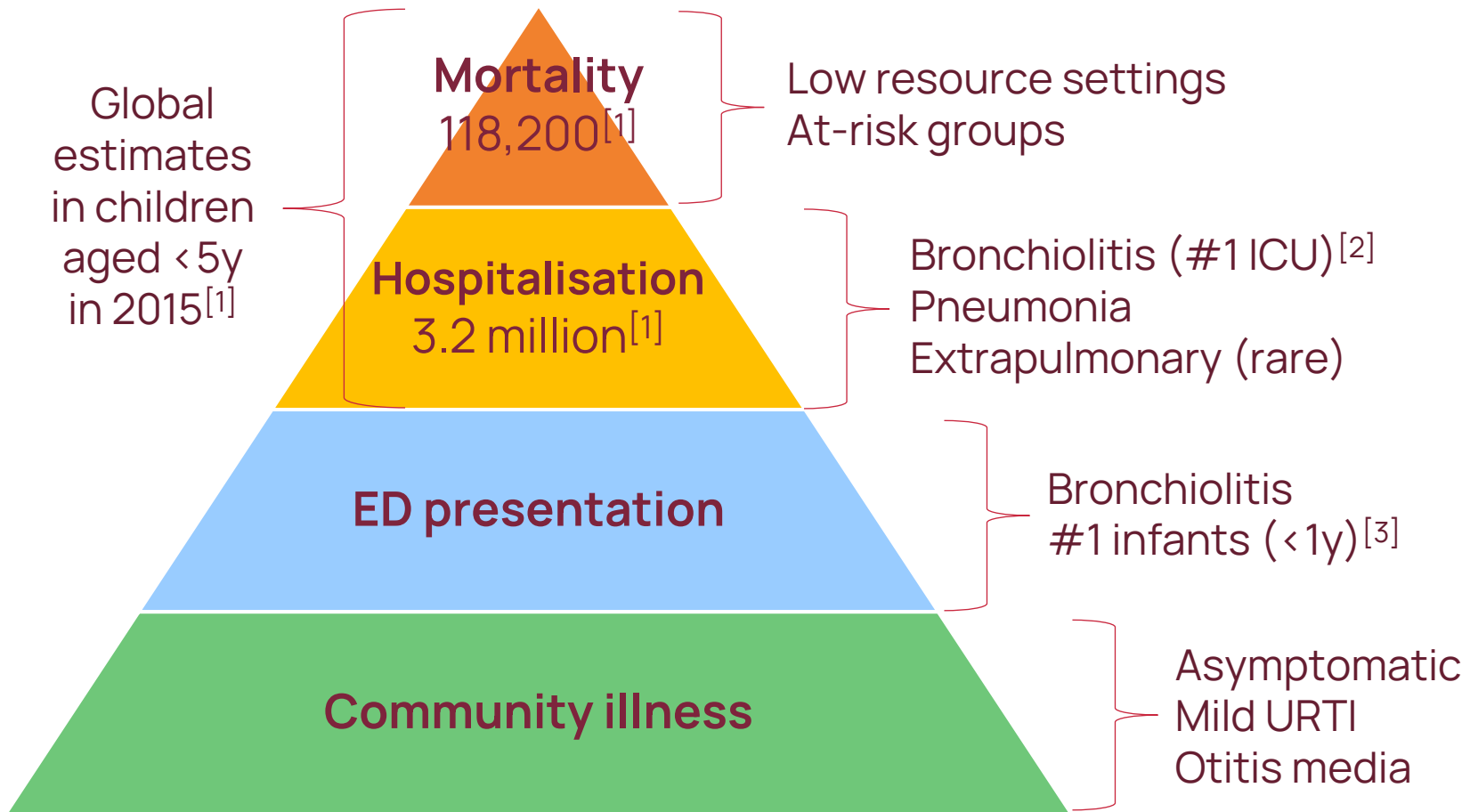
Leading cause of acute lower respiratory infection

- Infants & young children^[1]
 - Majority hospitalised are healthy^[2]
- Prematurity, chronic comorbidities^[3,4]
- Older adults^[4]
- Indigenous populations^[5,6]

Prevention & treatment

- No licenced vaccine
- Monoclonal antibody immunoprophylaxis (Palivizumab)
- Infection prevention & control
- Supportive treatment

Estimating the RSV Disease Burden



[1] Shi, et al. The Lancet, 2017. [2] ANZICS, <https://www.anzics.com.au/annual-reports/> 2018.

[3] Acworth, et al. Emergency Medicine Australasia, 2009.

“The burden of RSV in children in the UK exceeds that of influenza”

Taylor et al. BMJ Open, 2016.

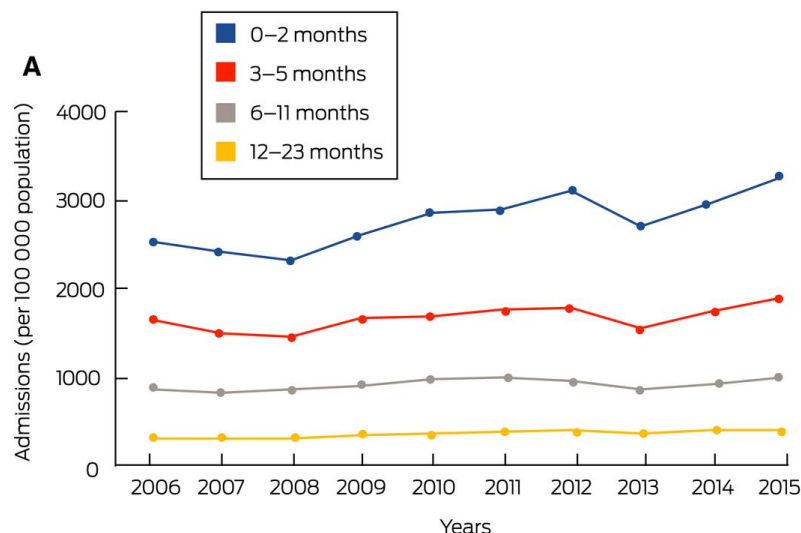
RSV disease in young children

Community disease^[1]

- GP visits & antibiotic use
- Most children infected by age 2-3y
- 34% community medical care
- 2% hospitalised

Hospitalisations in Australia^[2,3]

- >7,000 children aged <5y in 2015
- LOS 3 days (IQR 1-4)
- Indigenous children IR 1.8 (1.8-2.0)
- AU >\$6,350 per hospital episode^[4]
- AU\$20,000 per ICU episode^[5]



National RSV-coded hospitalisations

National Hospital Morbidity Database ICD-10-AM codes - RSV organism (B97.8), RSV pneumonia (J12.1), RSV bronchitis (J20.5), RSV bronchiolitis (J21.0)

[1] Takashima et al. Eur J Pediatr, 2021. [2] Saravanos et al. Med J Aust, 2019. [3] Gebremedhin et al. Scientific Reports, 2022. [4] Homaira et al. Epidemiol Infect, 2016. [5] Pham et al. Journal of Paediatrics & Child Health, 2019.

RSV disease in young children



“RSV is terrifying and all but completely unknown to parents.” Mother of 3 week old bub Navy

RSV-associated child deaths

RSV is an important contributor to < 5y child mortality^[1]

- Up to 118,200 (UR 94,600-149,00) hospital & community deaths (2015)
- Majority in low-income or lower-middle income countries (LMIC)

RSV-GOLD mortality database^[2]

- RSV-associated death in children < 5y
- Clinical & socioeconomic characteristics
- 358 children from 23 countries



Characteristic	LMIC	UMIC	HIC
Median age (months)	5.0 (IQR 2.3-11.0)	4.0 (2.0-10.0)	7.0 (3.6-16.8)
Medical comorbidity	28%	47%	70%

[1] Shi et al. The Lancet, 2017. [2] Scheltema et al. Lancet Glob Health, 2017.

RSV-associated child deaths

RSV deaths in NSW Australia, 1998-2018

- RSV-attributable in-hospital death in children < 16y
- Paediatric tertiary/quarternary referral hospital
- Total of 20 RSV-attributable deaths



Characteristic	
Population death rate	1.2 (0.5-2.7) per million in NSW
Median age (months)	28.7 (IQR 8.8-75.0)
Medical comorbidity <ul style="list-style-type: none">• Malignancy with immunosuppression, neurological disease, cardiorespiratory disease, immunodeficiency	100%
Healthcare associated infection	55%
RSV diagnosis code (principal & additional)	85%

“RSV is associated with a substantial disease burden in adults comparable to influenza, with most of the hospitalisation and mortality burden in the elderly.”

Fleming et al. BMC Infectious Diseases, 2015.

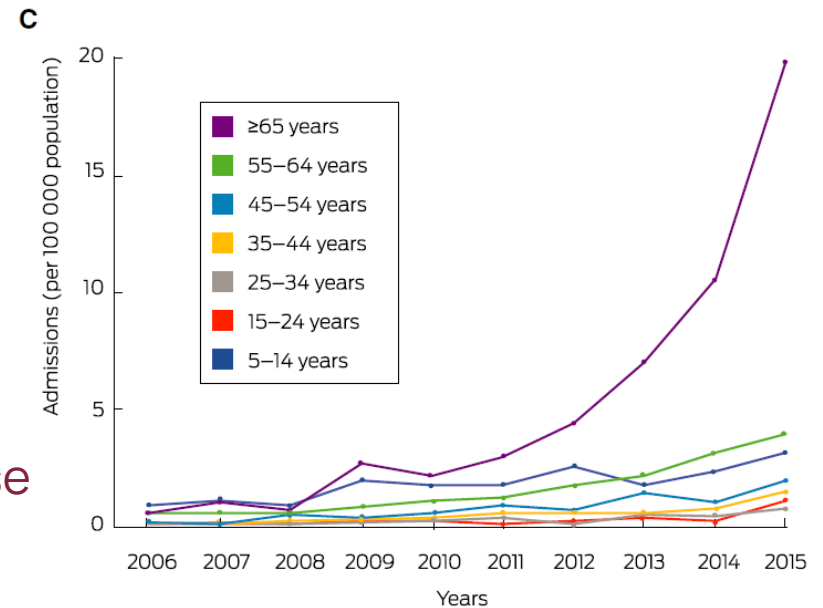
RSV disease in adults

Hospitalisations in Australia [1]

- RSV pneumonia ($\geq 65y$)
- LOS 6 days (IQR 4-9)
- \uparrow RSV-associated deaths
- Rates \uparrow Indigenous adults (35-64y)

Associated diagnoses [2]

- Chronic obstructive pulmonary disease
- Asthma
- Congestive heart failure
- Immunocompromise



National RSV-coded hospitalisations

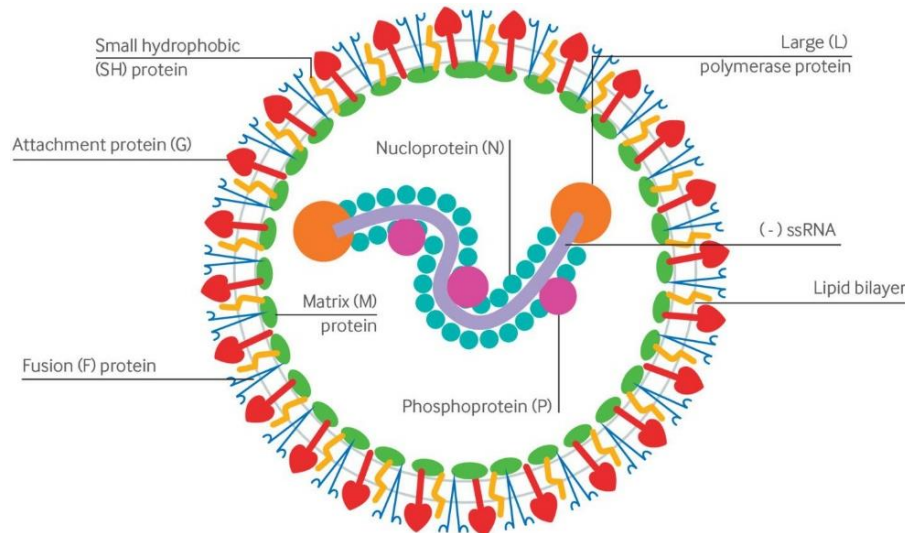
National Hospital Morbidity Database ICD-10-AM codes - RSV organism (B97.8), RSV pneumonia (J12.1), RSV bronchitis (J20.5), RSV bronchiolitis (J21.0)

[1] Saravanos et al. Med J Aust, 2019. [2] Branche & Falsey, Drugs Aging, 2015

The development of safe, effective and affordable RSV prevention is a global priority.

RSV-specific prevention

Paediatric	Maternal	Elderly
Immunoprophylaxis Vaccines <ul style="list-style-type: none">• Live attenuated• Protein-based• Nucleic acid• Recombinant vectors	Vaccines <ul style="list-style-type: none">• Protein-based	Vaccines <ul style="list-style-type: none">• Protein-based• Nucleic acid• Recombinant vectors



F (Fusion) protein

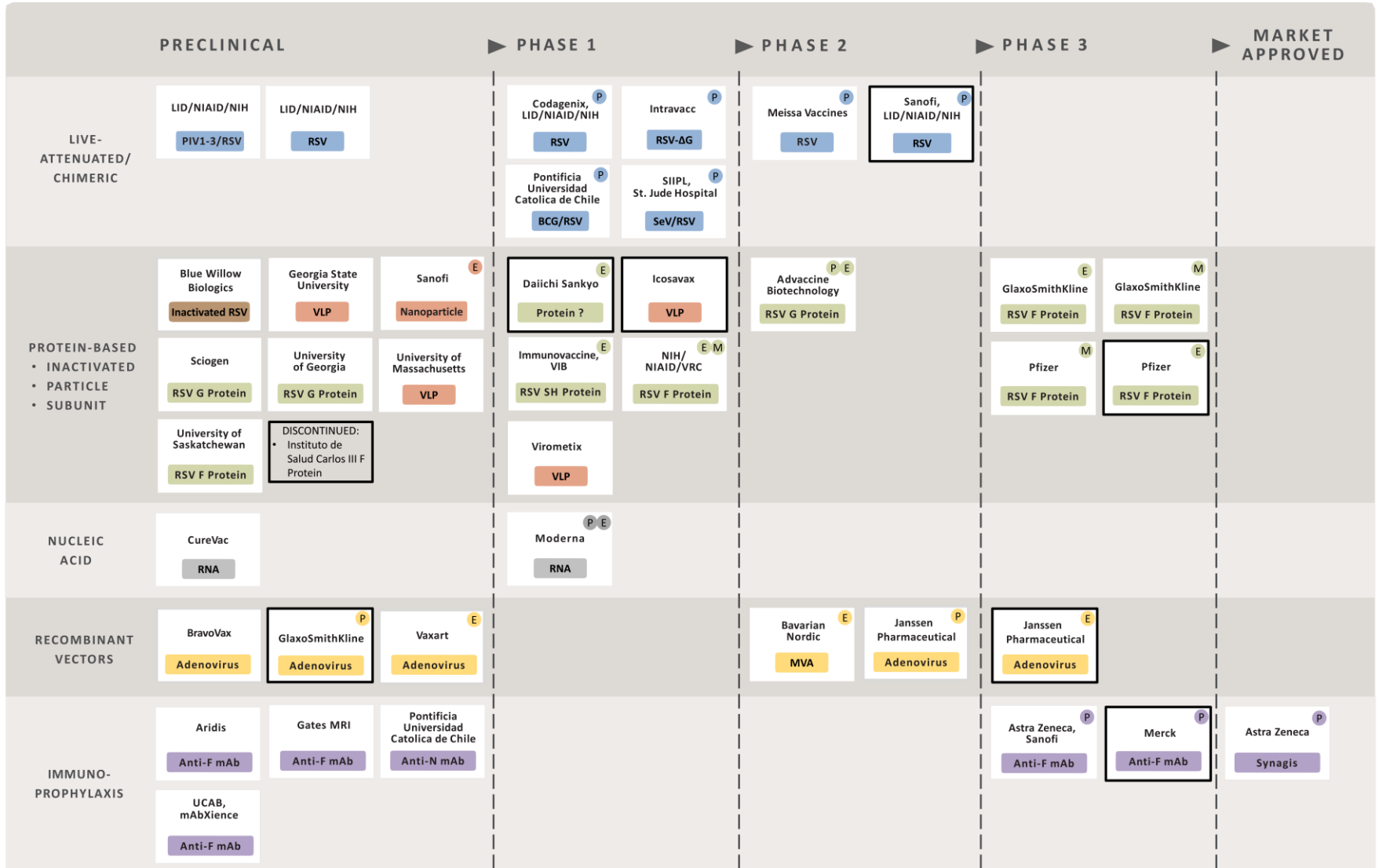
- Common vaccine target
- Highly conserved
- Pre & post fusion form

G (attachment) glycoprotein

- Variable
- Subtypes RSV-A & RSV-B

RSV Vaccine and mAb Snapshot

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



UPDATED: September 28, 2021

Indicates Change

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

RSV-specific prevention

Company	Phase	Vaccine Type	Target Group	Efficacy
[1]Novavax	3 N=4,636	F protein nanoparticle	Pregnant women (infants)	39% (5-61) RSV-ALRI 44% (20-62) with hospitalisation
[2]Janssen “CYPRESS study”	2b N=5,728	Adenovirus vector PreF	Older adults (≥65y)	80% (52-93) RSV-ALRI 70% (43-85) symptomatic RSV infection
[3]AstraZeneca/Sanofi “Nirsevimab”	2b N=1,453	Monoclonal Ab PreF (single-dose)	Healthy pre-term infants	78% (52-90) RSV-ALRI

[1] Mahdi et al. N Engl J Med 2020. [2] <https://www.nj.com/janssen-announces-phase-2b-data-demonstrating-its-investigational-rsv-adult-vaccine-provided-80-protection-against-lower-respiratory-infections-in-older-adults> [3] Griffin et al. N Engl J Med, 2020.

“Awareness of RSV as a global health problem is lacking.”

<https://rsvgold.com/awareness/>

Awareness of RSV disease

- Pregnant women and midwives have low awareness of RSV^[1,2]
- RSV in older adults is under recognised^[3]
- Busy immunisation schedules
- Challenges with uptake of existing vaccines

Education for key groups

- Health care workers
- Pregnant women
- Early childhood & aged care

Of 495 pregnant Australian women attending an antenatal clinic **83%** had never heard of RSV^[1]

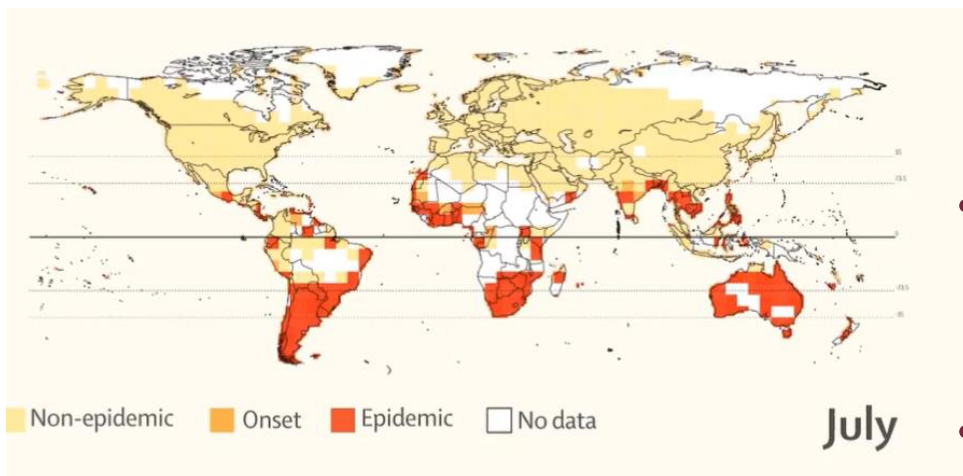


[1] Giles et al. Vaccine, 2019. [2] Wilcox et al. Pediatr Infect Dis J, 2019. [3] Branche & Falsey. Drugs Aging, 2015. Image: <https://www.facebook.com/protectlittlelungs/>

Understanding RSV activity is key information for planning health service delivery & timing of interventions.

RSV epidemic seasonality

Predicted global changes in RSV prevalence by month



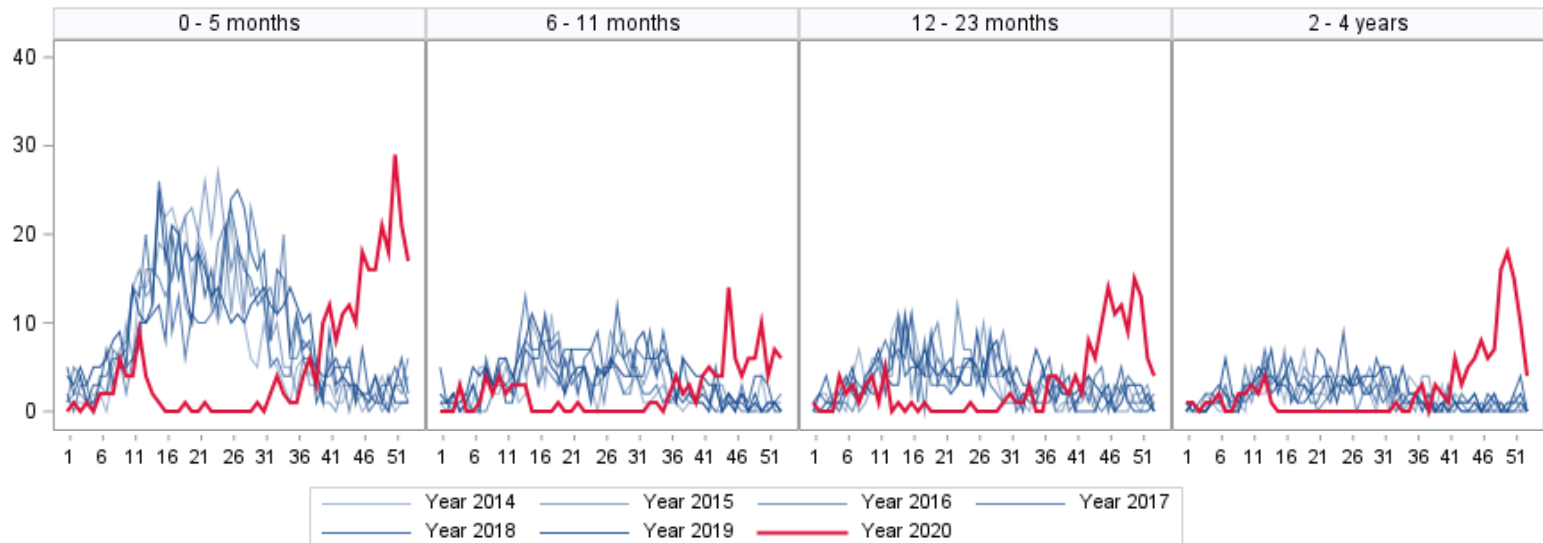
- Key information for planning
 - Health service delivery
 - Prophylaxis & immunisation
- Clear seasonal epidemics
 - Tropics – late summer
 - Temperate sites – winter
- Precedes influenza season
- Duration 4.6 (4.3-4.8) months

RSV epidemic seasonality in 2020

COVID-19 public health measures disrupted RSV activity globally

→ Single major lockdown in NSW in 2020

- Suppression of typical RSV season → unseasonal 'summer' epidemic
- RSV infections in children aged 2-4y ↑ 84% (34 to 192) $P < 0.01$
- RSV hospitalisations ↓ 32% (-41 to -19) $P < 0.01$



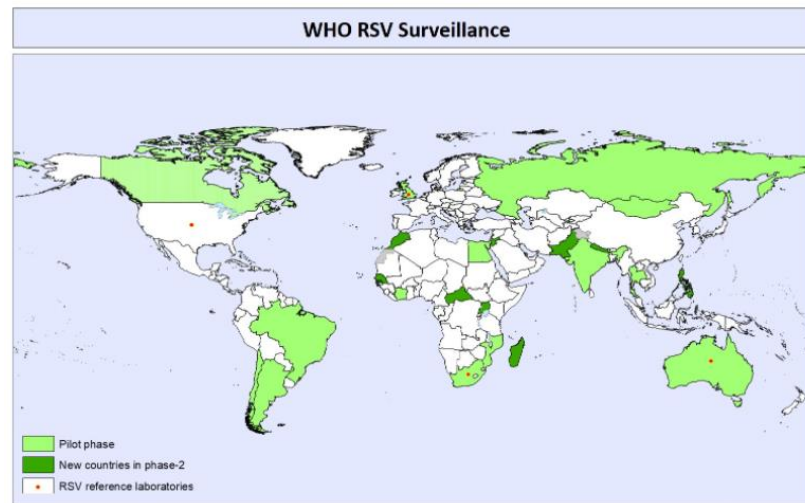
RSV prevention - looking forward

RSV Surveillance

- Australia – RSV notifiable
- Global – WHO Flu/RSV
- Clinical
- Virological

RSV Research

- Paediatric & adult
- At-risk groups
- Data-linkage
- Social

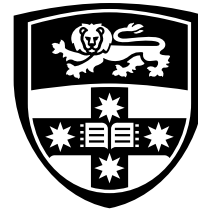


Thank you!

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SYDNEY



The Sydney **children's**
Hospitals Network



NCIRS National Centre for
Immunisation Research
and Surveillance