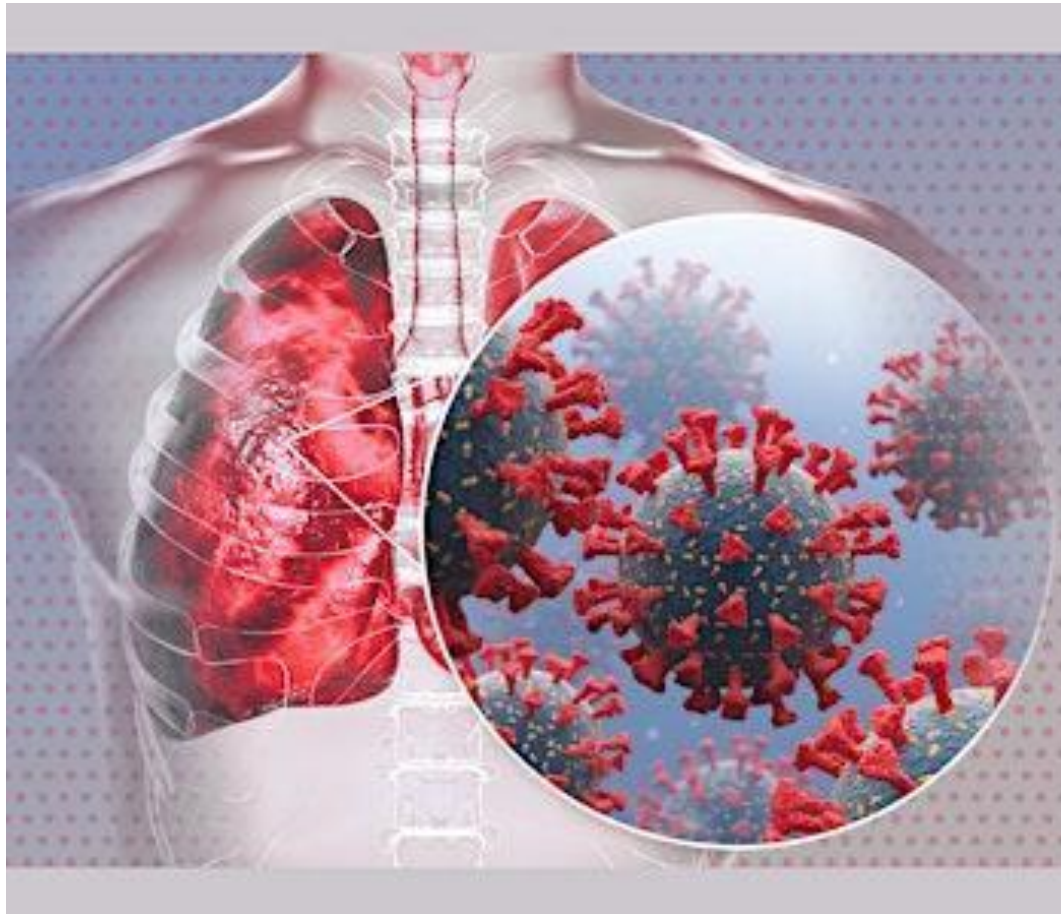


# Masterclass: Vaccination of Older People



## Charles Feldman

*Emeritus Professor, University of the Witwatersrand*

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*Honorary Consultant (non-clinical), Monash Medical Centre*

## RSV in Older Adults

# Declaration of interest

- Charles Feldman has acted on the speakers bureau and advisory boards of MSD (Merck) and Pfizer.
- Other declarations of no interest to the current presentation.
- Affiliations:
  - Emeritus Professor, University of the Witwatersrand, South Africa
  - Adjunct Senior Lecturer, Monash University, Australia
  - Honorary Consult (non-clinical), Monash Medical Centre, Australia

# Topics to be covered



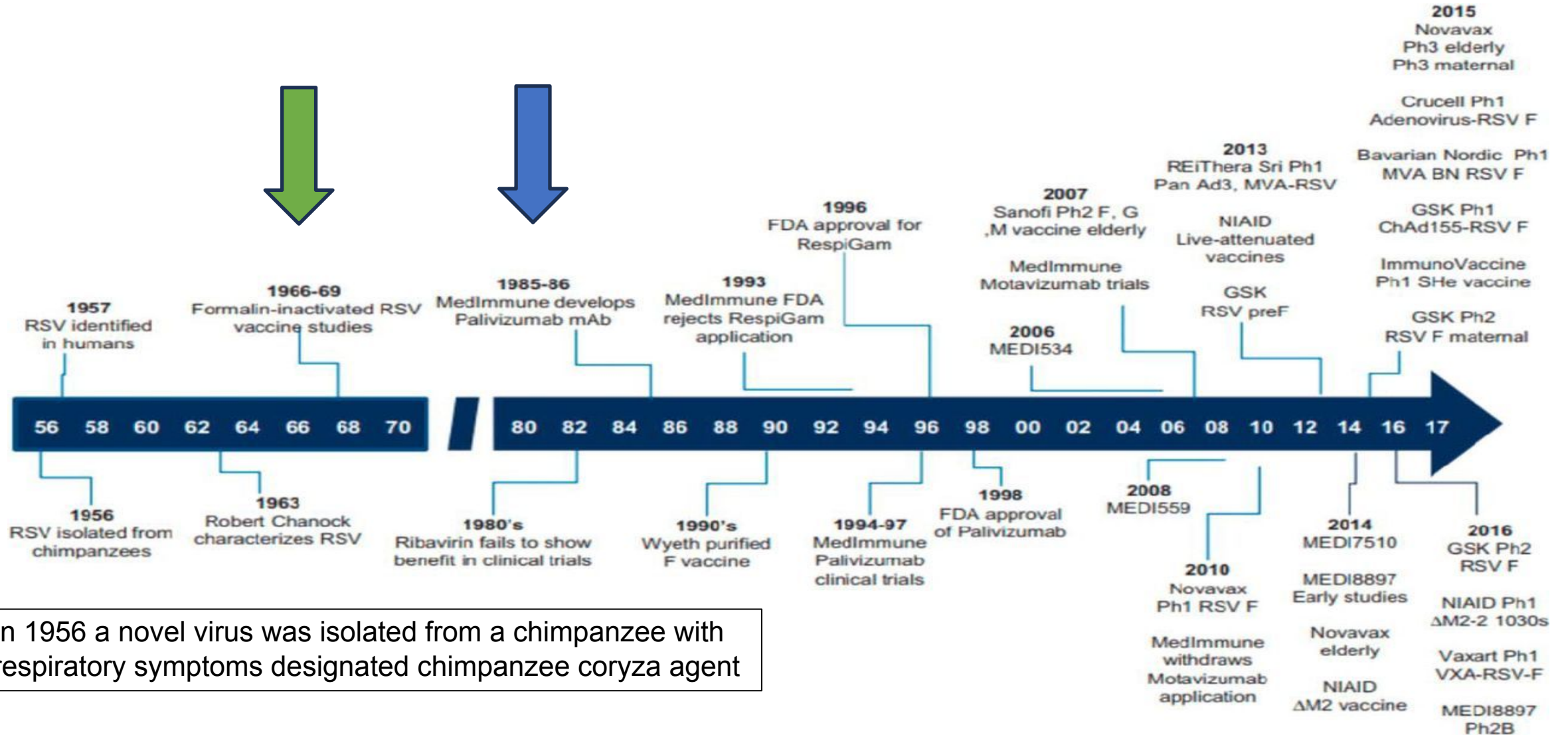
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- Emerging role of RSV in RTI
- Structure and function of the virus
- Burden of the disease, including Australia
- Risk factors for severe infection
- Immunological aspects of RSV infection
- Consequences of co-infections with viruses and bacteria
- Cardiorespiratory events following RSV infection
- Vaccine and monoclonal antibody recommendations

# Looking back into the history of RSV



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In 1956 a novel virus was isolated from a chimpanzee with respiratory symptoms designated chimpanzee coryza agent



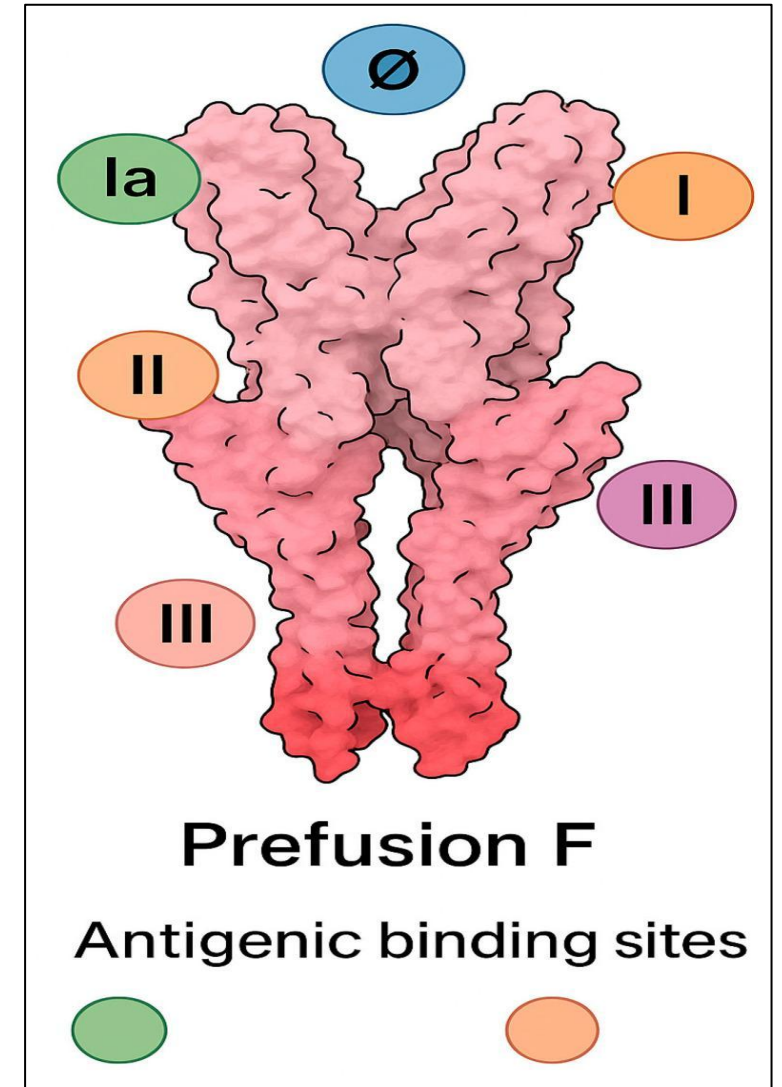
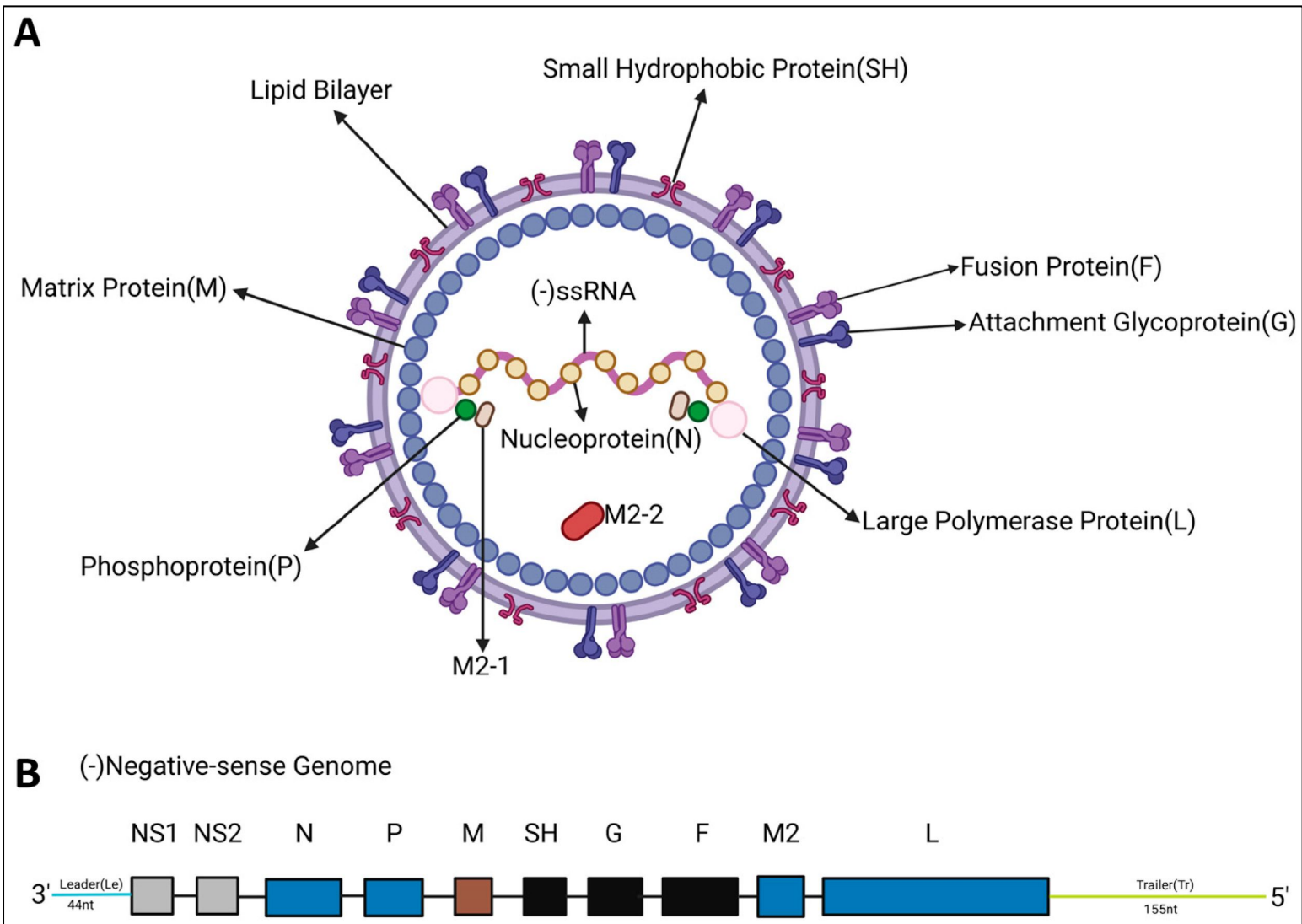
## Description of the virus

- Respiratory syncytial virus (RSV) is an enveloped, negative-sense, single-stranded RNA genome of approximately 15 kb that encodes 11 viral proteins.
- Since its discovery in 1957, RSV has been classified into a single serotype, yet it exhibits a wide diversity of viral strains, which has led to the classification of two major antigenic subgroups, RSV-A and RSV-B, each containing multiple genotypes.
- These genotypes are differentiated based on variability in antigen reactions against the attachment (G) and fusion (F) glycoproteins and to date, the ON1 genotype of subtype A and the BA9 genotype of subtype B are the dominant genotype in the global epidemic.

# Description of the virus



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# What is the burden of RSV?



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- RSV is a leading cause of respiratory disease globally, causing infections across all ages, with the most severe disease burden among young infants.
- Overall, more than 92% of all RSV-associated acute LRTI episodes and nearly 99% of related fatalities occur in low- and middle-income countries.
- Among older adults ( $\geq 65$  years), 2015 GBD data recorded about 1.5 million episodes in industrialized countries and of these, approximately 14.5% (214,000 episodes) were admitted to hospitals.
- In sum, RSV infections impose a substantial burden on patients, caregivers, healthcare systems and broader society around the world.



# Overview of RSV infections

- RSV is a common virus that causes upper and lower respiratory tract infections.
- It is spread through droplets from an infected person's cough or sneeze, which can be inhaled by others or land on surfaces where the virus can live for several hours.
- While it may be a mild disease for some, it can cause serious illness, complications, and hospitalisation in otherwise healthy adults.
- Infections most commonly occur in autumn and winter, usually between April and September with peaks in June and July, often before influenza season.
- RSV vaccines can be given at any time of the year, although vaccination should be offered to patients before the start of the RSV season, where possible.

# RSV is a burden throughout life



Birth	Infancy (<18 Mo)	Young Childhood (19 Mo - 5 Yr)	Childhood (6-16 Yr)	Adulthood (17-70 Yr)	Older Adulthood (>70 Yr)
RSV bronchitis	Postbronchiolitic wheeze				
		Exacerbation of asthma/COPD			
				Insidious respiratory illness	
	Colds due to infection or reinfection				
<b>Partial protection from RSV reinfection</b>					
Transfer of maternal Ab					
Immature	Innate immunity			Declining	
Immature	Th1 immunity			Declining	
Th2/Th17 bias					

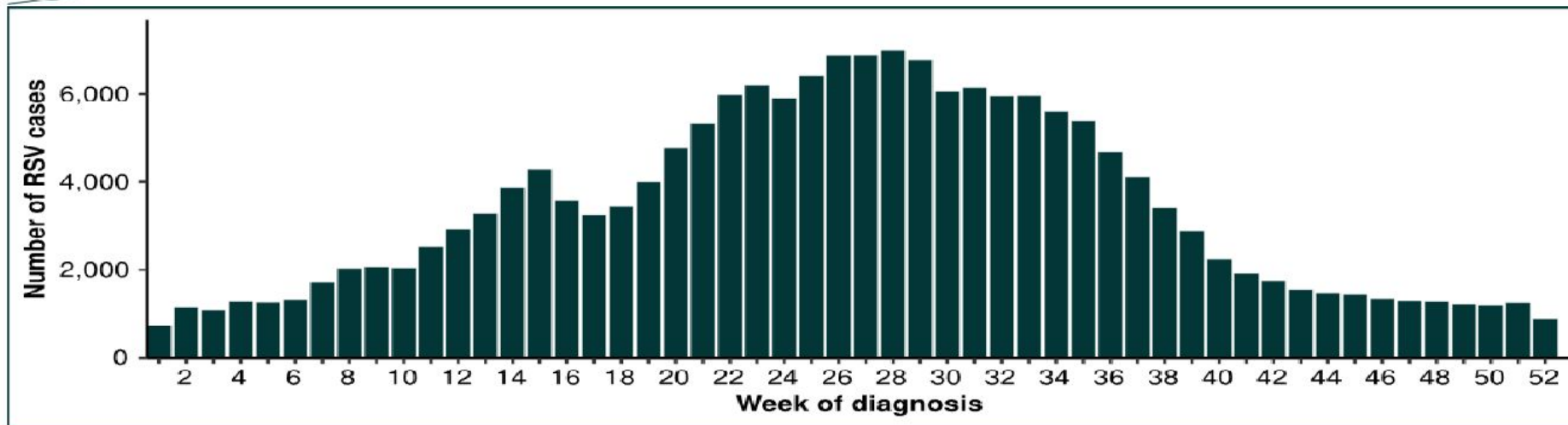
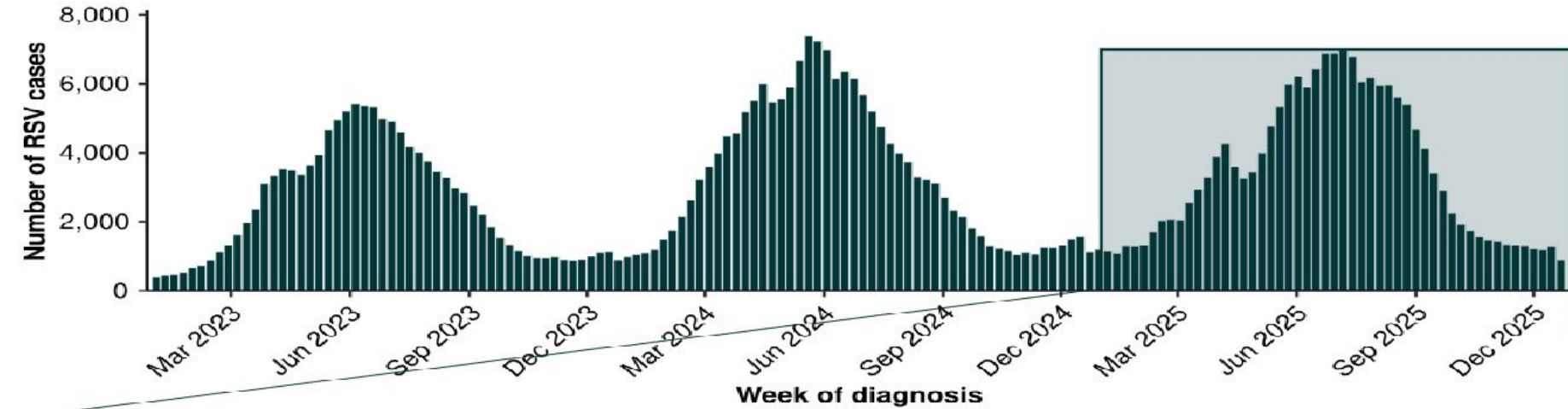
**Clinical features**

**Immune responses**

# Surveillance for RSV in Australia by year and week



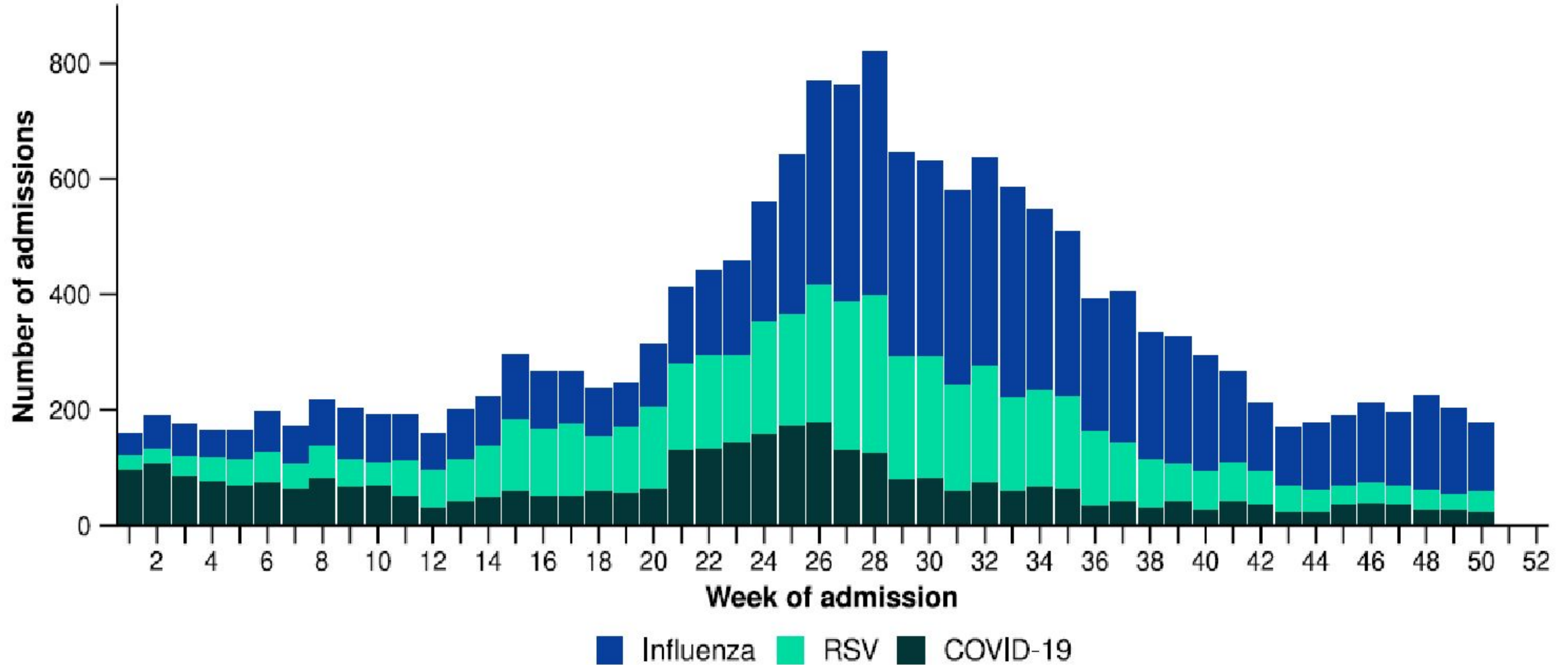
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COALITION



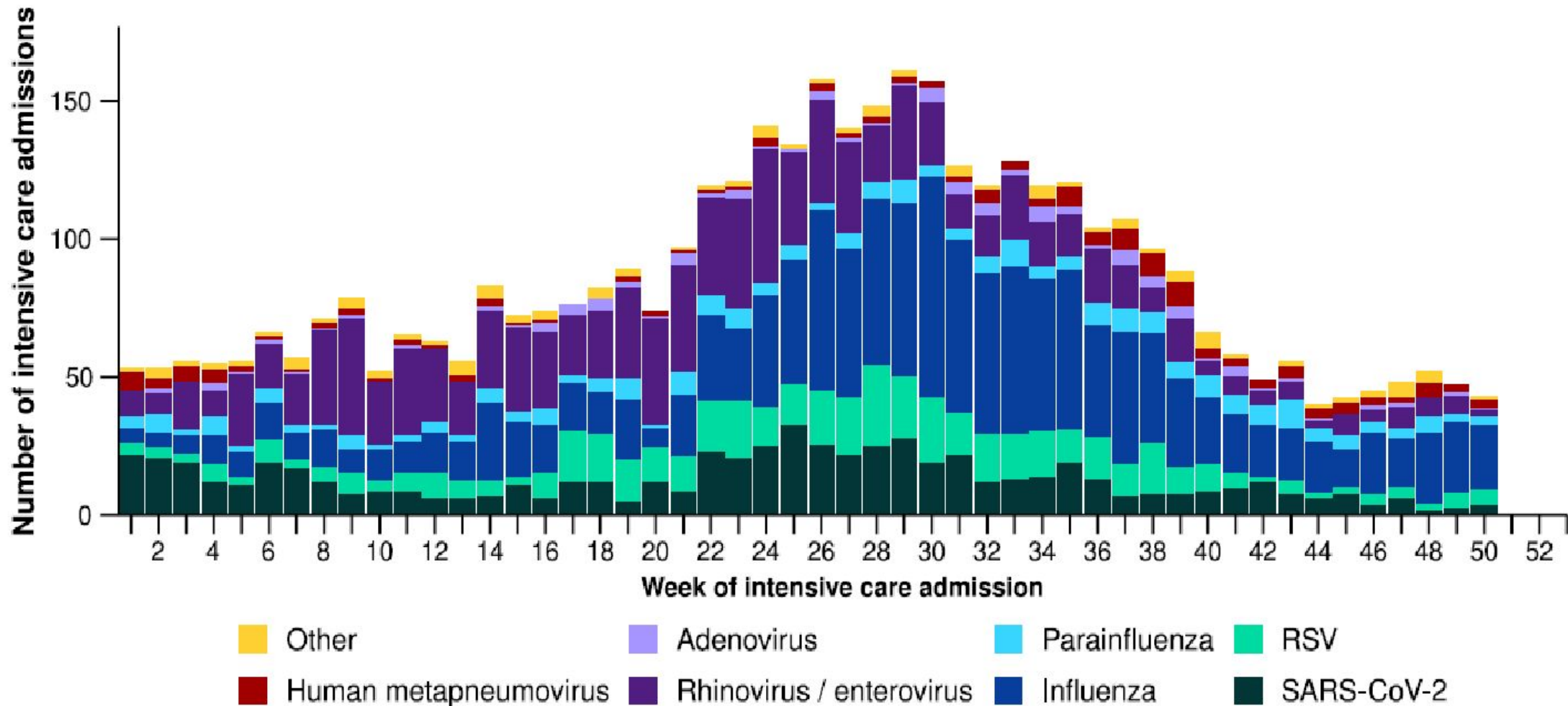
# SARI hospital admissions in Australia for 2025



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COALITION



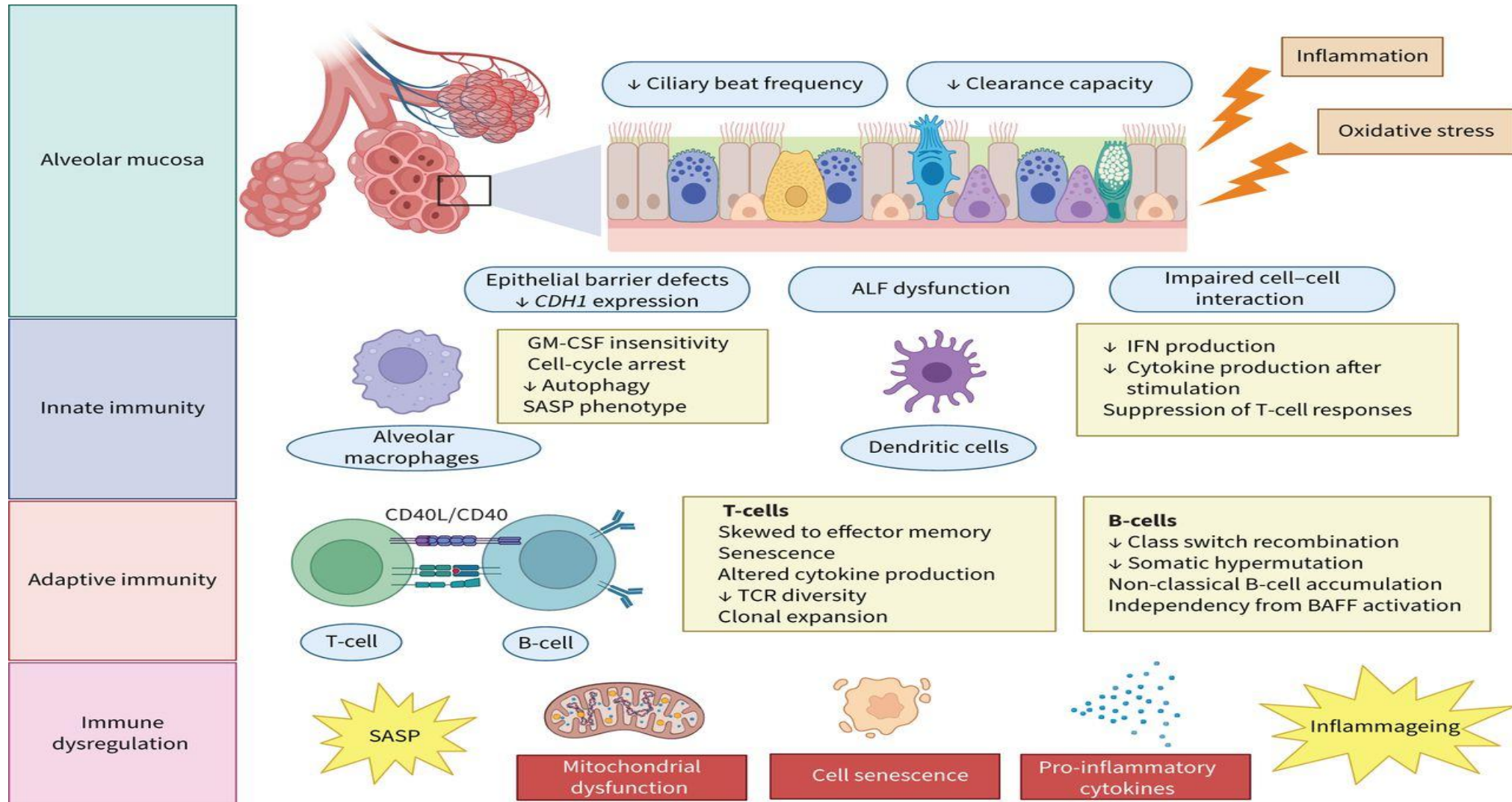
# SARI admissions to ICU at a sentinel hospital in 2025



# Immunosenescence and susceptibility to viral infections



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# Increased risk of severe RSV in adults



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## Risk category

## Example medical condition

Cardiac disease

- Congenital heart disease
- Congestive heart failure
- Coronary artery disease

Chronic respiratory conditions

- Suppurative lung disease
- Bronchiectasis
- Cystic fibrosis
- Chronic obstructive pulmonary disease
- Chronic emphysema
- Severe asthma (requiring frequent medical consultations or the use of multiple medications)

Immunocompromising conditions

- HIV
- Malignancy
- Immunocompromise due to disease or treatment
- Asplenia or splenic dysfunction
- Solid organ transplant
- Haematopoietic stem cell transplant
- CAR T-cell therapy

# Increased risk of severe RSV in adults



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## Chronic metabolic disorders

- Type 1 or 2 diabetes
- Amino acid, carbohydrate, cholesterol biosynthesis disorders
- Fatty acid oxidation defects
- Lactic acidosis, Mitochondrial disorders
- Organic acid, urea cycle, vitamin/cofactor disorders
- Porphyria

## Chronic kidney disease

## Chronic neurological conditions

- eGFR <30 mL/min (stage 4 or 5)
- Hereditary and degenerative CNS diseases
- Seizure disorders
- Spinal cord injuries and neuromuscular disorders
- Other conditions

## Chronic liver disease

- Conditions with progressive deterioration including cirrhosis and other diseases

## Obesity

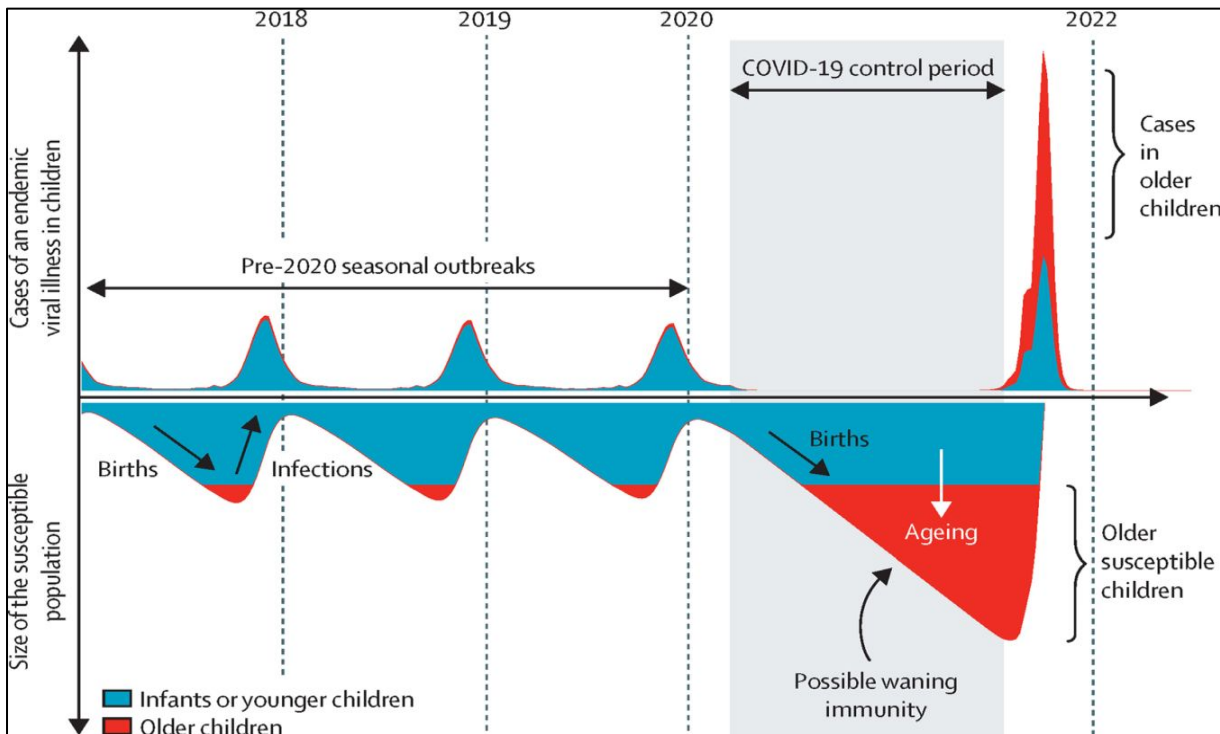
- Body mass index  $\geq 30$  kg per m<sup>2</sup>

# Overview of immunity to RSV



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- Experimental data suggests that humoral, mucosal and cell-mediated immunity play a role in protection, recovery from, and immuno-pathogenesis of RSV disease

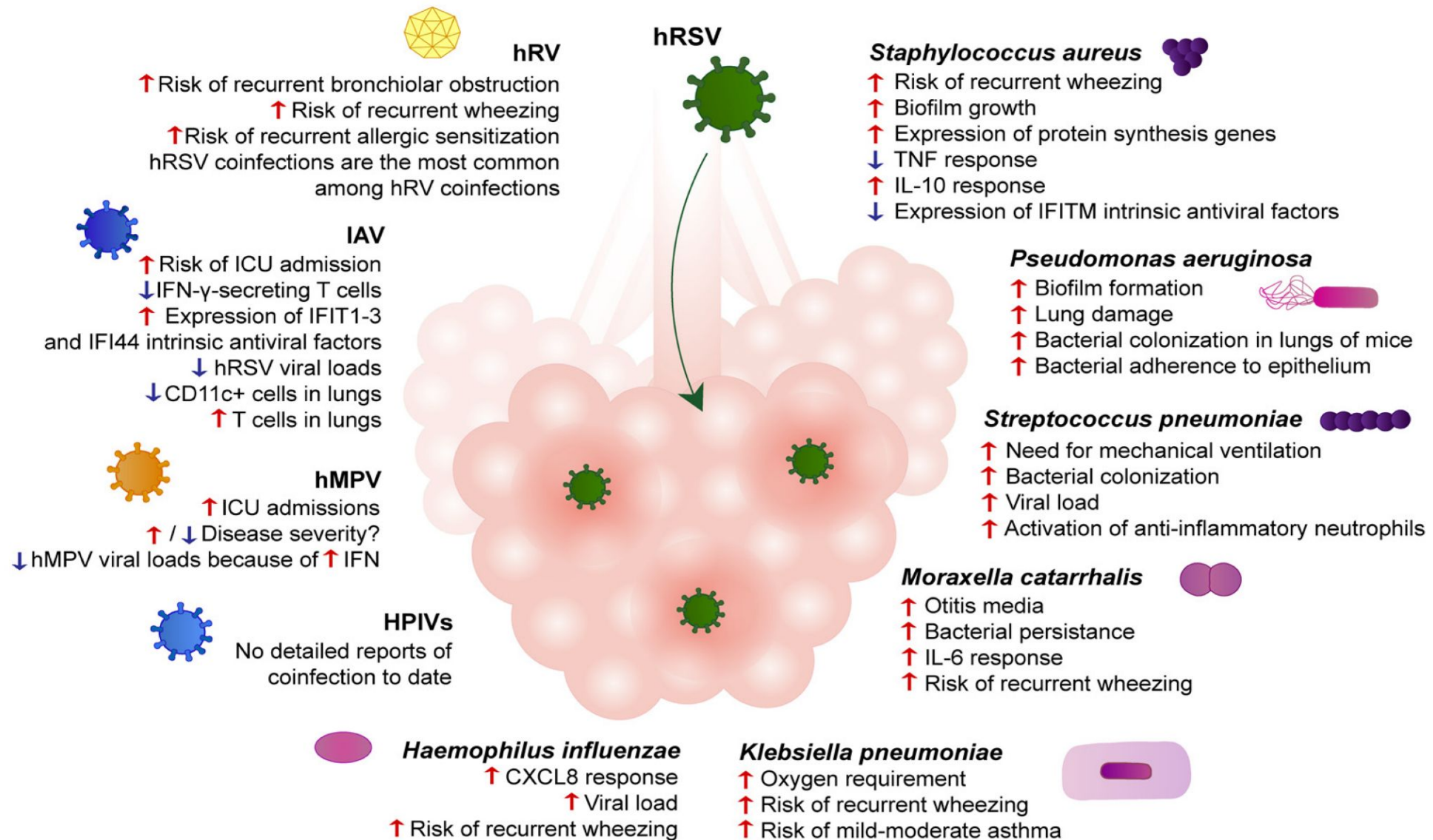


- Possible trajectory of seasonal outbreaks of cases of an **endemic viral illness** in children pre-2020 and post-2020 following COVID-19 non-pharmaceutical interventions (NPIs).
- There is a delayed circulation of the virus and therefore an immunity gap/debt/pause/deficit – the susceptible population increases.
- Ages of the children infected may change and subsequent outbreaks may be larger and at different times of the year – peaks likely to occur in winter.

# Co-infections that may occur with RSV



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# Co-infections modulate disease pathogenesis



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**Respiratory syncytial virus**



***Streptococcus pneumoniae***



IP10/CXCL10 cytokine expression

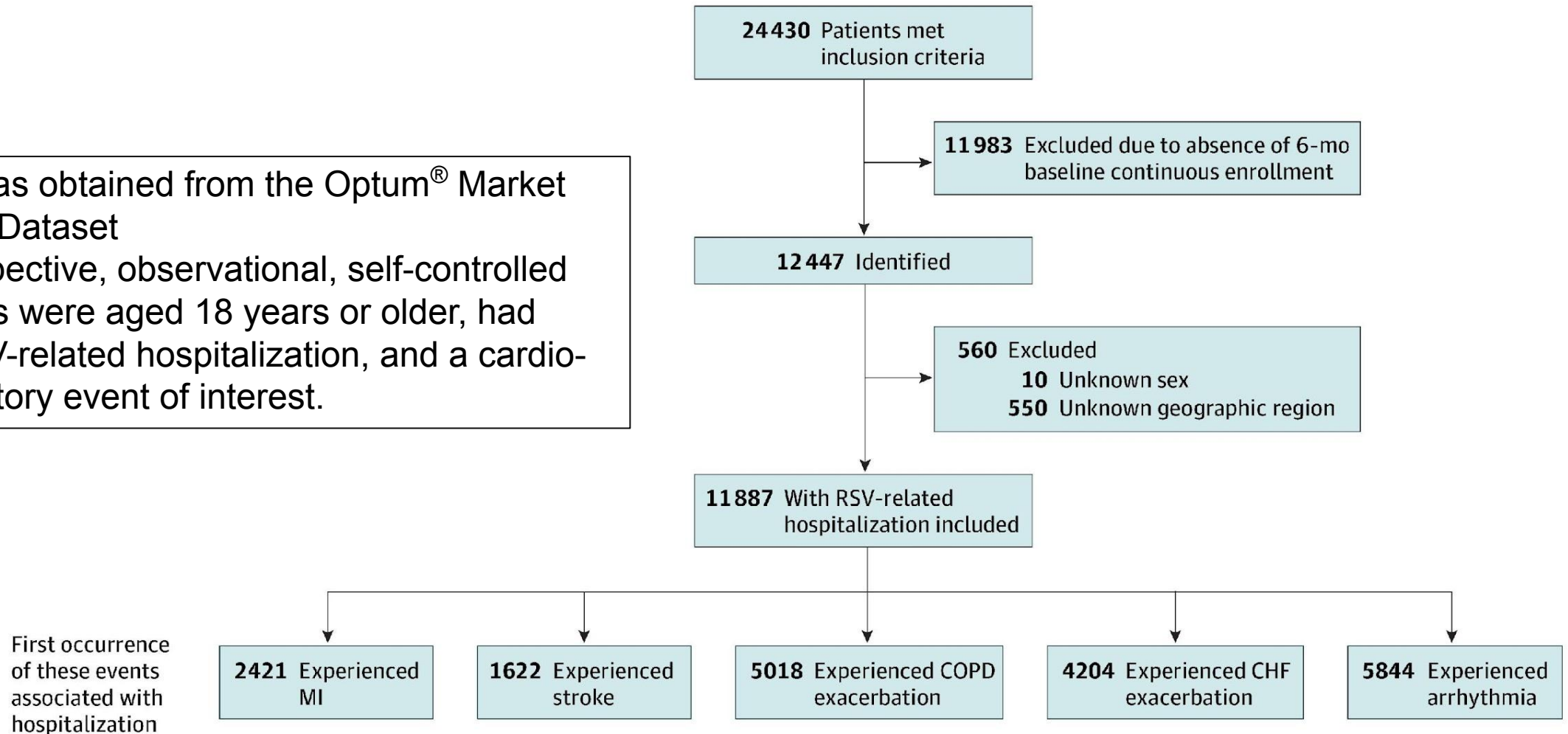


**Human Macrophages**

# Cardiorespiratory events following RSV hospitalisation



- Data was obtained from the Optum<sup>®</sup> Market Clarity Dataset
- Retrospective, observational, self-controlled
- Patients were aged 18 years or older, had an RSV-related hospitalization, and a cardiorespiratory event of interest.




# What cardiologists are saying about vaccine benefits



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## Adult Vaccination



### Protect your heart with the vaccines you need

Staying up to date with your vaccines is an important part of living heart healthy – just like:

- Eating well
- Getting good sleep
- Being active
- Taking heart medicines
- Not smoking
- ... and

### Getting vaccinated!

Having heart disease makes you more likely to become seriously ill from infections such as influenza (the flu), COVID, and pneumonia.

These infections can strain the heart. They also can lead to heart attack, heart damage, stroke, and even death. So make sure you are protected.

**Vaccines:**

- Prevent diseases
- Make the illness milder if you do get sick
- Save lives
- Keep other people healthy too

#### Vaccines you might need


Ask about and make sure you're up to date with vaccines that protect against:

- Influenza (flu)
- COVID
- Respiratory syncytial virus (RSV)
- Pneumonia
- Shingles
- Diphtheria, Tetanus and Whooping cough (pertussis)
- Hepatitis B

Depending on your age, lifestyle and job, you may need other vaccines.

#### Where to get vaccines

Start by asking your heart doctor or primary care provider. You can also go to [Vaccines.gov](https://www.vaccines.gov) to find vaccines near you.



For more information, visit [CardioSmart.org/HealthyLiving](https://www.CardioSmart.org/HealthyLiving)  
@ACCinTouch #CardioSmart

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# Ongoing developments for the prevention of RSV infection



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## RSV Vaccine and mAb Snapshot


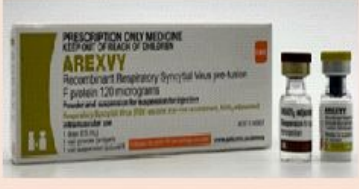


- P = PEDIATRIC
- M = MATERNAL
- A = ADULT
- O = OLDER ADULT
- = LIMITED TO INCREASED RISK
- = LIVE/CHIMERIC
- = VECTORED
- = SUBUNIT
- = mAb
- = PARTICLE
- = NUCLEIC ACID

VACCINES	▶ PHASE 1		▶ PHASE 2			▶ PHASE 3	▶ MARKET APPROVED		
Codagenix, LID/NIAID/NIH RSV (P, O)	Blue Lake PIV5/RSV (O)	Pfizer RSV F Protein (P)	Advaccine Biotechnology RSV G Protein (O)	Daiichi Sankyo RSV F Protein (O)	Baiyiwuyou RSV F Protein (O)	Sanofi, LID/NIAID/NIH RSV (P)	AREXVY GSK RSV F Protein (A, O)	ABRYSCO Pfizer RSV F Protein (A, M, O)	mRESVIA Moderna RSV F Protein (A, O)
Immorna RSV F Protein (O)	GSK RSV F Protein (O)	Clover Biopharma RSV F Protein (O)	Innorna RSV F Protein (O)	Sanofi RSV F Protein (O)	RNAfa RSV F Protein (O)	Maxvax RSV F Protein (O)			
Abogen RSV F Protein (O)	NanoRibo RSV F Protein (O)	Patronus Biotech SVLP (O)	Blue Lake PIV5/RSV (P)	RII Russia RSV/Flu (O)	Moderna RSV F Protein (P, M)				
FuBiologics RSV F Protein (O)	Viromelix SVLP (O)								
<b>COMBINATIONS</b>									
Moderna Flu/RSV/SARSCoV2 (O)	Moderna RSV/hMPV (O)	Sanofi RSV/hMPV/PIV3 (O)	Ilusdvax RSV/hMPV (O)						
Sanofi RSV/hMPV (O)	Clover Biopharma RSV/hMPV (O)	Clover Biopharma RSV/hMPV/PIV5 (O)							
		Vicebio RSV/hMPV (O)							
<b>IMMUNOPROPHYLAXIS</b>									
Gates MRI Anti-F mAb (P)	Genrix Anti-F mAb (P)	Shanghai Institute of Biological Products Anti-F mAb (P)				Trinomab Biotechnology Anti-F mAb (P)	ENFLONIA Merck Anti-F mAb (P)	BEYFORTUS AstraZeneca, Sanofi Anti-F mAb (P)	SYNAGIS AstraZeneca Anti-F mAb (P)

# Current recommendations for prevention of RSV infections Australia



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Administration of RSV vaccines and monoclonal antibodies by age group or cohort				
Age group or cohort	RSV vaccines for adults		RSV monoclonal antibodies for infants	
	Abrysvo® 0.5mL (Pfizer) 	Arexyv® 0.5 mL (GSK) 	Beyfortus™ (Nirsevimab) 0.5 mL (Purple) (Sanofi) 	Beyfortus™ (Nirsevimab) 1 mL (Blue) (Sanofi) 
Women from 28 weeks pregnancy	<b>NIP FUNDED</b>	<b>DO NOT USE</b>	<b>DO NOT USE</b>	<b>DO NOT USE</b>
Infants & children ≤24 months	<b>DO NOT USE</b>	<b>DO NOT USE</b>	<b>STATE &amp; TERRITORY FUNDED</b>	<b>STATE &amp; TERRITORY FUNDED</b>
Adults 60-74 years Adults with medical conditions that increase risk of severe RSV	<b>AVAILABLE PRIVATELY BASED ON CLINICAL DECISION</b>	<b>AVAILABLE PRIVATELY BASED ON CLINICAL DECISION</b>	<b>DO NOT USE</b>	<b>DO NOT USE</b>
Adults ≥ 75 years Aboriginal and Torres Strait Islander people ≥60 years	<b>AVAILABLE PRIVATELY BASED ON CLINICAL DECISION</b>	<b>NIP FUNDED</b>	<b>DO NOT USE</b>	<b>DO NOT USE</b>