Respiratory Syncytial Virus

The virus, the illness and its management

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The KIDS Research Institute Australia | Wesfarmers Centre of Vaccines & Infectious Diseases
The University of Western Australia
Perth Children's Hospital
PathWest Laboratory Medicine WA

Summary

A common virus infecting ciliated epithelial cells of the upper and lower airway

Infection stimulates a rapid immune response but waning results in recurrent infection through one's lifetime

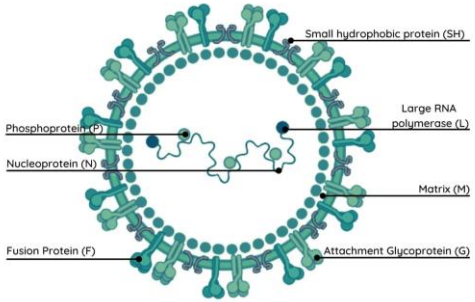
More severe disease observed at the extremes of age, particularly infants and the elderly

Most common cause of respiratory infection in infants and underappreciated in older individuals

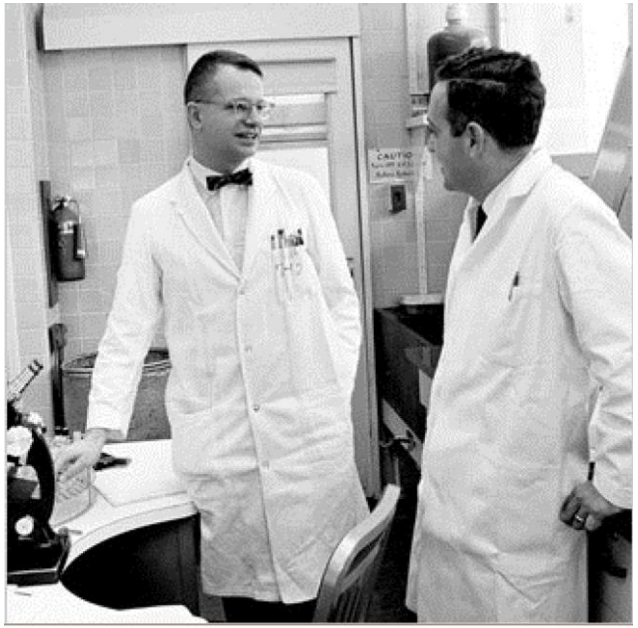
Morbidity significant locally; morbidity and mortality significant globally

Management is supportive; Prevention is possible

The virus



RSV
Paramyxoviridae (Pneumovirus)
Two subgroups: A and B
15.2kb genome
ssRNA; negative sense
Non-segmented genome
Replicate: respiratory epithelium
Key proteins: Glycoprotein and Fusion protein



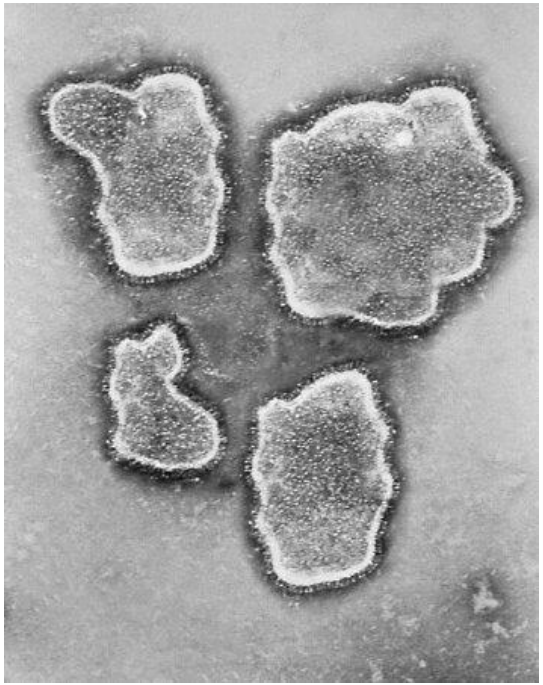
RECOVERY FROM INFANTS WITH RESPIRATORY ILLNESS OF A VIRUS RELATED TO CHIMPANZEE CORYZA AGENT (CCA)

II. EPIDEMIOLOGIC ASPECTS OF INFECTION IN INFANTS AND YOUNG CHILDREN [1]

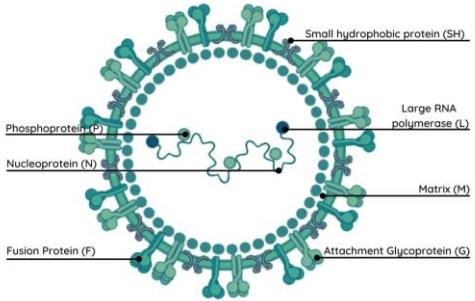
By

ROBERT CHANOCK [2] AND LAURENCE FINBERG [3]

(*Received for publication July 22, 1957*)



RSV (compared with influenza and SARS-CoV-2)



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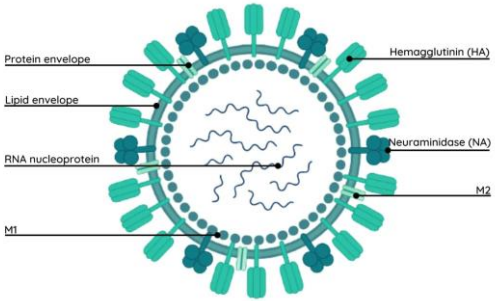

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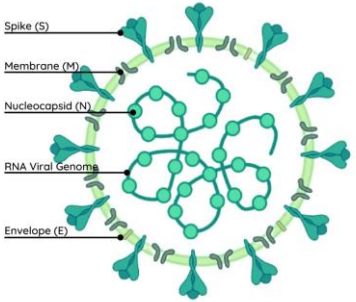

SARS-CoV-2

Coronaviridae (β coronavirus)
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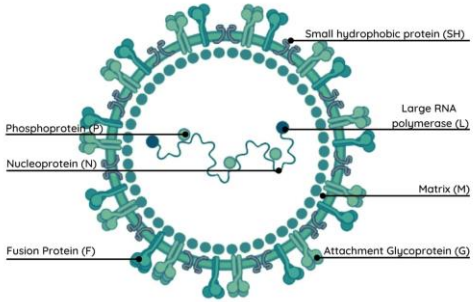

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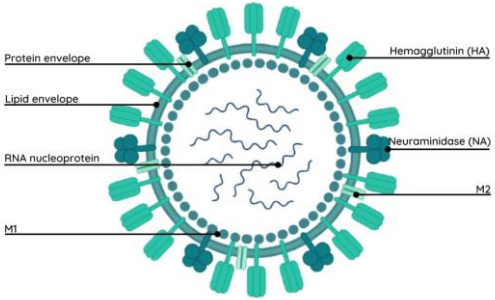

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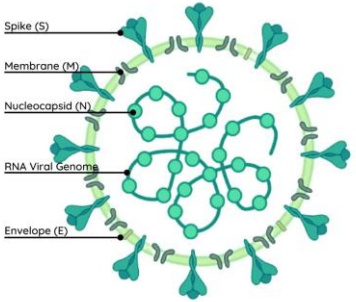

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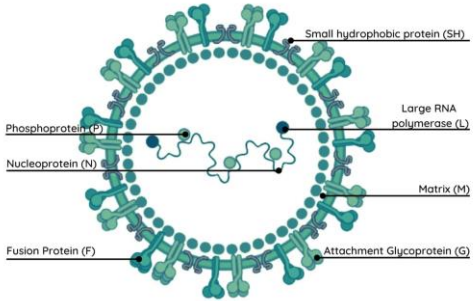

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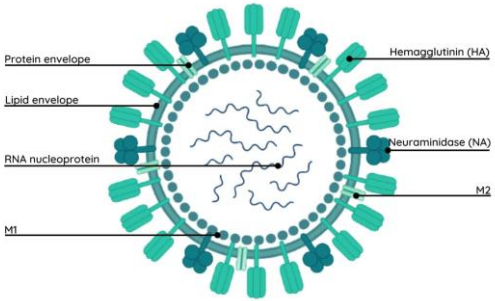

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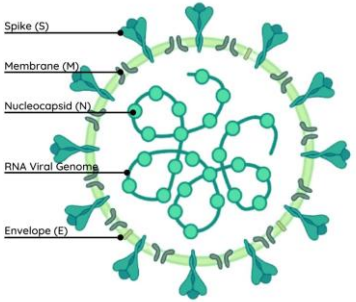

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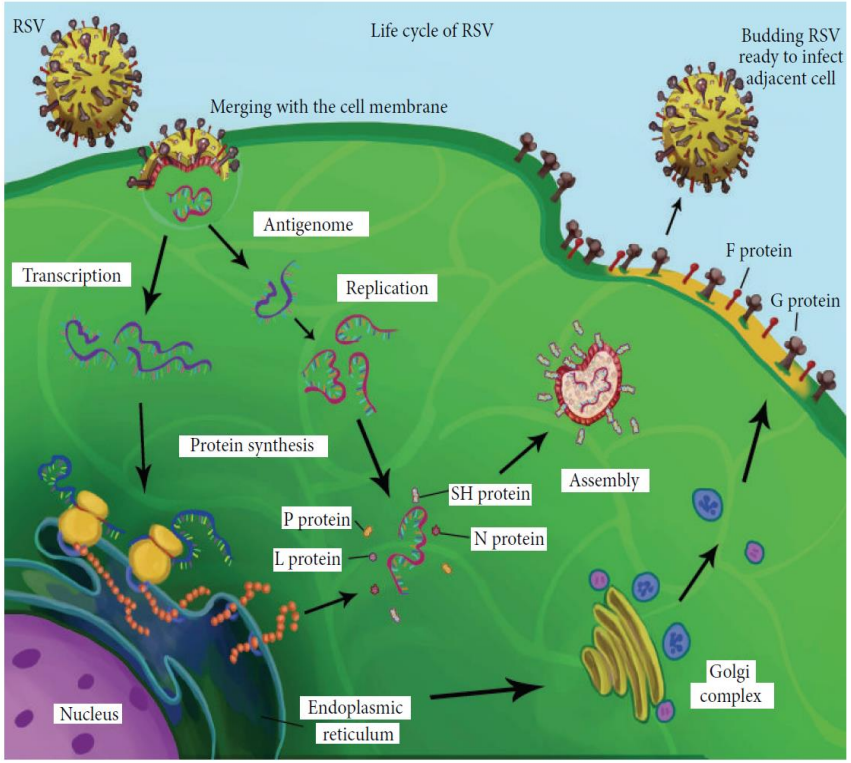
The virus

G protein = targets ciliated cells of the airway facilitating adherence

F protein = initiates viral penetration and promotes cells to cell spread

Both F & G are key in eliciting a neutralizing antibody response

Humoral or cytotoxic T cell-mediated immunity is viral



The virus – the F protein story

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Virology®

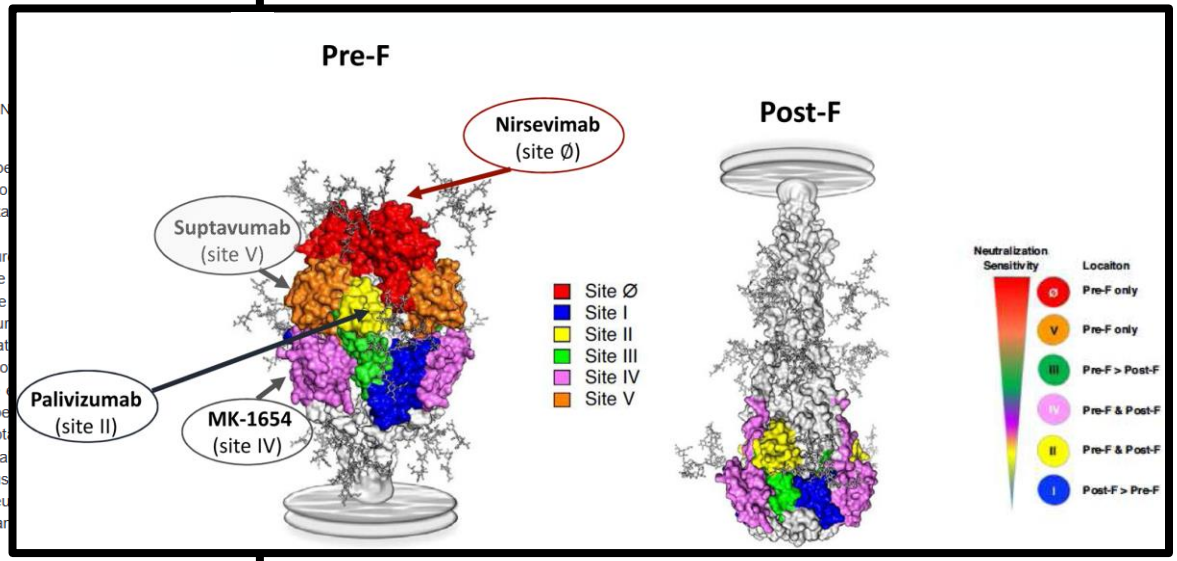
STRUCTURE AND ASSEMBLY
1 August 2011 Volume 85 Issue 15
https://doi.org/10.1128/jvi.00555-11

Structure of Respiratory Syncytial Virus Fusion Glycoprotein in the Postfusion Conformation Reveals Preservation of Neutralizing Epitopes

Jason S. McLellan*, Yongping Yang, Barney S. Graham, Peter D. Kwong

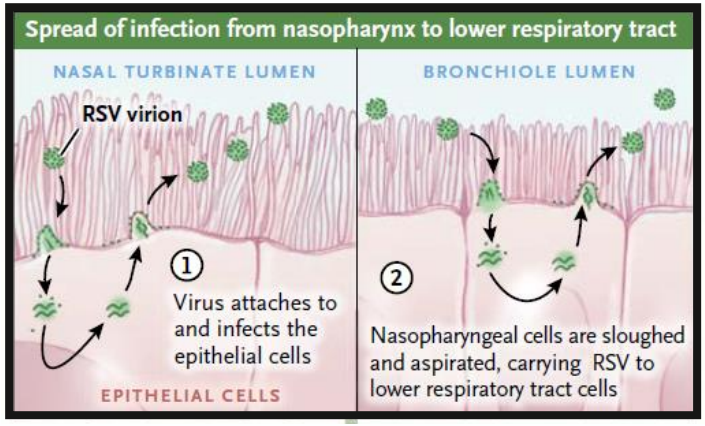
Vaccine Research Center, National Institute of Allergy and Infectious Diseases, N
Bethesda, Maryland 20892

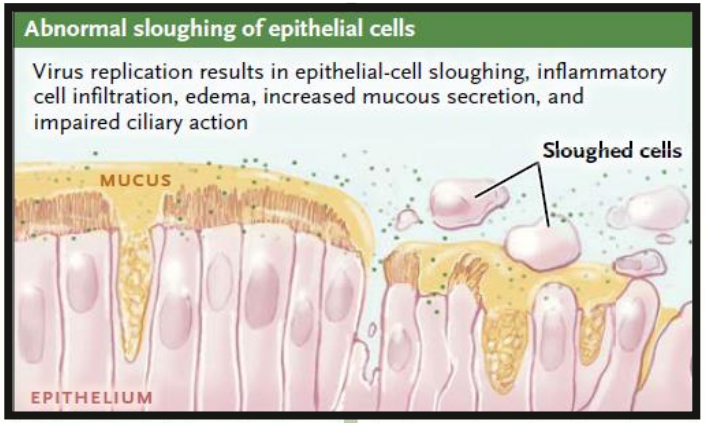
ABSTRACT Respiratory syncytial virus (RSV) invades host cells via a type that undergoes dramatic structural rearrangements during the fusio monoclonal antibodies, such as 101F, palivizumab, and motavizumab, ta sites on the RSV F glycoprotein. The structures of these sites as motavizumab and 101F have been previously determined, but a structur glycoprotein ectodomain has remained elusive. To address this issue, we biophysical studies on stable ectodomain constructs. Here, we present the the trimeric RSV F ectodomain in its postfusion conformation. The structur and motavizumab epitopes are present in the postfusion state and that similar to those observed in the antibody-bound peptide structures. Bo postfusion F glycoprotein with high affinity in surface plasmon resonance the antibodies bound to the F glycoprotein predicts that the 101F epitope peptide and restricted to a single protomer in the trimer, whereas mot residues on two protomers, indicating a quaternary epitope. Mechanistica that 101F and motavizumab can bind to multiple conformations of the fus neutralize late in the entry process. The structural preservation of neu postfusion state suggests that this conformation can elicit neutralizing ar useful vaccine antigen.

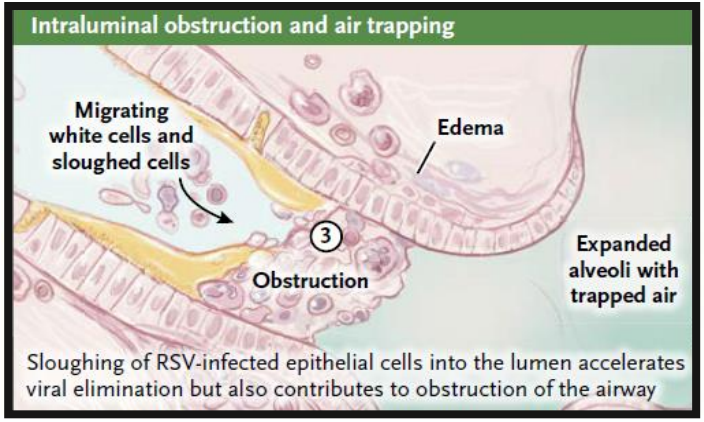


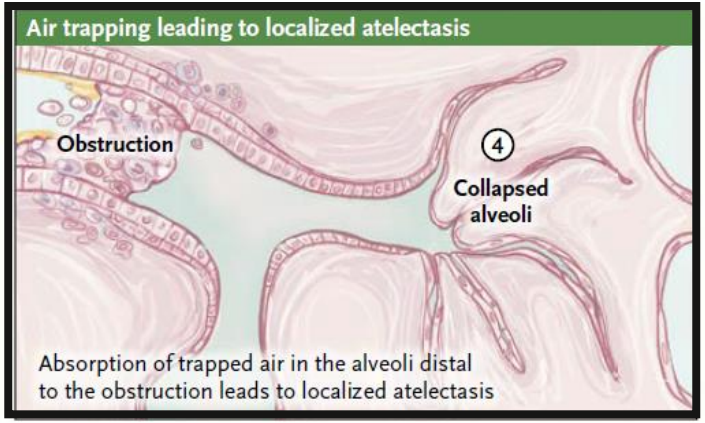
McLellan JS et al, J Virol 2011

The virus – pathogenesis









Cody Meissner H et al. NEJM 2016

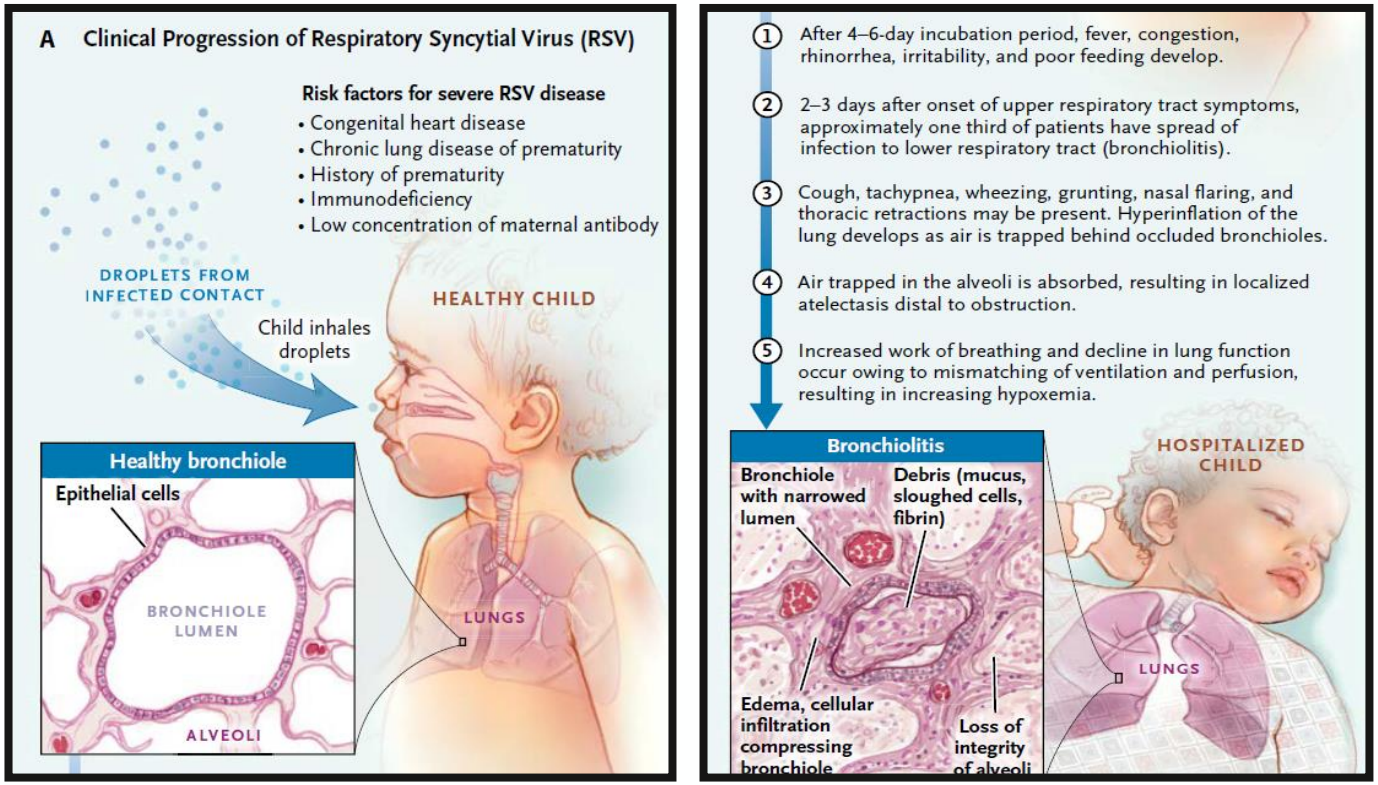
The illness – the impact

The most common pathogen associated with acute lower respiratory infection in young children:

- **Globally**: 33.1m episodes of RSV-ALRI, 3.6mill hospitalisations, 100K deaths in those < 5 years of age (mostly LMICs)
- **Australia:** 1 in 30 Australian infants hospitalised (8 times more common than influenza in those < 5 years of age)

https://www.ifa.org.au

The illness – bronchiolitis



Cody Meissner H et al. NEJM 2016

The illness – pneumonia

Prevalence of respiratory viruses in community-acquired pneumonia in children: a systematic review and meta-analysis

Mitchell T G Pratt, Tasnim Abdalla, Peter C Richmond, Hannah C Moore, Thomas L Snelling, Christopher C Blyth*, Mejbah U Bhuiyan*

Summary

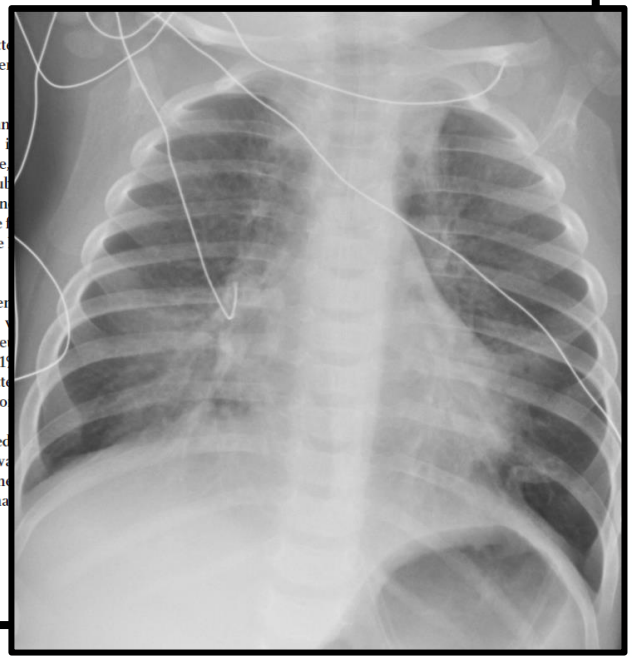
Background Respiratory viruses are increasingly detecte
prevalence estimates vary substantially. We aimed to syste
associated with community-acquired pneumonia.

Methods We conducted a systematic review and meta-an
respiratory viruses detected by any diagnostic method i
pneumonia. We searched MEDLINE, PubMed, Embase
restrictions for relevant published articles and reports pub
review to pre-COVID-19 pandemic years. Three indepen
predefined protocol. We calculated the pooled prevalence
Laird random-effects models. We assessed bias using the
in PROSPERO (CRD42016034047).

Findings We identified 186 eligible articles that represen
acquired pneumonia. One or more respiratory viruses
patients with a diagnosis of community-acquired pne
syncytial virus (22·7%, 20·9–24·5) and rhinovirus (22·1
paediatric pneumonia globally, with other viruses detecte
prevalence by the country's national income, under-5 mo

Interpretation Respiratory viruses are frequently detected
ages and geographical regions, with non-significant v
strategies to limit antibiotic use in children with viral pn
targeting common respiratory viruses are expected to ha
pneumonia.

Funding None.



	Overall		
	Number of studies	Prevalence (%)	I^2 (%)
Respiratory syncytial virus	150	22·7%	98·1%
Human rhinovirus	83	22·1%	98·5%
Human bocavirus	45	8·6%	98·1%
Human adenovirus (non-typed)	110	7·3%	97·0%
Human metapneumovirus	95	6·5%	96·3%
Human parainfluenza virus	58	6·6%	94·0%
Human parainfluenza virus 1	44	2·1%	88·6%
Human parainfluenza virus 2	40	1·1%	86·6%
Human parainfluenza virus 3	52	4·4%	94·4%
Human parainfluenza virus 4	20	2·0%	81·3%
Influenza (non-typed)	48	6·5%	89·9%
Influenza virus (non-typed)	61	5·5%	90·1%
Influenza virus H1N1	27	4·6%	93·9%
Influenza virus H3N2	16	4·8%	91·9%
Influenza B virus	58	1·8%	87·7%
Influenza C virus*	4	0·4%	50·8%
Human coronaviruses (non-typed)	32	3·5%	89·5%
Human coronaviruses NL63	19	1·0%	58·7%
Human coronaviruses 229E	15	1·2%	81·2%
Human coronaviruses OC43	20	2·3%	89·0%
Human coronaviruses HKU1	12	1·5%	87·7%
Enterovirus	33	3·7%	88·5%

Pratt MTG et al, Lancet Child Adoles Health 2022

The illness – respiratory morbidity

Open Forum Infectious Diseases

MAJOR ARTICLE

Factors Predicting Secondary Respiratory Morbidity Following Early-Life Respiratory Syncytial Virus Infections: Population-Based Cohort Study

Mohinder Sarna,[1,2,a,©] Amanuel Gebremedhin,[1,2,a] Peter C. Richmond,[1,3,4] Kathryn Glass,[1,5] Avram Levy,[6,7] and Hannah C. Moore[1,2]

[1]Wesfarmers Centre of Vaccines and Infectious Diseases, Telethon Kids Institute, University of Western Australia, Perth, Western Australia, Australia, [2]Curtin School of Population Health, C University, Bentley, Western Australia, Australia, [3]School of Medicine, University of Western Australia, Nedlands, Western Australia, Australia, [4]Perth Children's Hospital, Nedlands, Weste Australia, Australia, [5]National Centre for Epidemiology and Population Health, ANU College of Health and Medicine, Australian National University, Canberra, Australian Capital Territory, Aust [6]PathWest Laboratory Medicine, QEII Medical Centre, Nedlands, Perth, Western Australia, Australia, and [7]School of Biomedical Sciences, University of Western Australia, Nedlands, Perth, We Australia, Australia

Background. The association between early-life respiratory syncytial virus (RSV) infections and later respiratory morbidit well established. However, there is limited evidence on factors that influence this risk. We examined sociodemographic a perinatal factors associated with later childhood respiratory morbidity requiring secondary care following exposure t laboratory-confirmed RSV episode in the first 2 years.

Methods. We used a probabilistically linked whole-of-population-based birth cohort including 252 287 children born Western Australia between 2000 and 2009 with follow-up to the end of 2012. Cox proportional hazards models estima adjusted hazard ratios (aHRs) of the association of various risk factors with the first respiratory episode for asthma, wheezi and unspecified acute lower respiratory infection beyond the age of 2 years.

Results. The analytic cohort included 4151 children with a confirmed RSV test before age 2 years. The incidence of subsequ respiratory morbidity following early-life RSV infection decreased with child age at outcome (highest incidence in 2–<4-year-o 41.8 per 1000 child-years; 95% CI, 37.5–46.6), increased with age at RSV infection (6–<12-month-olds: 23.6/1000 child-years; 9 CI, 19.9–27.8; 12–<24-month-olds: 22.4/1000 child-years; 95% CI, 18.2–22.7) and decreasing gestational age (50.8/1000 child-ye 95% CI, 33.5–77.2 for children born extremely preterm, <28 weeks gestation). Risk factors included age at first RSV episode (6–< months: aHR, 1.42; 95% CI, 1.06–1.90), extreme prematurity (<28 weeks: aHR, 2.22; 95% CI, 1.40–3.53), maternal history of asth (aHR, 1.33; 95% CI, 1.04–1.70), and low socioeconomic index (aHR, 1.76; 95% CI, 1.03–3.00).

Conclusions. Our results suggest that in addition to preterm and young infants, children aged 12–<24 months could also be potential target groups for RSV prevention to reduce the burden of later respiratory morbidities associated with RSV.

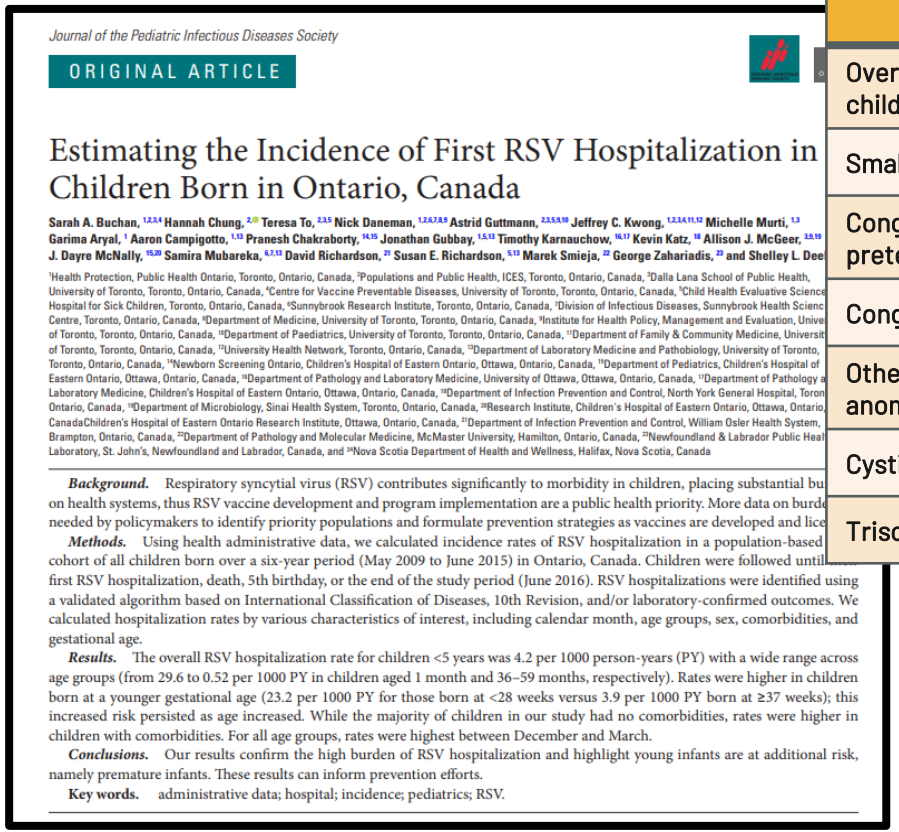
Keywords. age at RSV infection; asthma; linked data; respiratory morbidity; respiratory syncytial virus; wheeze.

Subgroup	No.	Time at Risk, Child-Years	Rates/1000 (95% CI)
Overall	458	23 708.7	19.3 (17.6–21.2)
Age group of subsequent respiratory morbidity[a]			
2–<4 y	322	7705.4	41.8 (37.5–46.6)
4–<6 y	80	6165.7	13.0 (10.4–16.2)
≥6 y	56	9837.6	5.7 (4.4–7.4)
Age at first RSV episode			
<3 mo	117	7218.2	16.2 (13.5–19.4)
3–<6 mo	116	6754.0	17.2 (14.3–20.6)
6–<12 mo	138	5859.6	23.6 (19.9–27.8)
12–<24 mo	87	3877.0	22.4 (18.2–27.7)
Gestational age			
<28 wk	22	433.0	50.8 (33.5–77.2)
29–32 wk	21	693.2	30.3 (19.8–46.5)
33–36 wk	55	2993.1	18.4 (14.1–23.9)
≥37 wk	360	19 589.5	18.4 (16.6–20.4)

[a] defined as hospitalisation or ED presentation for asthma, wheezing or unspecified ALRI

Sarna M et al, Open Forum ID 2023

The illness – risk factors for RSV hospitalisation



Journal of the Pediatric Infectious Diseases Society

ORIGINAL ARTICLE

Estimating the Incidence of First RSV Hospitalization in Children Born in Ontario, Canada

Sarah A. Buchan, Hannah Chung, Teresa To, Nick Daneman, Astrid Guttmann, Jeffrey C. Kwong, Michelle Murti, Garima Aryal, Aaron Campigotto, Pranesh Chakraborty, Jonathan Gubbay, Timothy Karnauchow, Kevin Katz, Allison J. McGeer, J. Dayre McNally, Samira Mubareka, David Richardson, Susan E. Richardson, Marek Smieja, George Zahariadis, and Shelley L. Dee

[1]Health Protection, Public Health Ontario, Toronto, Ontario, Canada, [2]Populations and Public Health, ICES, Toronto, Ontario, Canada, [3]Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada, [4]Centre for Vaccine Preventable Diseases, University of Toronto, Toronto, Ontario, Canada, [5]Child Health Evaluative Science, Hospital for Sick Children, Toronto, Ontario, Canada, [6]Sunnybrook Research Institute, Toronto, Ontario, Canada, [7]Division of Infectious Diseases, Sunnybrook Health Scienc Centre, Toronto, Ontario, Canada, [8]Department of Medicine, University of Toronto, Toronto, Ontario, Canada, [9]Institute for Health Policy, Management and Evaluation, Unive of Toronto, Toronto, Ontario, Canada, [10]Department of Paediatrics, University of Toronto, Toronto, Ontario, Canada, [11]Department of Family & Community Medicine, Universit of Toronto, Toronto, Ontario, Canada, [12]University Health Network, Toronto, Ontario, Canada, [13]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada, [14]Newborn Screening Ontario, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada, [15]Department of Pediatrics, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada, [16]Department of Pathology and Laboratory Medicine, University of Ottawa, Ottawa, Ontario, Canada, [17]Department of Pathology a Laboratory Medicine, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada, [18]Department of Infection Prevention and Control, North York General Hospital, Toron Ontario, Canada, [19]Department of Microbiology, Sinai Health System, Toronto, Ontario, Canada, [20]Research Institute, Children's Hospital of Eastern Ontario, Ottawa, Ontario, CanadaChildren's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada, [21]Department of Infection Prevention and Control, William Osler Health System, Brampton, Ontario, Canada, [22]Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada, [23]Newfoundland & Labrador Public Heal Laboratory, St. John's, Newfoundland and Labrador, Canada, and [24]Nova Scotia Department of Health and Wellness, Halifax, Nova Scotia, Canada**

Background. Respiratory syncytial virus (RSV) contributes significantly to morbidity in children, placing substantial bu on health systems, thus RSV vaccine development and program implementation are a public health priority. More data on burde needed by policymakers to identify priority populations and formulate prevention strategies as vaccines are developed and lice

Methods. Using health administrative data, we calculated incidence rates of RSV hospitalization in a population-based cohort of all children born over a six-year period (May 2009 to June 2015) in Ontario, Canada. Children were followed until first RSV hospitalization, death, 5th birthday, or the end of the study period (June 2016). RSV hospitalizations were identified using a validated algorithm based on International Classification of Diseases, 10th Revision, and/or laboratory-confirmed outcomes. We calculated hospitalization rates by various characteristics of interest, including calendar month, age groups, sex, comorbidities, and gestational age.

Results. The overall RSV hospitalization rate for children <5 years was 4.2 per 1000 person-years (PY) with a wide range across age groups (from 29.6 to 0.52 per 1000 PY in children aged 1 month and 36–59 months, respectively). Rates were higher in children born at a younger gestational age (23.2 per 1000 PY for those born at <28 weeks versus 3.9 per 1000 PY born at ≥37 weeks); this increased risk persisted as age increased. While the majority of children in our study had no comorbidities, rates were higher in children with comorbidities. For all age groups, rates were highest between December and March.

Conclusions. Our results confirm the high burden of RSV hospitalization and highlight young infants are at additional risk, namely premature infants. These results can inform prevention efforts.

Key words. administrative data; hospital; incidence; pediatrics; RSV.

	<28w	28-31w	32-36w	37w+
Overall hospitalisation for children < 5 years	23.15 per 1000PY	12.51 per 1000py	7.67 per 1000py	3.86 per 1000py
Small for gestational age	37.97	14.16	7.95	4.38
Congenital lung disease / preterm lung disease	25.88	15.01	13.99	14.96
Congenital heart disease	25.91	18.22	17.38	12.87
Other congenital anomalies	19.44	21.59	13.67	6.47
Cystic fibrosis	-	-	-	11.66
Trisomy 21	-	-	34.01	23.37

Rates are 2-3 higher in First Nations children

BUT: >80% admission occur in those without risk factors

Buchan SA et al. JPIDS 2024

The illness – risk factors for severe disease

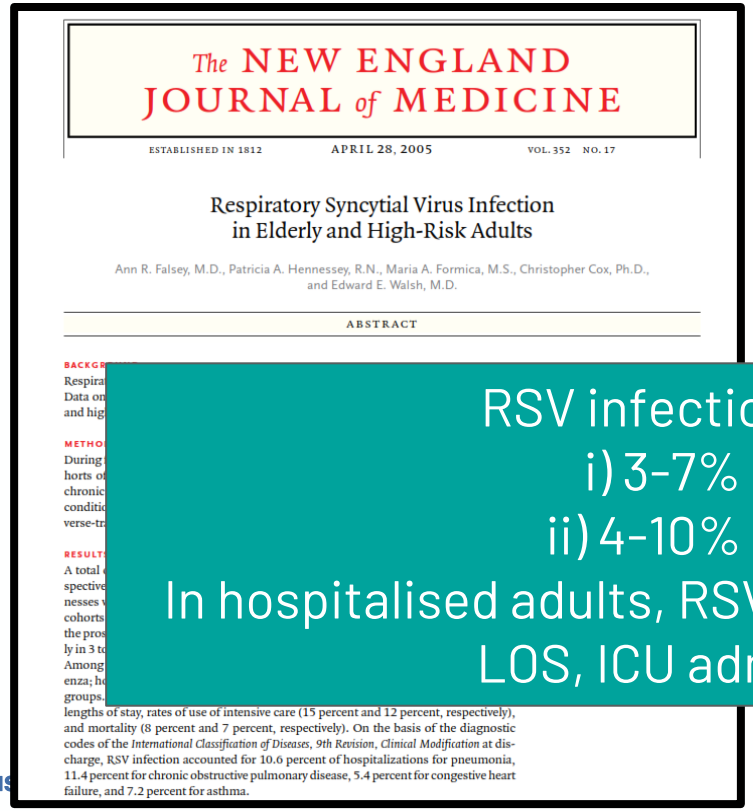
ICU admission	Crude OR (95%CI)	Adjusted OR* (95%CI)	Significance
Age <12 months	1.67 (0.72; 3.90)	1.91 (0.70; 5.19)	NS
Age 12+ months	Reference		
Comorbidity present	**5.87 (2.54; 13.57)**	**4.96 (1.78; 13.81)**	**p < 0.01**
Comorbidity absent	Reference		
Preterm <36w	**3.60 (1.44; 9.04)**	1.26 (0.40; 3.91)	NS
Term	Reference		
Aboriginal	**0.66 (0.45; 0.96)**	0.73 (0.49; 1.10)	NS
Non Aboriginal	Reference		

O2 and/or resp support	Crude OR (95%CI)	Adjusted OR* (95%CI)	Significance
Age <12 months	1.23 (0.86; 1.77)	1.26 (0.87; 1.84)	NS
Age 12+ months	Reference		
Comorbidity present	**1.97 (1.22; 3.18)**	1.39 (0.82; 2.38)	NS
Comorbidity absent	Reference		
Preterm <36w	**2.74 (1.58; 4.76)**	**2.25 (1.25; 4.02)**	**p < 0.01**
Term	Reference		
Aboriginal	0.88 (0.70; 1.11)	0.93 (0.74; 1.18)	NS
Non Aboriginal	Reference		

*adjusted by age group, comorbidity, preterm status, Aboriginal status and Nirsevimab immunisation

Blyth CC et al, OPTIONS XII 2024

The illness – other important populations



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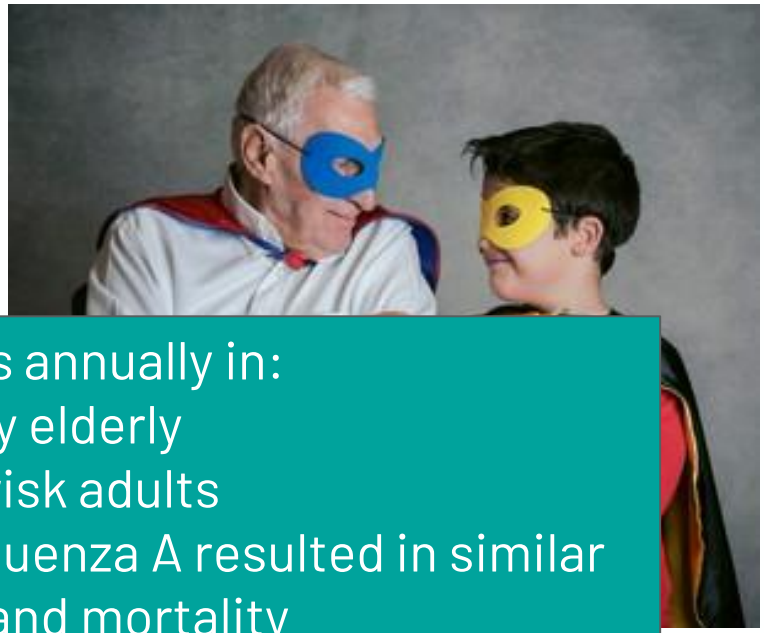
Respiratory Syncytial Virus Infection in Elderly and High-Risk Adults

Ann R. Falsey, M.D., Patricia A. Hennessey, R.N., Maria A. Formica, M.S., Christopher Cox, Ph.D., and Edward E. Walsh, M.D.

ABSTRACT

lengths of stay, rates of use of intensive care (15 percent and 12 percent, respectively), and mortality (8 percent and 7 percent, respectively). On the basis of the diagnostic codes of the *International Classification of Diseases, 9th Revision, Clinical Modification* at discharge, RSV infection accounted for 10.6 percent of hospitalizations for pneumonia, 11.4 percent for chronic obstructive pulmonary disease, 5.4 percent for congestive heart failure, and 7.2 percent for asthma.



RSV infection occurs annually in:
i) 3-7% of heathy elderly
ii) 4-10% of high-risk adults
In hospitalised adults, RSV and influenza A resulted in similar LOS, ICU admission and mortality

Falsey AR et al. NEJM 2025

The illness – other important populations

viruses

MDPI

Article

The Changing Detection Rate of Respiratory Syncytial Virus in Adults in Western Australia between 2017 and 2023

David A. Foley [1,2,3,*], Cara A. Minney-Smith [1], Andrew Tjea [1], Mark P. Nicol [2,4], Avram Levy [1,4], Hannah C. Moore [2,5,†] and Christopher C. Blyth [1,2,3,6,†]

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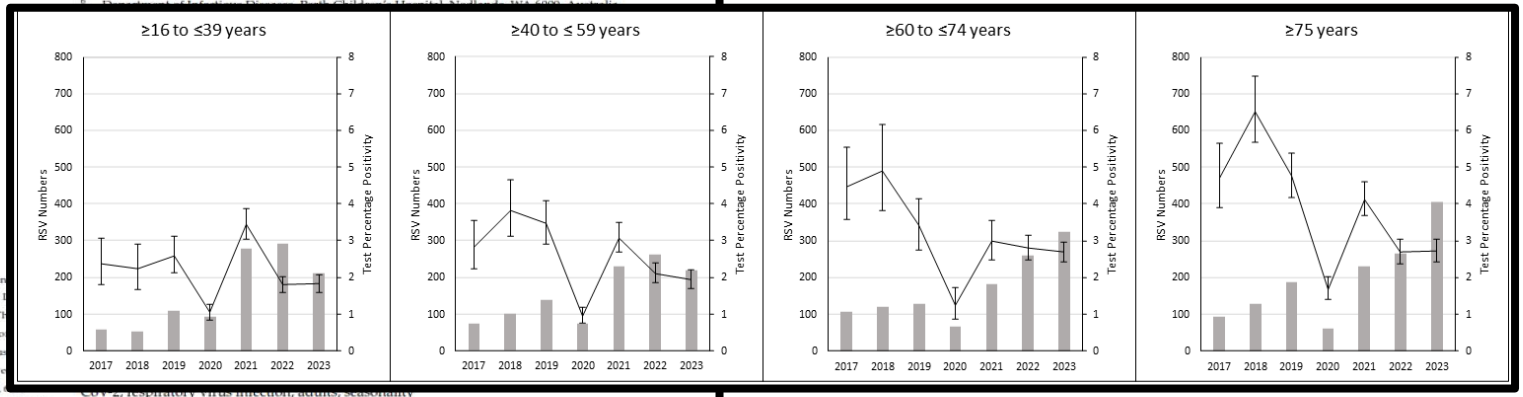
5 School of Population Health, Curtin University, Perth, WA 6009, Australia



Citation: Foley, D.A.; Minn
C.A.; Tjea, A.; Nicol, M.P.;
Moore, H.C.; Blyth, C.C. Th
Changing Detection Rate o
Respiratory Syncytial Virus
in Western Australia betwe
and 2023. *Viruses* **2024**, *16*,
https://doi.org/10.3390/v16050656

The true burden of RSV disease in adults remains uncertain, because traditionally we have not tested for RSV.
Post COVID research is shedding new light on the burden in adults

Foley DA et al, Viruses 2024

The illness – seasonality

viruses

MDPI

Article

The Changing Detection Rate of Respiratory Syncytial Virus in Adults in Western Australia between 2017 and 2023

David A. Foley [1,2,3,*], Cara A. Minney-Smith [1], Andrew Tjea [1], Mark P. Nicol [2,4], Avram Levy [1,4], Hannah C. Moore [2,5,†] and Christopher C. Blyth [1,2,3,6,†]

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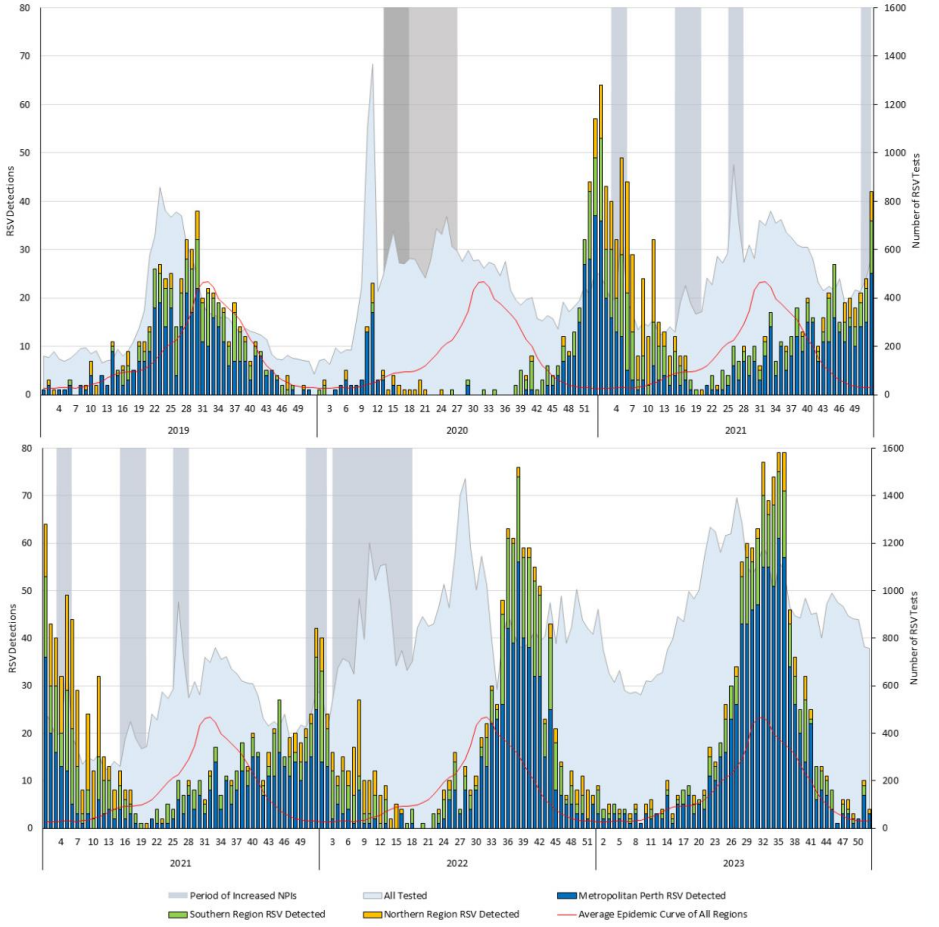
Abstract: The incidence of respiratory syncytial virus (RSV) in adults is inadequately defined and the impact of SARS-CoV-2-related non-pharmaceutical interventions (NPIs) is underexplored. Using laboratory data, we described the detection rate of RSV in adults ≥16 years in Western Australia (WA) between 2017 and 2023. With the exception of 2020, RSV detections rose annually between 2017 and 2023, reaching 50.7 per 100,000 in 2023 (95% confidence interval [CI], 47.9–53.8). RSV testing expanded considerably across the study period, with the testing in 2023 more than five times the 2017 total. The detection rate was highest in adults ≥60 years between 2017 and 2019, particularly those ≥75 years. Following 2020, the detections in all age groups increased, with the highest detection rate in 2023 in those ≥75-years (199.5 per 100,000; 95% CI, 180.5–220). NPIs significantly impacted RSV seasonality; the preceding winter pattern was disrupted, resulting in an absent 2020 winter season and two major summer seasons in 2020/21 and 2021/22. The RSV season began to realign in 2022, reverting to a winter seasonal pattern in 2023 and the largest season in the study period. Ongoing surveillance will be required to understand the stability of these increases and to delineate the impact of new immunisation strategies.

Keywords: respiratory infection; respiratory syncytial virus; non-pharmaceutical intervention; SARS-CoV-2; respiratory virus infection; adults; seasonality

check for updates

Citation: Foley, D.A.; Minney-Smith, C.A.; Tjea, A.; Nicol, M.P.; Levy, A.; Moore, H.C.; Blyth, C.C. The Changing Detection Rate of Respiratory Syncytial Virus in Adults in Western Australia between 2017 and 2023. *Viruses* **2024**, *16*, 656. https://doi.org/10.3390/v16050656



Foley DA et al, Viruses 2024

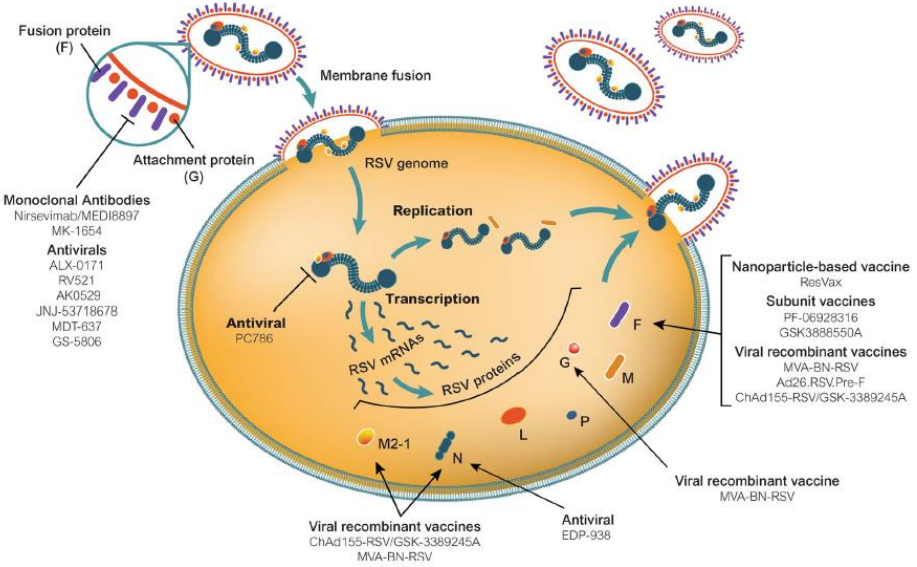
Management of RSV

RSV is self-limiting in most children and adults – supportive care is required

Current licenced antivirals (e.g. ribavirin) are poorly effective

Emerging antivirals are showing promise

- PhIII trial showing a 5 days course of AK0529 resulted in a 30% reduction in bronchiolitis score and 77% reduction in viral load



Domachowske JB et al, Infect Dis Ther 2021

Summary

A common virus infecting ciliated epithelial cells of the upper and lower airway

Infection stimulates a rapid immune response but waning results in recurrent infection through one's lifetime

More severe disease observed at the extremes of age, particularly infants and the elderly

Most common cause of respiratory infection in infants and underappreciated in older individuals

Morbidity significant locally; morbidity and mortality significant globally

Management is supportive; Prevention is possible